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Укладачі: Матерієнко А. С., Нетьосова К. Ю., Сурікова І. О., Григорів Г. В., Равшанов Т. Б.

Актуальні питання створення нових лікарських засобів: тези доповідей XXIV міжнародної науково-практичної конференції молодих вчених та студентів (20 квітня 2017 р.). в 2-х.т., Т.1. – Х.: Вид-во НФаУ, 2017. – 414 с.

Збірка містить матеріали науково-практичної конференції молодих вчених та студентів «Актуальні питання створення нових лікарських засобів». Матеріали згруповано за провідними напрямками науково-дослідної та навчальної роботи Національного фармацевтичного університету. Розглянуто теоретичні та практичні аспекти синтезу біологічно-активних сполук і створення на їх основі лікарських субстанцій; стандартизації ліків, фармацевтичного та хіміко-технологічного аналізу; вивчення рослинної сировини та створення фітопрепаратів; сучасної технології ліків та екстемпоральної рецептури; біотехнології у фармації; досягнень сучасної фармацевтичної мікробіології та імунології; доклінічних досліджень нових лікарських засобів; фармацевтичної опіки рецептурних та безрецептурних лікарських препаратів; доказової медицини; сучасної фармакотерапії, соціально-економічних досліджень у фармації, маркетингового менеджменту та фармакоекономіки на етапах створення, реалізації та використання лікарських засобів; управління якістю у галузі створення, виробництва і обігу лікарських засобів; інформаційниих технологій у фармації та медицині; основ педагогіки та психології; суспільствознавства; філології. Для широкого кола наукових і практичних працівників фармації та медицини.

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Editorial board: academician of NAS of Ukraine Chernykh V. P, prof. Kotvitska A. A., ass. prof. Krutskyh T. V., Danylchenko S. Yu.
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Topical issues of new drugs development: Abstracts of XXIV International Scientific And Practical Conference Of Young Scientists And Student (April 20, 2017) in 2 vol., Vol.1. – Kh.: Publishing Office NUPh, 2017. – 414 P.

Book of Abstracts includes materials of Scientific and Practical Conference of Young Scientists and Students «Actual questions of development of new drugs». Materials are groupped according to the main directions of scientific, research and educational work of the National University of Pharmacy. Teoretical and practical aspects of the synthesis of biologically active compounds and development of medicinal substances on their basis; standardization of drugs, pharmaceutical and chemical-technological analysis, the study of raw materials and herbal remedies development, modern drug technology and extemporal recipe; biotechnology in pharmacy, modern advances in pharmaceutical microbiology and immunology, clinical trials of new drugs, pharmaceutical care for prescription and OTC-drugs, evidence-based medicine, modern pharmacotherapy, socio-economic studies in pharmacy, marketing management and pharmacoeconomics during the development, implementation and use of drugs, quality management in development, production and traffi cking of drugs; information technologies in pharmacy and medicine; basics of pedagogy and psychology; social science; philology are presented. For a wide audience of scientists and pharmaceutaical and medicinal employees.

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Dear colleagues!

This book contains 593 abstracts, that were send to the Organizing Committee of the XXIV International Scientific And Practical Conference Of Young Scientists And Students ‘Topical issues of new drugs development’ from Belarus, Kazakhstan, Uzbekistan, Turkmenistan, Armenia, Saudi Arabia, Lithuania, Poland, Germany, Russia and Ukraine.

All this materials have two features in common: they were written in English and their authors are talented youth together with their skilled scientific supervisors.

Nowadays English is the language of communication and modern science. It is the official language in 54 countries. English is native language to 335 million people and over 1.3 billion people speak it all over the world.

This is the main reason why our traditional Conference of young scientists and students has been holding in English for the six years already.

We want our students and young scientists to be successful and to become well-known specialists not only in our native Ukraine. That's why they need to understand the importance of good knowledge of English language for their future career. And the first step on this way is to write abstracts, articles and prepare reports in English. Fortunately, scientific supervisors are always alongside with their students, because they do understand that youth is our future.

When I was a student I was also enchanted with the beauty of organic chemistry, especially – with organic synthesis. By the time of graduating from the university I have almost finished my candidate thesis. Today I am proud to represent pharmacy in the highest echelon of science of our country – in the National Academy of Sciences of Ukraine. And I am pleased to see new generation, that really enjoy scientific work.

22 key areas sessions are presented in this book of abstracts. Among them: synthesis, analysis, phytochemical, technological, biological, pharmacological research, social pharmacy, organization and economics, philology. That is because pharmacy begins with the tiniest atoms and molecules and resulted in preservation and maintenance of health of people. So everyone can find something interesting for scientific pharmaceutical research, while studying in National University of Pharmacy. Students' Scientific Societies of each department and Young Scientists' Council unite all our students and postgraduate students, who want to launch their scientific career. And International Scientific And Practical Conference Of Young Scientists And Students 'Topical issues of new drugs development' gives many of them the first chance to present the obtained results to a great audience.

I congratulate all the participants of the Conference and wish everyone good health, successful scientific career and, of course, love!

Rector of National University of Pharmacy,
Academician of NAS of Ukraine,
prof. Valentyn P. Chernykh

Section 1.

SYNTHESIS OF PHYSIOLOGICALLY ACTIVE SUBSTANCES

CONSTRUCTION, SYNTHESIS AND EVOLUTION OF NEW P-SULPHONAMIDOBENZOYLAMINO 2-OXINDOLE DEREVATIVES WITH POTENTIAL CHEMOTHERAPEUTIC PROPERTIES

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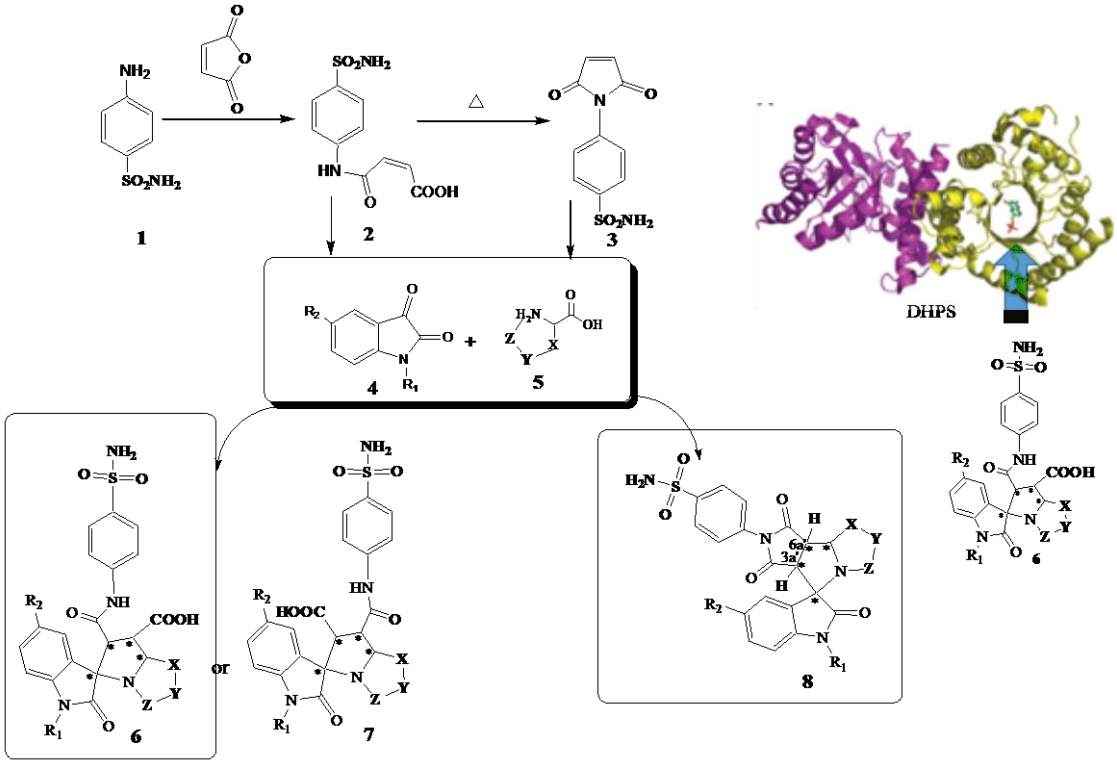
Introduction. Spiro-2-oxindoles called privileged molecules to search for and construction of new biologically active substances. They have significant chemotherapeutic potential. Thus, among them, compounds with antimicrobial and anti-tuberculosis activity have been found, some of them are capable of suppressing HIV. At the same time it would be interesting to include in their composition pharmacophore of sulfonamide. The rapid expansion of extensive resistance to the sulfonamides soon after their introduction and the growing use of the broader-spectrum penicillins in the treatment of infectious disease diminished the usefulness of sulfonamides. Sulfa drugs interrupt the essential folate pathway in bacteria and primitive eukaryotes; they target the enzyme dihydropteroate synthase (DHPS). It has been demonstrated as a primary target for the longest standing antibiotic class, the sulfonamides. Today, sulfonamides occupied a rather small place in the list of therapeutic agents that can be used for infectious disease. Therefore, the need for new antimicrobials is great in face of a growing pool of resistant pathogenic organisms.

Aim. Construction, synthesis and evolution of *p*-sulphonamidobenzoylamino spiro-2-oxindole derivatives and search potential chemotherapeutical activities.

Materials and methods. Synthesis of compounds using three-component condensation in alcoholic-aqueous medium; proof of the structure was performed by X-Ray, ^{1}H, ^{13}C NMR spectroscopy. ^{1}H NMR spectra were recorded on instruments Varian Mercury VX-200 (200 MHz) in DMSO-d_6 solution, TMS internal standard. Commercially available reagents and solvents were used without further purification. AtomicChargeCalculator (ACC) offers an efficient, user-friendly, interactive and platform independent environment for the calculation, visualization and analysis of conformationally dependent, quantum mechanics quality atomic charges in both biomacromolecules and drug-like molecules (https://webchem.ncbr.muni.cz). It was employed to predict the chemical reactivity and regioselectivity of reaction. The CADD Group's Chemoinformatics Tools and user Services online server (https://cactus.nci.nih.gov) was used to predict *in silico* toxicity, and specific antimicrobial activity according to QSAR models (Ampc Beta-Lactamase Inhibitor, inhibition of HIV-1 integrase, HIV-1 reverse transcriptase etc.). Molinspiration web

server (Molinspiration Cheminformatics, 2016) were respectively used for predicting bioactivity of the compound too.

Results and discussion. For synthesis of key synthons **2** and **3** was used streptocide **1**. The regioselective three-component condensation of azomethine ylides derived from isatins **4** and α-amino acids **5** with **2** or **3** as dipolarophiles has been realized through a one-pot 1,3-dipolar cycloaddition protocol in boiling aqueous alcohols afforded to the spirooxindoles (amides **6** and imides **8**) in moderate to excellent yields. The possible regioisomers **7** were not observed. The regiochemical outcome of the cycloaddition was unambiguously confirmed by Rotating-frame Overhauser Effect Spectroscopy experiments ^{1}H NMR and chemical reactivity and regioselectivity of reaction. Some classical (e.g. DHPS) and new potencial targets (e.g. Ampc Beta-Lactamase Inhibitor, inhibition of HIV-1 integrase, HIV-1 reverse transcriptase) for library of compounds **6** and **8** were been evoluted *in silico*. Spiro compounds **6** and **8** were tested according standard test-strains of microorganisms.



Conclusions. The 1,3-dipolar cycloaddition of azomethine ylides generated *in situ* from isatins and α-amino acids to N-(*p*-sulfonamido)-maleaminic acid **2** and N-(*p*-sulfonamido)-maleimide **3** afforded regio- and stereoselectively the spirooxindoles **6** and **8** in moderate to good yields. By using chemoinformatics complex computational analysis *in silico* we have found, that the obtained compounds are potentially non-toxic, does not have mutagenic and carcinogenic properties, and their potential as new chemotherapeutical and antiviral (HIV-1 reverse transcriptase) activity was been evaluated.

OBTAINING AND RESEARCH OF 2-PHENYLIMINOTHIAZOLE DERIVATIVES CONTAINING HYDROXYETHYL MOIETY

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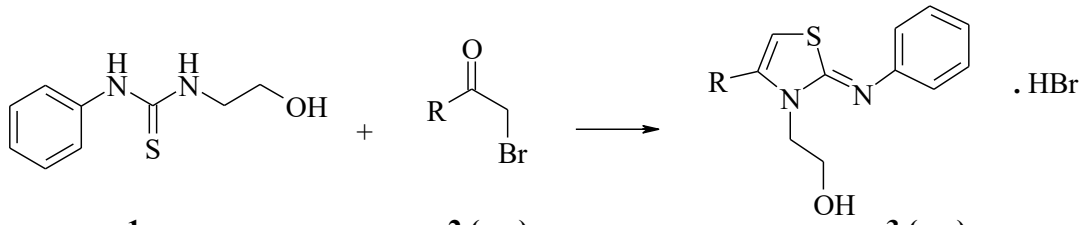
Introduction. Analysis of scientific literature shows that iminothiazole-containing heterocycles are prospective biologically active substances with antimicrobial, anti-inflammatory, antihistaminic, antihypertensive, hypnotic and anticonvulsant activity.

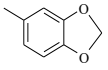
Aim. To continue the search of new biologically active substances among 2-phenyliminothiazole derivatives which possess anti-inflammatory activity.

Materials and methods. The synthesis of series 2-[4-aryl(adamantyl)-2-phenyliminothiazol-3-yl]-ethanol derivatives has been carried out:



1 **2 (a-g)** **3 (a-g)**

a) R=C_6H_5, b) R=4-$CH(CH_3)_2C_6H_4$, c) R= 4-$OCH_3C_6H_4$, d) R=3-$OCH_3C_6H_4$,

e) R=4-BrC_6H_4, f) R=3-$NO_2C_6H_4$, g) R=  , h) R=  .

To optimize the pharmacological screening of 2-[4-aryl(adamantyl)-2-phenyliminothiazol-3-yl]-ethanol derivatives «drug-like» parameters have been calculated and computer prognosis of biological properties by PASSonline programme has been done.

Results and discussions. The series 2-[4-aryl(adamantyl)-2-phenyliminothiazol-3-yl]-ethanol derivatives by interaction thiourea 1 and α-haloketones 2a-g in ethanol medium has been synthesized. Structure and purity of synthesized compounds 3a-g confirmed by elemental analysis, ^{1}H NMR and chromato-mass spectra. According to obtained results of virtual screening compounds 3a, 3b for anti-inflammatory activity have been tested.

Conclusions. Thus we have synthesized an eight new 2-[4-aryl(adamantyl)-2-phenyliminothiazol-3-yl]-ethanol derivatives, confirmed their structure and purity. The virtual screening of synthesized compounds and pharmacological screening of most promising compounds for anti-inflammatory activity have been performed. The results of virtual screening confirm results of pharmacological screening. It was established that tested compounds possess moderate anti-inflammatory activity.

SYNTHESIS OF N'-ARYLIDENE-6-OXO-4,4-DIPHENYL-5,6-DIHYDRO-4*H*-THIENO[3,4-*C*]PYRROLE-1-CARBOHYDRAZIDES AS NEW PROMISING BIOLOGICALLY ACTIVE SUBSTANCES

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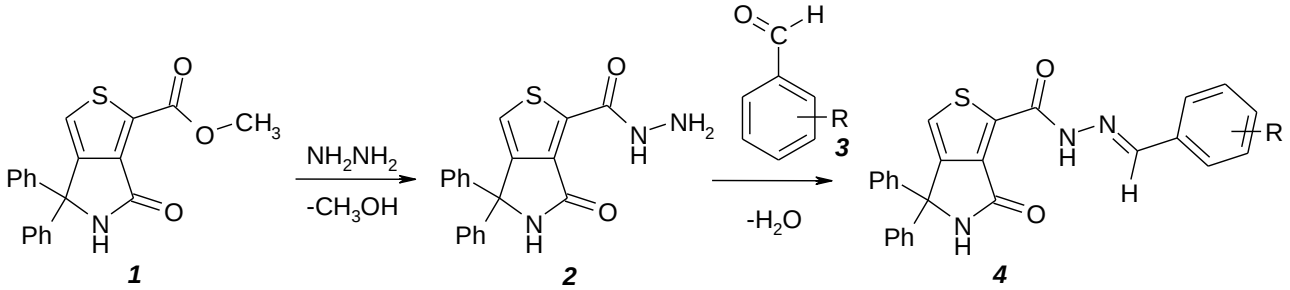
Introduction. Previously, we have worked out an efficient procedure to synthesize esters of 6-oxo-4,4-diphenyl-5,6-dihydro-4*H*-thieno[3,4-*c*]pyrrole-1-carboxylic acid by means of acidochromal cyclocondensation of benzylic acid amides. The formers comprise the novel heterocyclic system and this fact gives a great opportunity to investigate biological properties of such acids and their derivatives. It was established that abovementioned esters are effective antihypoxic and psychostimulating agents. In continuation of these researches, we decided to modify the ester group of the fused heterocycles to extend the series of thieno[3,4-*c*]pyrroles and to determination of "structure-bioactivity" relations. One of the effective methods for modifying of an ester group is synthesis of hydrazides.

Aim. Our research was focused on the synthesis of 6-oxo-4,4-diphenyl-5,6-dihydro-4H-thieno[3,4-*c*]pyrrole-1-carboxylic acid hydrazide and its further interaction with aromatic aldehydes.

Materials and methods. We used a common methods of organic synthesis. Also we used ^{1}H NMR spectroscopy to confirm the structure of the synthesized compounds.

Results and discussion. Initial hydrazide 2 was obtained by treating of methyl ester 6-oxo-4,4-diphenyl-5,6-dihydro-4*H*-thieno[3,4-*c*]pyrrole-1-carboxylic acid **1** with hydrazine hydrate. Interaction of hydrazide **2** with various aromatic aldehydes **3** allowed to obtain the target hydrazones **4** in good yields.



Conclusion. Thus, we significantly increased the number of potentially biologically active substances belonging to N'-arylidene-6-oxo-4,4-diphenyl-5,6-dihydro-4*H*-thieno[3,4-*c*]pyrrole-1-carbohydrazides. Structure synthesized compounds was proved by modern physico-chemical methods.

SYNTHESIS OF SILVER NANOPARTICLES GENERATED BY METHANOLIC EXTRACT OF EUPHORBIA FISCHERIANA

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Introduction. Nanotechnology has potential future for enhancing therapeutic efficacy and reducing the unwanted effects of herbal drugs. The biological research on Euphorbia species has been supported by the use of some plants in traditional medicines. In the present research work silver nanoparticles of Euphorbia fischeriana's methanolic extract (Ag-EF) were synthesized, characterized and tested for different activities.

Aim. According to it, the purpose of this work is to work up silver nanoparticles generated by methanolic extract and to synthesize complex compound from this plant.

Material and methods. Object of this researching was radix of the plant Euphorbia fischeriana, which was harvested on June of 2016^{th} year from the mountains Pskom.

3 g powder of Euphorbia fischeriana's radix was taken and dissolved in methanol (Extract was made in a ratio 1:10); any suspended particles were removed by filtration and was obtained 30 ml of extract. This solution was treated as a source extract (containing plant extract) and was utilized for subsequent operations.

Ag-EF was obtained when we mixed 1 mM solution of silver nitrate with powder of Euphorbia fischeriana's radix generated by methanol. For homogenously mixing methanolic extract with silver nitrate, was used magnetic interference. 200 ml of 1 mM silver nitrate's solution was prepared. Before adding silver nitrate's solution the color of methanolic extract was yellow. After adding this solution extract has been blured. Silver nitrate's solution and methanol extract were mixed in a ratio 1:1-3. The mixture was stirred uniformly for 2, 4, 6 and 8 hours on Magnetic mixer. By this way, we could find an optimal time of synthesis. At the bottom of the flask appeared sticky and red nanoparticle's precipitation. Then we separated it and washed two times with methanol, and dried it.

Results and discussion. We defined an optimal condition of silver nanoparticles and methanol extract. Silver nitrate's and methanol extracts were made in a ratio 1:2, and we found an optimal time of synthesis. This time was 4 hours.

Conclusions. During experiment ,was obtained an optimal condition of silver nanoparticle's and methanol extract's synthesis for the first time.

MORPHINE: PAST, PRESENT AND FUTURE?

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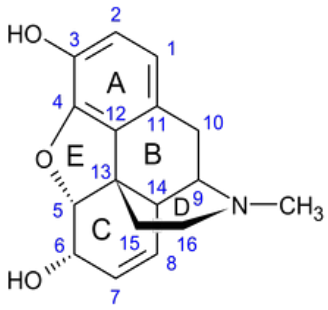
Introduction. According to the World Health Organization pain syndrome tends to happen in 90% of all disease, but only in 10% of them people use opioid analgesics. This class of drugs includes derivatives of phenanthrene, piperidine, benzomorphan and morphinan. Morphine is one of the most widely used narcotic analgesics in the world. An interest generated by the Morphine molecule relates to it`s chemical structure and mechanism of action and not only with it's actuality.



Aim. The aim of is work is the study of chemical structure and comparison of it's pharmacological activity. Analysis of available methods of synthesis of Morphine and studying the mechanism of it's action. Comparison mechanisms of action of narcotic analgesics and endogenous opioid peptides, analysis of their interaction with receptors in our organism.

Materials and methods. We used methods of scientific-bibliographic research. Information published in open sources by leading universities in the USA and Australia we're also applied.

Results and discussion. We studied historical facts about Morphine and Heroin, chronology from the time of structure opening and their formulas (including discovering of syringe and opioid receptors) till using opioid analgesics in present time, in this work. Besides, we examined four possible interactions of Morphine with protein receptors, considered structures of endogenous opioid peptides, including "message sequence" in details.

Conclusion. It was found that Morphine is optically active and has five asymmetric carbon atoms (C_5, C_6, C_9, C_{13}, C_{14}), 8 pair of racemic isomer, but only the levorotatory isomer of this drug is effective analgesic. Morphine is widely applied in clinical pain treatment, especially for terminal cancer pain and post-surgery pain. Synthesized dextrorotatory isomer of Morphine is completely devoid of any analgesic properties. The molecule is rigid, and it's T-shaped structure plays a key role in the interaction with the protein receptor and the manifestation of pharmacological activity. That's why Morphine is one of the most widely used narcotic analgesics all over the world.

THE OLD NEW CARBON

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It is well-known fact, that organic chemistry is a science studying carbon and its derivatives. Carbon's characteristics are deeply and rather wide explored. Carbon and its derivatives are used in industry, medicine and many other types of human activities. But nature still keeps a lot of secret and does not stop to surprise scientists.

Emergence process of new causative agents of dangerous diseases, including protected from antibiotics (most of them or even all of them) is well-discussed in scientific circles. Requirements in new effective and safe medicines come just after such increase, which could be cause of epidemics or even pandemics.

One of the course of the new medicine's development, which is necessary to be highlighted is research in new biologically active substances. Taking into account, that carbon is an accepted champion in amount of possible modifications and potential compounds, this element is a perspective "launch site" for every pharmaceutical researches. Moreover, the carbon's structure is rather suitable for such role: carbon's atoms compiled into spheres with surface consists from 20 hexagons and 12 pentagons. The discovery of fullerenes greatly expanded the number of known carbon allotropes, which until recently were limited to graphite, graphene, diamond, and amorphous carbon such as soot and charcoal.

In 1970, R. W. Henson (Atomic Energy Research Establishment) proposed the structure and made a model of Fullerene. Unfortunately, the evidence for this new form of carbon was very weak and was not accepted by scientific circles. Harold Kroto from University of Sussex and team of scientists from Rice University were the scientists who was interested in carbon. The first fullerene molecule to be discovered by their hard and exhaustive research in 1985. For his researches in the area of carbon (extracted from space dust) in 1985, Kroto and his American colleges were presented with the Nobel prize of 1996 in chemistry.

They separate a new carbon's variety: a fullerene. It is an elementary substance in a form of soft yellow crystals, which becomes an object of interest of many scientists in nanoelectronic industry for the purposes of displays (from active bigboards to flexible computers) producing. Fullerene production processes includes the following five stages:

1. synthesis of fullerenes or fullerene-containing soot; (ii)
2. extraction; (iii)
3. separation (purification) for each fullerene molecule, yielding pure fullerenes

such as C_{60}; (iv)

4. synthesis of derivatives (mostly using the techniques of organic synthesis);
5. other post-processing such as dispersion into a matrix.

There are a lot of previously unknown substances that are perspective to use in different areas (including pharmacy) created on the base of fullerene. Also, fullerene allows scientist to use nanometrs in their activities except micrometers.

Fullerene has a noticeable pharmacological activity: biological active substances with fullerene and with addition of some vitamins, antibiotics, hormones become very useful in healing of damaged brain cells. The first experiment with fullerene in such area was committed on experimental animals in Tel-Aviv by Israel scientist. Potentially, such substances may become a revolution in healing of disseminated sclerosis and Alzheimer's disease, other forms of gerontic dementias.

After usability in the above-stated practical issues, which are ready to massive producing, fullerene is a core element of several perspective pharmacological and medical novelties. There are methods of viruses' genom destruction without vaccines developed on the base of fullerene. Fullerene may become an integral part of many detoxes against animal and non-biological poisons. There are some positive results of using fullerene in healing of cancer. From the viewpoint of military and space medicine, fullerene attracts the great interest as potential radioprotective agent. Hydrated fullerenes C_{60} prove themselves as effective radioprotectos for animals. Their molecules catalyzed recombination of free radicals. In case of high radioactivity, for example, in space flight out of magnetic field of Earth, fullerene based radioprotectos may be indispensable: for example, it can solve a problem of astronauts protection from star wind and other space radiation during mission on Mars. Scientists from Institute of physiological active compounds of Kharkov have already achieved some positive results on such course.

Even a new subdivision of chemistry was founded because of Fullerene explorations. Fullerene chemistry is a field of organic chemistry devoted to the chemical properties of fullerenes. Research in this field are oriented to functionalize fullerenes and tune their properties for commercial and industrial use. For example, fullerene is notoriously insoluble and adding a suitable group can enhance solubility. By adding a polymerizable group, a fullerene polymer can be obtained.

Taking into account the foresaid facts, despite the fact that many of the above-stated concepts are in the early stage of development, even now it is an obvious fact that development of new pharmacological and other compounds on the base of fullerene is now one of the most perspective development projects both from scientific, social and commercial viewpoints.

NEW ANTICONVULSANT DRUGS AMONG LITHIUM, POTASSIUM SALTS OF SOME SALICYLIDENE-AMINOACIDS

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The tendency to modify molecules of physiologically active compounds continues to play an important role in the development of new drugs. Studies on the development of new psychotropic drugs based on such neuroactive aminoacids as GABA, glutamic acid, glycine and β-alanine are the focus of the experimenters. GABA-ergic substances contain substances with nootropic, anticonvulsant, tranquilizing properties. The correct combination of various neuroaminoacids with the lithium cation is of particular interest in connection with the fact that lithium salts are used for the treatment and prevention of manic-depressive psychosis, various affective states.

The aim of this investigation was to study the anticonvulsant activity of 12 lithium, potassium salts of some salicylidene-amino acids (GABA, α-, β-alanine, valine, tryptophan, ε-aminocaproic acid, 5-aminosalicylic acid). The study of the anticonvulsant activity of compounds in doses of 50-150 mg / kg was carried out on outbred mice weighing 18-22g in accordance with common tests: antagonism with corazole, nicotine, maximal electroshock. Neurotoxic / muscle relaxant / effect of compounds and acute daily toxicity were also studied. The results of the experiments were tested statistically according the method of Litchfield and Wilcoxon and compared with the known anticonvulsant drug ethosuximide. Anticonvulsant activity was revealed in some compounds only for antagonism with corazole. The most active are the derivatives of β-alanine, β-phenyl-α-alanine, β-phenyl-β-alanine and 5-aminosalicylic acid. The compound for anticonvulsant activity is not inferior to ethosuximide, but they are more toxic compared to it. The activity of lithium derivatives in comparison with potassium derivatives and in L-derivatives of β-phenyl-α-alanine and tryptophan is more pronounced in comparison with their DL derivatives.

APPROACHES TO SYNTHESIS OF 3-(5-R-AMINO-[1,3,4]THIADIAZOL-2-YL)-1,2,2-TRIMETHYLCYCLOPENTANECARBOXYLIC ACIDS

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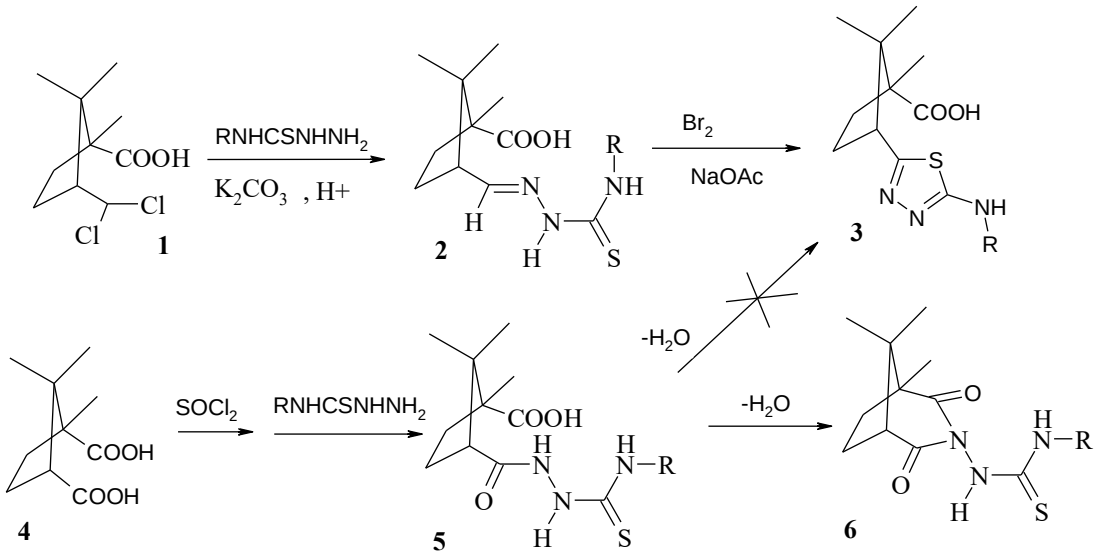
Introduction. This work is continuation of search for biologically active substances among the derivatives with 1,2,2-trimethylcyclopentanecarboxylic acid moiety.

Aim. The aim of the work is development a method for synthesis of 3-(5-R-amino-[1,3,4]thiadiazole-2-yl)-1,2,2-trimethylcyclopentanecarboxylic acids (3, scheme).

Results and discussion. At the first stage thiosemicarbazones (2) have been obtained by interaction beetween 3-dichloromethyl-1,2,2-trimethylcyclopentanecarboxylic acid (1) and 4-R-thiosemicarbazides. Followed cyclization of thiosemicarbazones (2) under the action of bromine leads to target acid 3.

An attempt to synthesize acids (3) using camphoric acid (4) as a starting compound was also made. But it was found that the dehydration of acylthiosemicarbazides (5) ended up with the formation of imide ring and compounds (6) were obtained.



Conclusion. 3-Dichloromethyl-1,2,2-trimethylcyclopentanecarboxylic acid has been proposed as the starting material for two step synthetic procedure of the desired product.

NEW 2-AMINO-4-ARYL-4*H*-PYRANS BASED ON 1,2-BENZOXATHIIN-4(3*H*)-ONE 2,2 DIOXIDE

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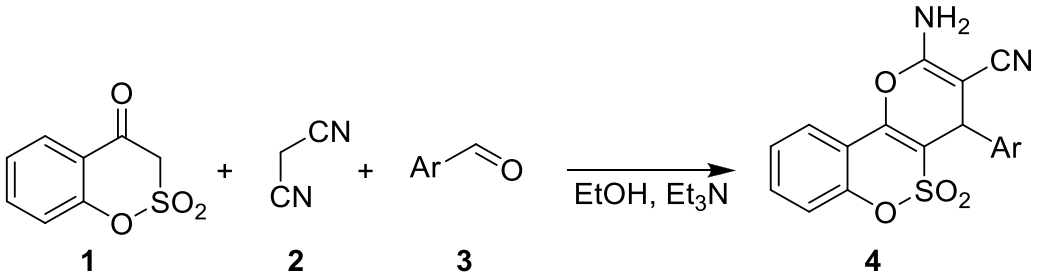
Introduction. To date 1,2-benzoxathiin-4(*3H*)-one 2,2-dioxide was not used in multicomponent reactions. This compound is a synthetic analogue of active methylene carbonyl compounds since it comprises $COCH_2SO_2$ moiety in its structure. These features open great opportunities to construct new condensed heterocyclic systems based on it. Thus, there is no information referred to fused heterocyclic systems combining 1,2-benzoxathiine 2,2 dioxide.

Aim. Current research was aimed to synthesize 2-amino-4-aryl-4*H*-pyrano[3,2-*c*][1,2]benzoxathiine-3-carbonitrile 5,5-dioxides based on three-component interaction of 1,2-benzoxathiin-4(*3H*)-one 2,2-dioxide with malononitrile and aromatic aldehydes, and also to prove the structure of the obtained compounds.

Materials and methods. As starting materials 1,2-benzoxathiin-4(*3H*)-one-2,2 dioxide, malononitrile and different substituted aromatic aldehydes were used. The methods of organic synthesis and ^{1}H NMR spectroscopy method were applied in the course of the research.

Results and discussion. The interaction of 1,2-benzoxathiin-4(3*H*)-one 2,2-dioxide (1) with malononitrile (2) and aromatic aldehydes (3) was carried out in refluxing ethanol for 1 hour (the molar ratio 1:1:1) and resulted into formation of target compounds (4) in moderate to high yields. The reaction products were obtained as colorless or yellow crystalline precipitates, further purification was not required. Triethylamine was used as easily available and inexpensive basic catalyst. The structures of the obtained compounds were confirmed by ^{1}H NMR.



Conclusions. During the research we have shown a possibility to synthesize new 2-amino-4-aryl-4*H*-pyrano[3,2-*c*][1,2]benzoxathiine-3-carbonitrile 5,5-dioxides *via* one-pot three-component interaction of 1,2-benzoxathiin-4(*3H*)-one 2,2-dioxide with malononitrile and arenecarbaldehydes. These investigations may be useful in further studies dedicated to this synthetic area.

SYNTHESIS AND CARDIOTROPIC PROPERTIES OF THE NEW 1,3-THIAZOLE DERIVATIVES

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Introduction. Experimental and clinical trials in recent years have observed that cardiotropic drugs of metabolic type have proven clinical effectiveness. And medicines with this kind of action, such as Meldonium and L-carnitine have taken the lead in treatment regimen for cardiovascular pathologies. Having analyzed data in the scientific and patent literature, it should be noted that derivatives of 1,3-thiazole are prospective for a search of potential cardiotropic agents among them, and also they have a high pharmacotherapeutical potential.

The **aim** of this work is to obtain new biological compounds of metabolic type with a high cardioprotective activity among derivatives of 1,3-thiazole.

Materials and methods. Methods of organic synthesis; physical and physicochemical methods of analysis of organic compounds (^{1}H NMR spectroscopy, elemental analysis), the study of biological properties using standard techniques; analysis of the results obtained and their generalization, statistical methods for processing experimental data.

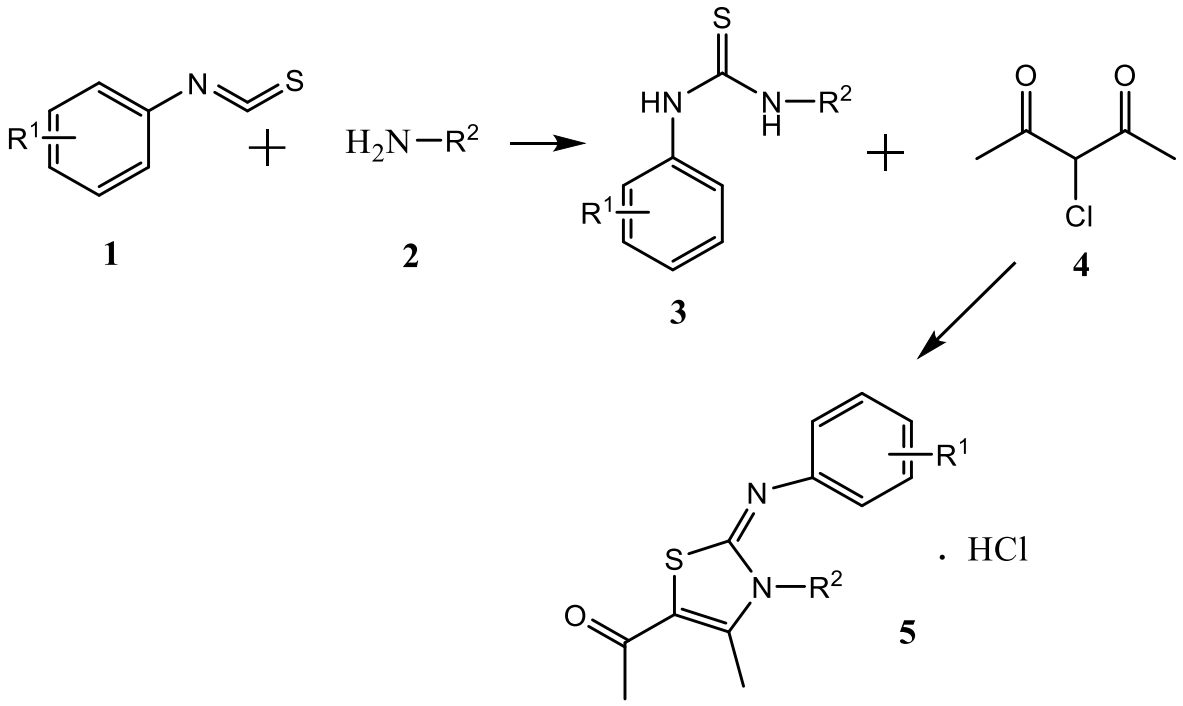
Results and discussion. In order to find new biologically active substances, the synthesis of new series of derivatives of 1-(4-methyl-2-(phenylimino)-2,3-dihydrothiazol-5-yl)ethan-1-one. has been conducted. As the initial products of the synthesis, by the interaction of substituted phenylisothiocyanates **1** and arylamines **2** the unsymmetrical thiourea solutions **3** were produced. The reaction was carried out in dry dioxan medium. The hydrochlorides of N-[4-methyl-2-R-phenyliminothiazole-3-yl]-morpholine **5** were obtained by boiling the equimolar amounts of unsymmetrical thioureas **3** with 3-chloropentane-2,4-dione **4** in Ethanol (Scheme 1). The structure and individuality of the compounds were confirmed by modern physical and chemical methods: thin-layer chromatography, elemental and ^{1}H NMR spectral analysis.

The cardiotropic action was investigated on the isolated of the thoracic aorta of laboratory mice. The effectiveness of examined compounds was compared with the negative control and the reference preparations: Meldonium and L-carnitine.

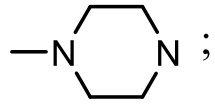
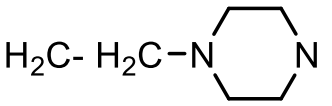
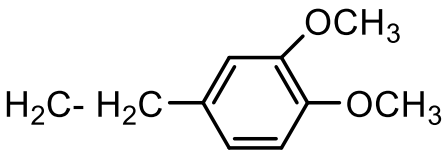
Two examined compounds at the level of reference preparations, and in some cases exceeding them, having reduced the normalized maximum rate of the contraction phase to hypoxia, which indicates the property of these compounds to

realize a decrease in the energy potential of the cardiomyocyte damaged by hypoxia.

Scheme 1



R^1 = -H, $-OCH_3$, $-CH_3$

R^2 =  ;  ; 

Conclusions. A purposeful synthesis of a new series of derivatives of 1-(4-methyl-2-(phenylimino)-2,3-dihydrothiazol-5-yl)ethan-1-one. has been carried out.

The structure and individuality of 4 compounds which have not described in the literature was confirmed by means of elemental analysis, ^{1}H NMR-spectroscopy, and thin layer chromatography.

The results of the pharmacological studies conducted of the synthesized compounds have confirmed the presence of cardiotropic properties that provides the prospectivity of the further research in this group.

NIMESULIDE. ADVANTEGES AND DISADVANTEGES OF PHARMACOLOGYCAL ACTIVITY.

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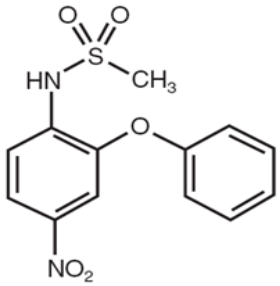
Nimesulide, an anti-inflammatory and analgesic drug, was originally synthesized by Dr George Moore and his research team at Riker Laboratories, Minnesota in 1971. The drug was synthesized with the intention of providing a better therapeutic alternative in comparison to the existing class of non-steroidal anti-inflammatory drugs.



One of the problems with NSAIDs is that they block both types of the COX enzyme, so while inflammation and pain were reduced. Nimesulide is selective inhibitor of COX-2. Selective NSAIDs inhibit only the COX-2 enzyme, allowing for the production of the prostaglandins that protect the stomach, while still relieving fever, pain and inflammation. They do no have the anti-platelet effects associated with nonselective NSAIDs and so do not alter clotting. The clinical data and information from studies in experimental animal models strongly supports the epidemiological data showing that nimesulide has a relatively low risk of serious collateral reactions.

In my work have been described history, structure, mehanism of action, role of sulphonamide group of Nimesulide. Therefore, it will be possible to say about different advanteges and disadvanteges of this substance.

The importance of sulphonamide moiety in medicinal chemistry cannot be ignored as it constitutes an important class of extensively used drugs.

Antibacterial sulfonamides target a bacterial metabolic pathway as competitive inhibitors of the enzyme dihydropteroate synthetase, DHPS. Dihydropteroate synthetase activity is vital in the synthesis of folate, and folate is required for cells to make nucleic acids, such as DNA or RNA. So if DNA molecules cannot be built, the cell cannot divide, and the effect is bacteriostatic. Sulfa drugs do not cause the same disruption in animal cells, because our cells do not synthesize folate.

SYNTHESIS AND INVESTIGATION OF THE 7-AMINO-4-METHYLCOUMARIN'S MALEIC DERIVATIVE IN THE DOMINO-THREE-COMPONENT REACTION WITH ISATIN AND *L*-VALINE

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Introduction. 7-Amino-4-methylcoumarin **1** is a far-famed useful fluorescent labeling reagent for trace determination of different proteins. Also useful as a reference standard in enzyme assays. Nevertheless, at 2011 R. Tandon and coauthors were discover that it displayed the lowest *MIC* of 1 mg/L against not only *Mycobacterium tuberculosis* H37Rv strain but also the susceptible as well as the multidrug-resistant clinical isolates. Certain 7-acylamino coumarins were also found to inhibit the aforementioned strains and isolates with MICs in the range of 1.0-3.5 mg/L. They were also found to act in synergy with isoniazid/rifampicin. Electron microscopy revealed the cell-wall-attacking characteristic of these compounds, while fluorescence microscopy indicated that mycolic acid might be the target of action.

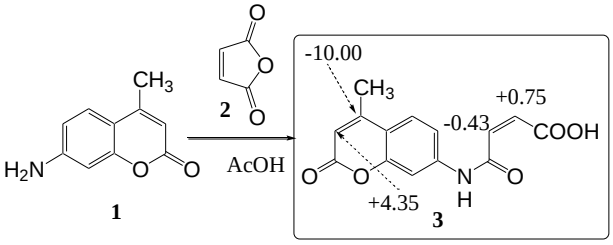
On the other hand, spiro-2-oxindoles are known for their antimicrobial potential. Therefore, we were interested to explore the possibility of 7-amino-4-methylcoumarin as dipolarofile using in the construction of new spiro-2-oxindoles.

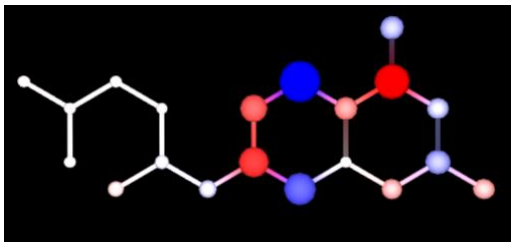
Aim. Investigation of chemical reactivity of 7-amino-4-methylcoumarin in the domino-tree-component reaction with isatin and *L*-valine.

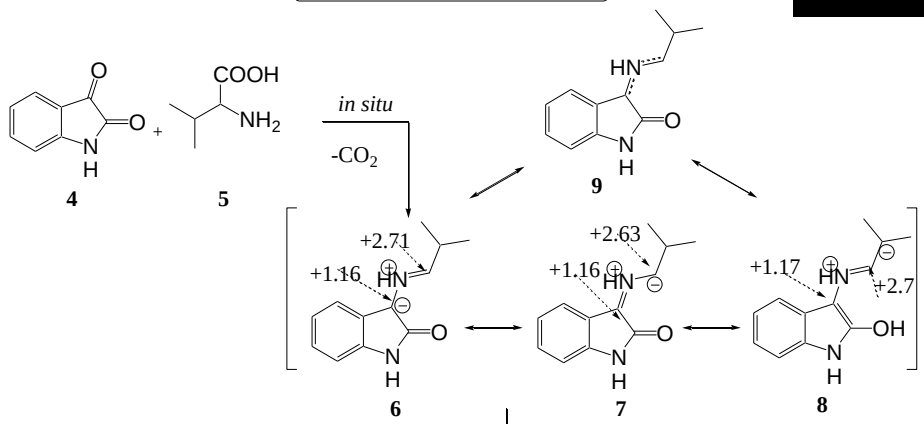
Materials and methods. Synthesis of compounds using acylation in glacial acetic acid, three-component condensation in alcoholic-aqueous medium; proofing of the structure was performed by UV-, ^{1}H NMR spectroscopy. ^{1}H NMR spectra were recorded on instruments Varian Mercury VX-200 (200 MHz) in DMSO-d_6 solution, TMS internal standard. UV-spectrums were record in EtOH on the SPEKOL-1500. AtomicChargeCalculator (ACC) offers an efficient based on the Electronegativity Equalization Method (EEM), user-friendly, interactive and platform independent environment for the calculation, visualization and analysis of quantum mechanics quality atomic charges in drug-like molecules (https://webchem.ncbr.muni.cz). It was employed to predict the chemical reactivity and regioselectivity of reaction. The CADD Group's Chemoinformatics Tools and user Services online server (https://cactus.nci.nih.gov) was used to predict *in silico* toxicity, and specific antimicrobial activity according to QSAR models.

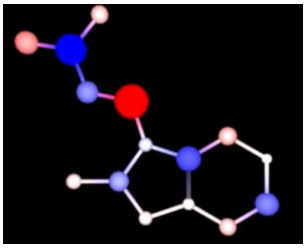
Results and discussion. The synthesis of 7-(N-maleylamino)-4-methylcoumarin **3** were carry out acylation of **1** by treatment with maleic anhydride **2**. Obtained N-(7-amino-4-methylchromen-2-one-7-yl)maleamiic acid **3** can be

considered as a bifunctional 1,3-dipolarophile. The calculation of atom charges using the ACC protocol for molecule **3** shows that the largest charge is concentrated on the π-bond of the lactone cycle and to a reduced extent on the π-bond maleic acid residue. Comparison with **1** and **3** chromophores, the difference of absorption ($\Delta\lambda_{max}$ 11 nm) between becomes less, and hence the absorption maxima would shift towards shortest wavelength for 7-acylamino chromophore, the *p*-electron is less free to move for **3**. One-pot protocol in boiling aqueous ethanol the regioselective three-component condensation of azomethine ylide (hybrid structures **6-9**) derived from isatin **4** and *L*-valine **5** *via* Shtreker reaction and then with **3** has been realized through a 1,3-dipolar cycloaddition with 92 % yield **10**. The possible regioisomer **11** were not observed. Adduct **10** absorbed at 329 nm.

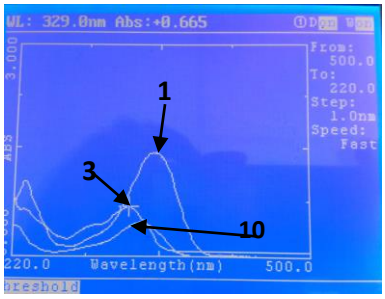


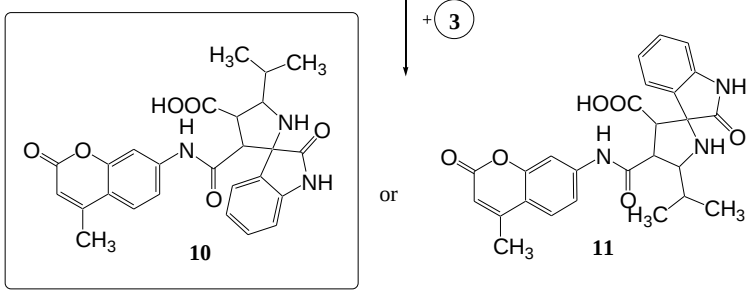






Absorption spectra of comp. **1,3,10**





Conclusions. The chemical reactivity of 7-amino-4-methylcoumarin in the domino-tree-component reaction with isatin and *L*-valine was been evaluated. The 1,3-dipolar cycloaddition of azomethine ylide generated *in situ* from isatin and *L*-valine to the spiro-adduct **10** to good yield. Despite the higher charges of the π-bond of the lactone cycle, the most reactive was the maleic acid residue at the 7 position of the 7-amino-4-methylcoumarin core. This may be due to steric limitation at the position 4 of the pyran ring, which are triggered by the 4-methyl group of lactone cycle.

SEARCH OF POTENTIAL ANTIOXIDANTS IN A ROW OF DERIVATIVES OF 8-HYDRAZINYL-1,3-DIMETHYL-7-ARYLALKYLXANTHINES

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Introduction. The leading role in the development of various critical states belongs to breaches of antioxidant status of an organism. That is a reason, the use of antioxidant therapy positively affects the results of treatment (even remoted one) and reduces the length of patients' stay at hospitals. Medicines of this type of pharmacological effect, available in the pharmaceutical market, do not fully meet the needs of modern medicine, therefore, the search of original substances with antioxidant properties is a perspective area of medicinal and pharmaceutical chemistries.

Aim. Among the known nitrogenheterocycles containing hydrazine group, the aim of our research was to identify a number of relevant functional derivatives, exhibiting antimicrobial, antihypoxytic, antiradical and other activities, thus exceeding or competing with reference drugs in action expressiveness. It seemed expedient for us to gain products of condensation of initial 7-arylalkyl-8-hydrazinotheophyllines with some reagents containing carbonyl, to explore their physical and chemical characteristics and pharmacological effects.

Materials and methods. 7-arylalkyl-8-hydrazinotheophyllines, related substances containing carbonyl, bases and solvents; condensation reaction, heterocyclization and salt formation; physicochemical studies using IR-, ^{1}H NMR-spectroscopy, chromato-mass-spectrometry; pharmacological screening *in vitro* and *in vivo*.

Results and discussion. Interaction of 7-arylalkyl-8-hydrazinotheophyllines with aldehydes and ketones of aromatic range, demanded the usage of acid catalysis and high-boiling solvents (heating for 1-4 hours) and accompanied with the high yields of target 7-*R*-8-ylidenhydrazinotheophyllines.

Modification of the initial materials in reactions with oxocarbonic acids and their functional derivatives varied depending on the conditions of the conversion. Thus, at room temperature during 24-36 hours in spirituous environment, in presence of catalytic amounts of concentrated hydrochloric acid, components of the mixtures formed corresponding [(7-*R*-theophylline-8-yl)hydrazono]alkyl(aryl-)carboxylic acids or esters of these acids.

Subsequently, with aim to improve the pharmaco-technological characteristics,

the synthesized acids were converted into salts by reacting with the bases of inorganic and organic nature. The processes took place in aqueous or spirituous environment under short-term heating with subsequent evaporation of the reaction mixtures and with salting target products using acetone.

Conducting reactions of 7-arylalkyl-8-hydrazinotheophyllines with dicarbonyle compounds (acetylacetone, acid 4-oxo-4-phenylbutanoate, 2-formil-(acetyl) benzoate) in «hard» conditions (acetic acid glacial environment, continuous heating of components of the mixture etc.) accompanied with obtaining products containing a heterocyclic fragment in 8-th position of the molecule. A similar result was also gained by further chemical modification of [(7-*R*-theophylline-8-yl)hydrazono]alkyl (aryl-)carboxylic acids or esters.

The substances, newly created for the analysis, were purified by recrystallization from ethanol, a mixture of ethanol – water or dimethylformamide – water in appropriate ratios.

The results of chromato-mass-spectrometric determination of synthesized compounds in conditions of APCI (chemical ionization at atmospheric pressure) confirmed their individuality and, in each case in different retention time, allowed to register correspondent intensive peaks of quasimolecular ions $[MH]^+$, mass of which corresponds to the calculated mass of protonated forms of derived substances.

IR spectra of the target products of reactions are characterized by intense absorption bands of CO-groups of xanthine fragment of molecules, valence fluctations of aromatic CH-bonds in the form of low intensity bands, absorption bands of absorbing -CH_2-aliphatic groups located in the 7 and 8 positions, valence fluctuations of substituted hydrazine-group etc.

Analysis of the ^{1}H NMR-spectra of the synthesized compounds allowed us to clearly confirm their structure, and, in some cases there were registered doubled signals of some protons, indicating the presence of tautomeric forms, but the identification of the last, needs some additional physical and chemical researches.

Evaluation of antioxidant and antiradical activities of the derived substances was conducted on the model of decelerating auto-oxidation of adrenaline into adrenochrome (this reaction in alkaline environment accompanied by the accumulation of superoxide radical), with inhibition: DPPH, $NO^{\bullet}$-radical (measured by the degree of inhibition of oxidation of ascorbic acid solution by trial indicators extinction at 265 nm) and oxidative modification of protein (quantified oxidized amino acid residues of proteins by reaction with 2,4-dinitrophenylhydrazine at 363 nm). The conducted researches revealed substances, which, by the expressiveness of action, exceeded the comparators.

Conclusions. Experimental results confirmed the prospects of the targeted of the original antioxidants in the range of 7,8-disubstituted theophylline.

FEATURES OF ALIPHATIC ALDEHYDES APPLYING IN THREE-COMPONENT INTERACTION WITH ACTIVE METHYLENE NITRILES AND 1-ETHYL-1*H*-2,1-BENZOTHIAZIN-4(3*H*)-ONE 2,2-DIOXIDE

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Introduction. 2-Amino-4*H*-pyran core is a structural motif of well-known biologically active compounds. The most straightforward route to this heterocyclic system is a three-component interaction of enol-nucleophiles with carbonyl compounds and active methylene nitriles. Various types of carbonyls were applied in this reaction, among which (*het*)arenecarbaldehydes and isatins are the most common one. Unlike these, aliphatic aldehydes have been studied poorly and rarely occurred in the literature as a possible component of such interactions. 1-R-1*H*-2,1-benzothiazin-4(3*H*)-one 2,2-dioxides being utilized in the reaction allow to fuse 2-amino-4*H*-pyran core with another known pharmacophore – 1*H*-2,1-benzothiazine 2,2-dioxide. We suspected that such combination might lead to increase of certain kinds of biological activity, for instance, antimicrobial. This is due to the numbers of 2-amino-4*H*-pyrans and 1*H*-2,1-benzothiazine 2,2-dioxides proved to be highly efficient antimicrobial agents.

Aim. Our research was focused on the scope and limitations of three-component 2-amino-4*H*-pyrans synthesis based on the aliphatic aldehydes, 1-ethyl-1*H*-2,1-benzothiazin-4(3*H*)-one 2,2-dioxide and active methylene nitriles and also on the confirmation of the synthesized compounds structure. We were additionally inspired in evaluation of antimicrobial activity of the obtained 2-amino-4*H*-pyrans.

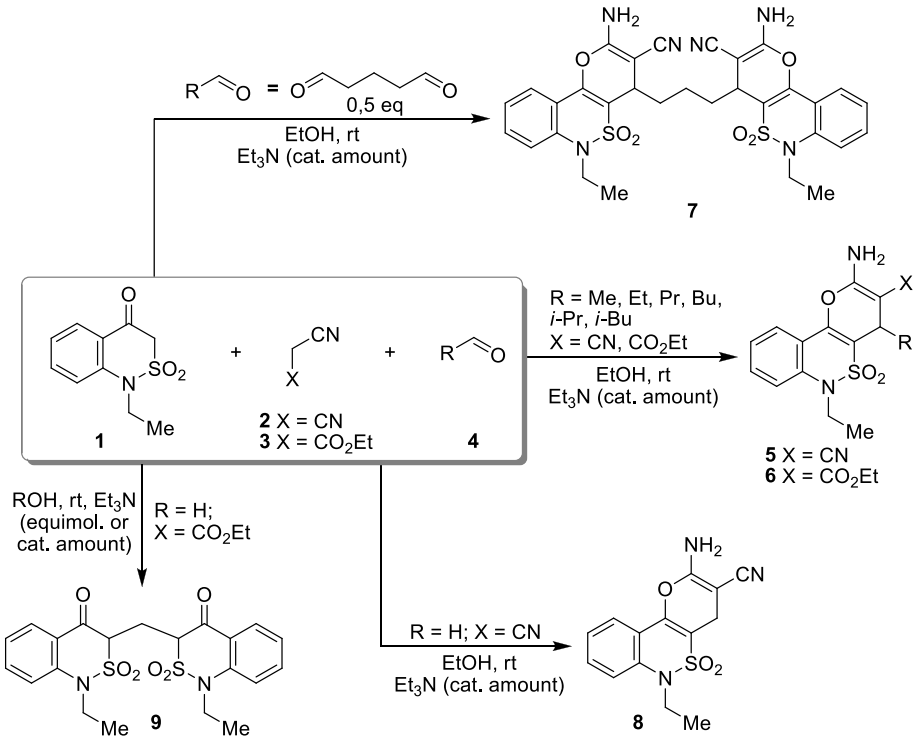
Materials and methods. We used different methods of organic synthesis as well as double serial dilution method in liquid growth medium to evaluate antimicrobial activity of synthesized compounds. We also employed ^{1}H and ^{13}C NMR spectroscopy to prove the structure of previously mentioned ones.

Results and discussion. Our investigations showed that three-component interaction of 1-ethyl-1*H*-2,1-benzothiazin-4(3*H*)-one 2,2-dioxide 1 with saturated aliphatic aldehydes 4 and malononitrile 2 proceeded under quite mild conditions and resulted into formation of 2-amino-6-ethyl-4-alkyl-4,6-dihydropyrano[3,2-*c*][2,1]benzothiazin-3-carbonitrile 5,5-dioxides 5 in moderate to high yields. The use of formaldehyde in the reaction allows to obtain 4-unsubstituted condensed 2-amino-4*H*-pyran 8. To date, there is no information in the literature about the possible application of aliphatic dialdehydes in the discussed three-component interactions. Therefore, we decided to utilize glutaric aldehyde with the purpose of obtaining of a

new class of 2-amino-4*H*-pyran bis-derivatives in which two fragments are linked by polymethylene bridge. As the result 1,3-bis(2-amino-6-ethyl-4,6-dihydropyrano[3,2-*c*][2,1]benzothiazine-3-carbonitrile-4-yl 5,5-dioxide)propan 7 was obtained in high yield.

Replacement of malononitrile 2 with ethyl cyanoacetate 3 in the three-component reaction led to decrease of the reaction efficiency and yields of target ethyl 2-amino-4*H*-pyran-3-carboxylates 6. Thus, in the case of glutaraldehyde we were not able to obtain desired bis-derivative. When formaldehyde was introduced in three-component interaction with 1 and 3 we got the unexpected result and the isolated product was bis(1-ethyl-1*H*-2,2-dioxido-2,1-benzothiazin-4(3*H*)-on-3-yl)methane 9. Taking into account the results we obtained before in the cases of (*het*)arenecarbaldehydes it was interesting, that product 9 was obtained in dicarbonyl form though one could expect to isolate it as triethylammonium salt.

Despite of our expectations, the 2-amino-4*H*-pyrans showed a low level of antimicrobial activity. The only activity against *C. albicans* was significant for these derivatives.



Conclusion. In the course of the research we synthesized the series of 4-alkyl substituted 2-amino-3-R-6-ethyl-4,6-dihydropyrano[3,2-*c*][2,1]benzothiazine 5,5-dioxides *via* three-component interaction of 1-ethyl-1*H*-2,1-benzothiazin-4(3*H*)-one 2,2-dioxide with aliphatic aldehydes and active methylene nitriles. Application of various aliphatic aldehydes as well as active methylene nitriles allows to establish certain regularities of the three-component interaction. Evaluation of antimicrobial activity of the synthesized compounds revealed their low potential to create antimicrobial drugs.

SYNTHESIS, DOCKING STUDIES OF THE DERIVATIVES OF 3-ALLYL-N,4-DIPHENYL-THIAZOLE-2-IMINE

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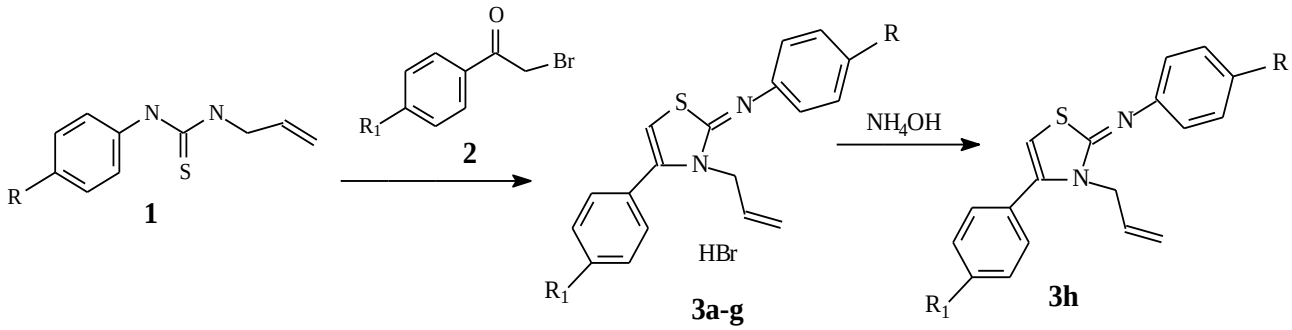
Introduction. Thiazoles, due to the presence of substituents capable of being modified, represent scientific value in organic synthesis for the production of new biologically active substances and therefore have a perspective to be used in medicine and pharmacy.

Aim. The purpose of this study is to synthesize new biologically active compounds in the series of the derivatives of 3-allyl-N,4-diphenyl-thiazole-2-imine, confirm the structure of synthesized compounds, conduct in silico probable molecular mechanisms of cardioprotective action of the obtained substances by the method of flexible molecular docking.

Materials and methods. The starting, auxiliary substances and solvents used in the work were obtained and purified using standard techniques. The purity of the obtained compounds was monitored by thin layer chromatography method using silica gel of Fluka (60 F254) plate (0.25 mm). Visualization was carried out by UV-radiation. Elemental analysis of the nitrogen content was carried out by the Dumas method. ^{1}H NMR-spectra were registered on a Varian Gemini 400 MHz device in DMSO-d6, tetramethylsilane (TMS) was used as an internal standard. For flexible molecular docking, the Autodock 4.2.6 software package was used. Preparation of ligands was carried out with the help of programs Vega ZZ (command line) and MGL Tools 1.5.6. The active center of the macromolecule from Protein Data Bank (PDB) of the gamma-butyrobetaine hydroxylase enzyme (PDB ID: 3O2G) was used as a biological target. Visual analysis of the complexes of the substances in the active center of the enzyme was carried out using the program Discovery Studio Visualizer 4.0.

Results and discussion. Under the conditions of the Hantzsch reaction, the synthesis of the derivatives of 3-allyl-N,4-diphenyl-thiazole-2-imine ***(3a-g)*** hydrobromide was carried out due to the interaction of the derivatives of unsymmetrical thioureas ***1*** with α-bromo-4-R-acetophenone ***2*** in equimolar amounts by boiling in ethanol for 3 hours, 3-allyl-N,4-diphenyl-thiazole-2-imine ***3h*** was obtained by neutralizing the corresponding hydrobromide with a 10% solution of NH_4OH:



where: ***3a*** R=CH_3, R_1 =OCH_3; ***3b*** R=CH_3, R_1 =Cl; ***3c*** R=CH_3, R_1 =2',4'-$(Cl)_2$; ***3d*** R=Br, R_1 =Cl; ***3e*** R=H, R_1 =Cl; ***3f*** R=Br, R_1 =NO_2; ***3g*** R=CH_3, R_1 =CH_3; ***3h*** R=CH_3, R_1 =OCH_3

The structure of the obtained compounds is confirmed by modern physicochemical methods of analysis: ^{1}H-NMR, 2DNMR-spectroscopy (NOESY, ROESY), elemental analysis, thin-layer chromatography. The conducted studies prove the regioselectivity of the reaction to the formation of substituted 3-allyl-N,4-diphenyl-thiazole-2-imines.

The conducted docking studies have shown that the pharmacological action of the synthesized compounds, as potential cardioprotective agents of metabolic action, is connected with inhibition of gamma-butyrobetaine hydroxylase (PDBID: 3O2G). Values of scoring functions for all investigated substances are negative and in absolute values are comparable or exceed values of scoring functions for standard substances, that indicates a high thermodynamic probability of the display of inhibitory activity in relation to this enzyme. The obtained results indicate the possibility of the formation of stable complexes of substituted thiazole-2-imines with a biological target in which the arrangement of the ligands in the active center of the receptor and the amino acids residues of the side chains, involved in the formation of non-covalent bonds, are analogous to the geometry and types of binding of levocarnitine and mildronate, established on the basis of crystallographic studies.

The derivatives of thiazole-2-imine can be considered as a promising scaffold for the formation of combinatorial libraries of potential biologically active substances, namely by introducing new pharmacophore centers into the 3 position of the thiazole cycle, as proved by the results of the conducted virtual screening procedures.

Conclusions. The synthesis of 8 new biologically active compounds of the derivatives of 3-allyl-N,4-diphenyl-thiazole-2-imine under the conditions of the Hantzsch reaction was carried out. The structure of the synthesized compounds is confirmed by the integrated use of modern physicochemical methods of analysis. The results of the docking studies allow to state that the new derivatives of 3-allyl-N,4-diphenyl-thiazole-2-imine are potential cardioprotective agents of metabolic action.

SYNTHESIS OF 3-ARYLIDENE-1-(2-AMINO-4-METHYL-THIAZOL-5-YL)-ETHANONES AS POTENTIALLY BIOLOGICALLY ACTIVE COMPOUNDS

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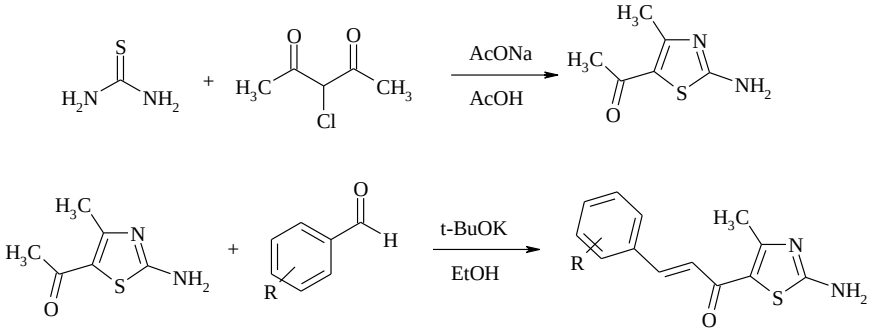
Introdaction. Synthesis of wide range pharmacologically active compounds with diverse structure, which causes their different biological activity, is actually problem of modern organic and medicinal chemistry.The studying of heterocycles, which contain 4-thiazolidinone core, is especially interesting, because they have anticancer, antimicrobial, anti inflammatory and antioxidant activities. In addition, the thiazolidinones form the central skeleton of many compounds displaying antidiabetic (agonists of PPAR-γ receptors- rosiglitazone, pioglitazone), diuretic (etozolin), dual inhibitors of cyclooxygenase-2/5 -lipooxygenase (darbufelon) activities.

Aim. Elaborating of preparative methods of synthesis of novel 3-arylidene-1-(2-amino-4-methyl-thiazol-5-yl)-etanones as potentially biologically active compounds.

Materials and methods. Organic synthesis, NMR spectroscopy.

Results and discussion. We first investigated the reaction of 3-chloroacetylacetone with thiourea in boiling acetic acid which afforded 1- (2-amino-4-methyl-thiazol-5-yl)–ethanones. To expand our investigation we then studied the reaction of 1-(2-amino-4-methyl-thiazol-5-yl)–ethanones with appropriate substituted benzaldehydes in the ethanol medium in the presence of potassium tert-butylate providing novel 3-arylidene-1-(2-amino-4-methyl-thiazol-5-yl)–ethanones. Structural elucidation of the newly synthesized compounds was accomplished using by NMR spectroscopy, as well as elemental analysis.



Conclusion. In summary, we have successfully developed an efficient method for the construction of 3-arylidene-1-(2-amino-4-methyl-thiazol-5-yl)-ethanone derivatives using 1- (2-amino-4-methyl-thiazol-5-yl)–ethanones and aromatic aldehydes. Overall, the biological tests revealed the necessity for further investigations of pharmacological potential of tested compounds for the construction of novel chemical entities with better pharmacological profiles.

SYNTHESIS OF 3-(2-METHYL-4-OXO-1,4-DIHYDROQUINOLINE-3-YL) PROPANOIC ACIDS AND THEIR EFFECT ON THE BLOOD COAGULATION SYSTEM

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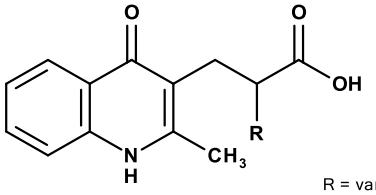
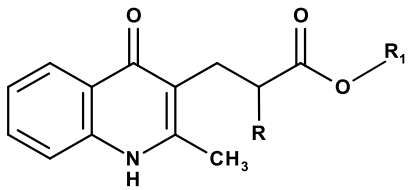
The study of the effect of new biologically active substances on the blood coagulation system is one of the important pharmacological investigation in modern medical chemistry. The use of such studies makes it possible to foresee the emergence of possible side effects of new medicines already at the early stages of drug discovery. Without any doubt, the effect on the blood coagulation system is desirable carried out in those cases when the receptor target with which the studied ligands are interacted is known and, accordingly, the spectrum of the revealed side effects is known. Special attention given to the search for new anti-inflammatory agents, in particular selective and non-selective COX-1 and COX-2 inhibitors, which can cause both thrombotic complications and an increase in the effect of anticoagulants, which can lead to internal bleeding.

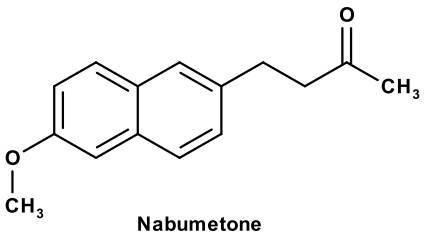


R = various substitutes
R_1 = lower alkyl

I

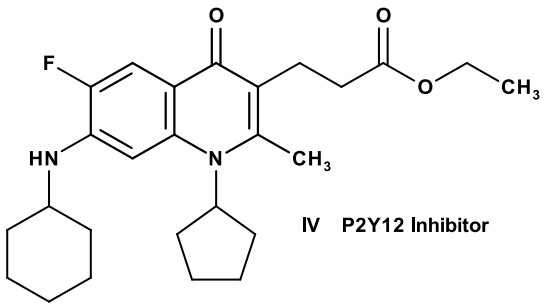


II



Nabumetone

III



IV P2Y12 Inhibitor

At the department of medical chemistry of the NUPh, carried out research of derivatives of 3-(2-methyl-4-oxo-1,4-dihydroquinolin-3-yl) propanoic acids (**I, II**) which can be effective NSAIDs and at the same time have a structural similarity to well-known platelet aggregation inhibitors **IV**. Performed in silico and in vitro studies allowed us to make some structure-activity relationships. In particular, the dependence of pharmacological activity such parameters as the molecular volume of substituents and logP was established.

SYNTHESIS AND INVESTIGATION OF PROPERTIES IN A RANGE OF 2-HYDROXY-4-OXO-7-METHYL-4H-PYRIDO [1,2 α] PYRIMIDINE-3-CARBOXYLIC ACID DERIVATIVES

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Introduction. Chemicals that are derivatives of pyrido [1,2-α] pyrimidine of major interest to the pharmaceutical and medical practice through a wide range of activities, including antimicrobial, antiviral and diuretic. The problem of identifying new classes of biologically active substances and create on their basis of highly efficient and safe medicines do not lose their relevance for quite a long time. Chemicals that have in their structure fused heterocyclic system pyrido [1,2-α] pyrimidine, recently attracted considerable attention chemists and pharmacologists synthetics through interesting pharmacological properties. Previously synthesized amides of 2-hydroxy-4-oxo-4H-pyrido [1,2-α] pyrimidine-3-carboxylic acid, in experiments on animals have shown anti-tuberculosis and diuretic properties. With this in mind, alkilamides of 2-hydroxy-4-oxo-7-methyl-4H-pyrido [1,2-a] pyrimidine-3-carboxylic acid are targets of great interest for further study.

Aim. The aim of this work was the synthesis of potential biologically active substances – alkilamides of 7 metylsubstituted 2-hydroxy-4-oxo-4H-pyrido [1,2-α] pyrimidine-3-carboxylic acid derivatives. The synthesized group of compounds to study for their biological types of activity.

Materials and methods. The melting point was determined by capillary Kofler on the block. 1H NMR spectra were recorded on a device Varian Mercury-VX-200 (200 MHz), Solvent - DMSO - d6, internal standard - tetramethylsilane (TMS). The chemical shifts are in the scale δ (ppm) correspond to calculated elemental analysis.

Results. According to the research using computer program PASS, the newly synthesized compounds are promising targets for further study of their biological activity. As it was shown by the data of the forecast, the mentioned above group of compounds have the potential antispasmodic, analgesic activity.

Conclusions. By the interaction of ethyl ester with 7-methylsubstituted of 2-hydroxy-4-oxo-4H-pyrido [1,2-α] pyrimidine-3-carboxylic acid derivatives with the corresponding alkylamine have synthesized a number of alkilamides of 7 methyl substituted of 2-hydroxy-4-oxo-4H -pirydo [1,2-α] pyrimidine-3-carboxylic acid derivatives with perspective types of biological activity. The structure of all the synthesized compounds has been confirmed by elemental analysis and 1 H NMR spectra.

BRANCH CHAIN AMINO ACIDS (BCAA) AS POTENTIAL PHYSIOLOGICALLY ACTIVE SUBSTANCES

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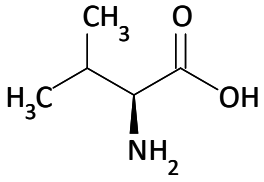
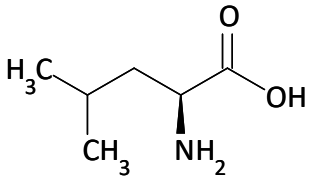
Introduction. In recent decades, most attention in the pharmaceutical industry of the drug development is directed on biologically active substances that are involved in the processes of human life. Amino acids, especially essential ones, are of great interest for medicine. Amino acids play important role for athletes as building material for muscles.

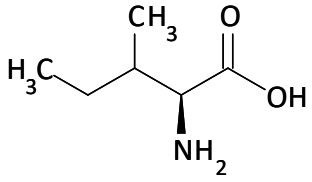
Materials and methods. BCAA (branch chain amino acids) – are popular among bodybuilders dietary supplement. BCAA – are three amino acids having a branched structure of the side chain. These substances are not synthesized in our bodies. They are essential. In this case, there are only three: valine + leucine + isoleucine with hydrophobic properties.



Valine



Leuicine



Isoleucine

Results and discussion. Valine is the source of energy for the muscles, as well as one of the important components of the synthesis of tissue. Isoleucine is required for hemoglobin synthesis, regulation of blood sugar, for leucine metabolism. By hydrophobic residues, an environment, that is necessary for binding oxygen from myoglobin, is created. Athletes, in the period of high muscle load, demand muscle oxygen, that is partly satisfied by oxygen released myoglobin.

Leucine is one of the main sources of energy. Its oxidation provides more ATP than glucose molecule. However, leucine and glucose oxidation differs in a way; the athlete gets just 2 powerful sources of ATP, restoring their strength much faster.

Additional reception BCAA increases the production of insulin and accelerates the transport of glucose and amino acids to the muscles.

It is clinically proven that these substances reinforce the immune system.

Conclusion. Modification of chemical structure of BCAA is productive direction for physiologically active substances research not only as food additives, but also as drugs.

SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF 3-ALKYLSUBSTITUTED 4-ARYLAMINO-2-METHYLQUINOLINES

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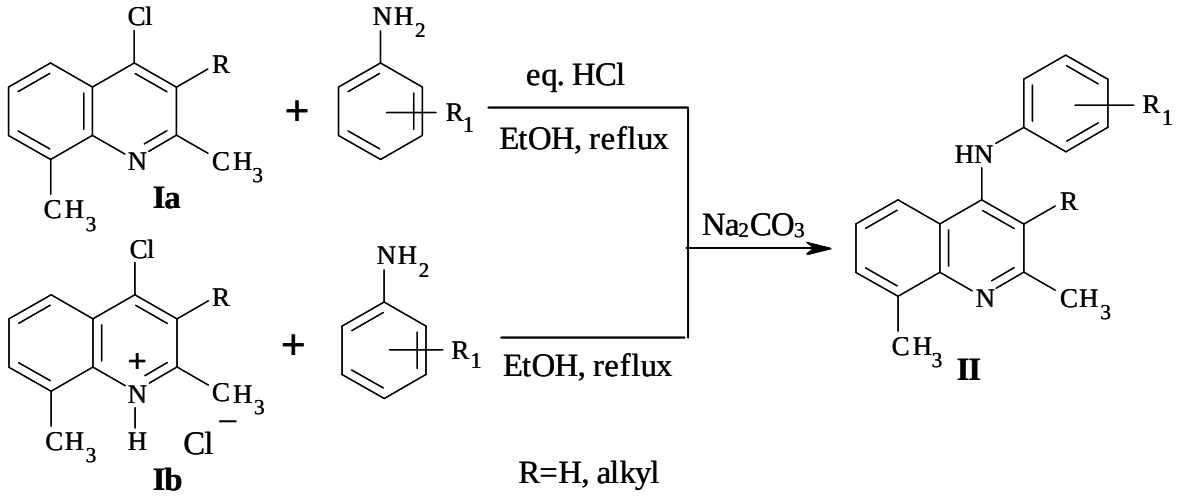
Introduction. The research of novel classes of antibacterial drugs actual more that ever due to the problem of antimicrobial resistance occurrence. This problem has rapidly escalated and became threatening.

Aim. Synthesis and study of the antimicrobial properties of novel 3-alkylsubstituted 4-arylamino-2-methylquinolines were the aim this research work.

Materials and methods. The target 3-alkyl-4-arylamino-2-methylquinolines **II** were synthesized by reaction of 3-alkyl-4-chloro-2-methylquinolin-4-ones **Ia** with substituted anilines in ethanol under the reflux in the presence of equimolar amounts of hydrochloric acid or starting with corresponding hydrochlorides **Ib** under the same conditions but without additional amounts of acid (Scheme).



The structure of the compounds synthesized was confirmed by ^{1}H-NMR spectroscopic method. The study of antimicrobial activity of the compounds **II** was carried out using the agar diffusion screening method known as “well method” against standard test-strains.

Results and discussion. The results of antimicrobial activity screening have shown that the most microbiologically active was less substituted 2,8-dimethyl-4-phenylaminoquinoline. This fact may be explained by higher water-solubility of this compound in comparison with 3-alkylsubstituted derivatives.

Conclusions. According to the SAR-analysis of the results obtained, further search for antimicrobial agents in the series of highly substituted 4-arylamino-3-alkyl-2-methylquinolines is unreasonable.

CHEMICAL DISCOVERIES BY APOTHECARIES OF THE WESTERN EUROPE IN THE XVIII – XIX CENTURIES

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Introduction. Many chemical discoveries of the XVII-XIX century were made in the drugstores, which functioned as the well-equipped chemical laboratories. Apothecaries were considered to be highly educated specialists, combining the work of a pharmacist and a chemist. On the basis of drugstores, scientific centers and even the Academy of Sciences were created (Italy, France).

Aim. To analyze the historical facts of the development of the chemistry in pharmacies, as the centers of scientific research in Western Europe.

Materials and methods. Literary sources and biographies of outstanding chemist-pharmacists of the XVIII-XIX century, who entered their names in the history of chemistry.

Results and discussion. Apothecaries-scientists discovered new elements and substances, perfected technologies and methods of chemical processing, invented more exact equipment for their researches. In this period incentives for the development of chemistry and pharmacy were appeared.

Martin Heinrich Klaproth, the discoverer of three chemical elements: Zirconium, Uranium (1789), Titanium (1803), emerged from Germany's pharmacists. He also explained the phenomenon of polymorphism for the first time.

The main Emil Erlenmeyer`s studies are devoted to the theory of structure. He synthesized isobutyric acid and α-aminoacids, guanidine, determined the structure of alcohols and carboxylic acids, studied the regrouping of enols to aldehydes and ketones independently of Eltekov, and determined the structural formula of naphthalene. He introduced a conical flask (Erlenmeyer flask).

Karl Friedrich Mohr worked in a volumetric analysis of drugs, applying burettes, pipettes in the analysis for the first time and created a scales, which have named after him. English scientist Robert Boyle synthesized acetone by distillation of potassium acetate, obtained phosphoric acid and phosphine.

The period of the chemistry development was promoted by the French pharmacists. Louis Nicolas Vauquelin discovered Chromium, Beryllium, Palladium, Osmium. He published one of the world's first manuals on chemical analysis - "Introduction to Analytical Chemistry" and created a school of chemists. Antoine Jérôme Balard discovered a new element "murid" (1826), which later was renamed in Bromine by Gay-Lussac.

The main scientific works of Pierre Jean Robiquet are devoted to the analysis of organic compounds, he discovered the first aminoacid asparagine (1806), pectin and malic acid, extracted camphor and quinic acid. The manager of the hospital drugstore, Joseph Louis Proust, investigated "honey sugar" and established its difference from "cane sugar". Also, his works about urea, enzymes, gluten are widely known. The military pharmacist Barnard Courtois discovered Iodine.

Jean Baptiste André Dumas is one of the authors of the theory of eaterine. He proposed a volumetric method for the quantitative determination of nitrogen (1830) in organic compounds (Dumas method), established the existence of the first homologous series in organic chemistry – a series of formic acid (1843).

The main studies of Georges-Simon Serullas are devoted to nitrogen-containing and organic halogen derivatives. He opened iodoform by the action of potassium on an alcohol solution of iodine, cyanamide (1827), cyanuric chloride (1827), iodide of nitrogen (1829), cyanuric acid, and (1824) methylene iodide, synthesized ethyl bromide (1827), the first organic bromine compound.

French chemist, pharmacist and technologist Antoine Bome was the author of a number of manuals on chemistry and pharmacy, including "Elements of theoretical and practical pharmacy" (1762) and "Experimental and theoretical chemistry" (1773), which details the chemistry of the late 18th century from the positions of the phlogiston theory

Pierre Eugène Marcellin Berthelot was a chemist and public figure, professor of chemistry at the Higher Pharmaceutical School in Paris (1859). He is an author of numerous works in organic chemistry, thermochemistry, agrochemistry, history of chemistry. He synthesized a huge number of organic compounds belonging to different classes, than he caused a final defeat to the ideas of "life force". He proved the possibility of synthesis of glycerin and fatty acids received (1853-1854) analogues of natural fats by their interaction. In addition, he found, that glycerin is a tritical alcohol. In 1851 he began working on the synthesis of organic compounds from simple substances, synthesized the simplest hydrocarbons - methane, ethylene, acetylene, benzene, and then based on them - more complex compounds. Of fundamental importance was the synthesis of ethyl alcohol by the hydration of ethylene in the presence of sulfuric acid (1854), before this ethyl alcohol was obtained only by fermentation of sugary.

Conclusions. In many bibliographic sources, the period of the XVII and the first half of the XIX century is called the "golden age of pharmacy". At that time, chemists opened new chemical compounds, while creating new drugs, and outstanding chemists, although they considered chemistry an independent science, combined their chemical research with pharmacy practice.

THE ANTIMICROBIAL ACTIVITY OF AMINO ACID DERIVATIVES

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Introduction. Taking into account the resistance of bacteria to antibiotics the WHO developed a global strategy on the problem of the growth inhibition of the antimicrobial resistance published in 2001. According to the WHO list of priority pathogens, *Pseudomonas aeruginosa* belongs to the 1st category of priority (a critical, high level of priority), and *Staphylococcus aureus* is in the second group (a high level of priority). Therefore, to create new antibiotics it is of interest to analyze the impact of derivatives of α-amino acids on some test strains for assessment of their antibacterial activity.

Aim. To determine the dependence of the antimicrobial activity on the nature of substituents the derivatives of alanine, serine, and threonine, as well as their N-hydroxymethyl, N,N-di(hydroxymethyl) and N,N-di(hydroxymethyl)-N-methyl derivatives were tested.

Materials and methods. The compounds studied were obtained from commercial sources or synthesized according to the synthetic methods previously developed. 1% aqueous solutions were tested in terms of the primary basis before modification.

Results and discussion. As the result of the preliminary microbiological studies it was found that the substituted amino acids showed the weak (*Escherichia coli*, *Proteus vulgaris*) or moderate (*Pseudomonas aeruginosa*) activity in relation to fungi and gram-negative microorganisms. Gram-positive bacteria are more sensitive to the action of the derivatives tested; moreover, the highest antimicrobial activity was shown by derivatives of threonine.

Conclusions. Based on the data obtained it follows that the chemically modified derivatives of α-amino acids mentioned above are promising for searching new compounds with the antimicrobial activity.

SYNTHESIS AND PHYSICS-CHEMICAL PROPERTIES OF SOME DERIVATIVES OF [1,3,4] OXADIAZOLES

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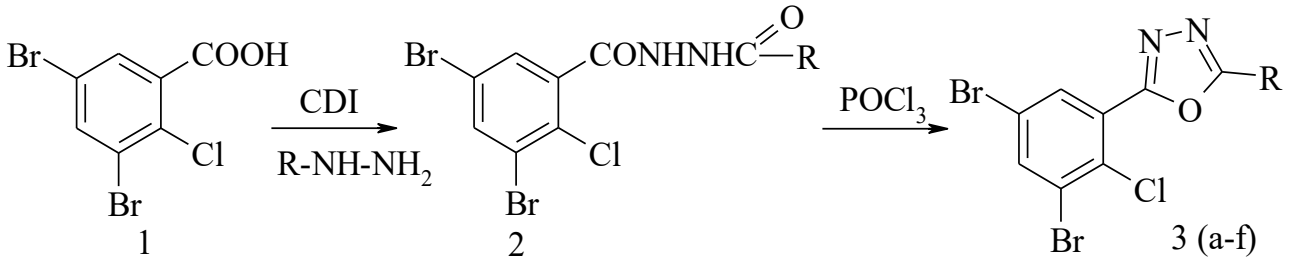
Introduction. According to the literature derivatives of 1,3,4-oxadiazoles exhibit, anticonvulsant and anti-inflammatory activity.

The aim of the study. Therefore, to study the pharmacological properties, we the synthesized hydrazides of 3,5-dibromo-2-chlorobenzoic acids and 1,3,4-oxadiazoles derivatives based on them.

Materials and methods. Synthesis of 2- (3,5-dibromo-2-chlorophenyl) -5-R-phenyl [1,3,4]oxadiazoles carried out by the scheme 1:

Scheme 1



a) R=Ph; b) R=Ph-4-CH_3; c) R=Ph-4-OCH_3;

d) R=Ph-4-C_2H_5; e) R=Ph-4-OC_2H_5; f) R= 

The synthesis of hydrazides of 2-chloro-3,5-dibromobenzoic acids derivatives (2) is carried out by reacting of 3,5-dibromo-2-chlorbenzoic acid (1) with hydrazines derivatives in the presence of carboxyl group activator carbonyldiimidazole.

The action of phosphorus oxychloride with heating in a 5 hours – hydrazide of 2-chloro-3,5-dibromobenzoic acids derivatives (2) cyclized in to 1,3,4-oxadiazoles (3).

The obtained results. The obtained 2- (3,5-dibromo-2-chlorophenyl) -5-R-phenyl [1,3,4]oxadiazoles are crystalline and amorphous substances, cream, white and brown color, insoluble in water and soluble in most organic solvents.

The structure of the synthesized compounds confirmed by elemental, IR- and NMR-spectral analysis, the individuality controlled by a thin layer chromatography.

Conclusions. The synthesized 2- (3,5-diabromo-2-chlorophenyl) -5-R-phenyl [1,3,4]oxadiazoles compounds may be promising in terms of finding bioactive substances with antimicrobial and anti-convulsive activity.

SCREENING EXAMINATION OF NANOCHROMIUM CITRATE EFFECT ON KIDNEY EXCRETORY FUNCTION

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Introduction. In different spheres of human activity the interest to nanotechnologies increases including nanobiology, nanomedicine and nanopharmacy. Chemical substances in nanometric range acquire new properties encouraging scientists to study their biological activity with the aim to make the scope of their use wider and safer. Chromium nanoparticles can be rather promising compounds to be used in medicine.

Aim. To study the effect of organic chromium compound obtained by Ukrainian scientists by means of electric-impulse aquananotechnology on the values of the kidney excretory function.

Materials and methods. The study was conducted on laboratory rats exposed to intra-gastric introduction of nanochromium citrate (NCC) during 14 days in increasing doses – 10-20-40 mkg/kg, that corresponds to 0,25%, 0,5%, 1% of DL_{50}. Renal function was examined under conditions of water diuresis.

Results and discussion. A long-term introduction of NCC in the doses of 10-20 mkg/kg against water load test increases diuresis by 21,3% and 12,2% respectively. Na^+ concentration in the urine and its secretion do not change significantly, K^+ concentration decreases in 1,8 and 2,8 times. Kaliuresis decreases in 1,5 and 2,5 times resulting in increased Na^+/K^+ coefficient in the urine. In the examined doses NCC does not considerably influence upon glomerular filtration rate (GFR) and creatinine concentration in the blood plasma. K^+ concentration increases reliably in the blood plasma against the ground of absent visible changes of Na^+ concentration. The concentration and excretion of protein in the urine becomes twice as big both in absolute values and standard ones concerning glomerular filtration rate (per 100 mcl of glomerular filtrate). Larger doses of NCC – 40 mgk/kg (1% from DL_{50}) affect diuresis. Increased diuresis under effect of less doses after introduction of larger doses decreases to the level of those control animals without considerable changes of Na^+- and K^+- uresis against the ground of hyperkalemia and increased renal protein loss. Glomerular filtration rate becomes 35% less, and creatinine concentration in the blood plasma increased in 1,5 times.

Conclusions. Nephrotoxicity NCC rises with increasing doses – diuresis, glomerular filtration rate reduce, retention azotemia and proteinuria increase against the ground of increased hyperkalemia.

SEARCH OF COMPOUNDS WITH ANTIMICROBIAL ACTIVITY INCLUDE DERIVATIVES OF [1,2,4]TRIAZOLO[4,3-*a*]PYRAZINE

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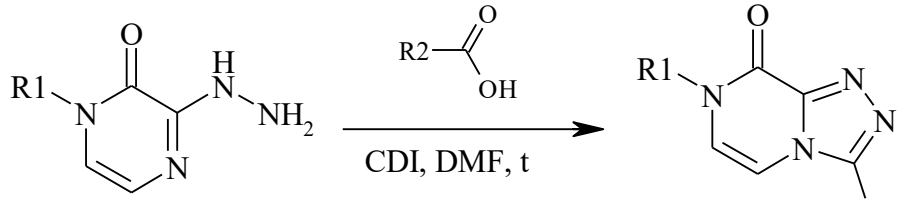
Introduction. Taking into account the wide spectrum of pharmacological activity of the [1,2,4]triazolo[4,3-*a*]pyrazine derivatives, it is very important to develop methods for the purposeful synthesis of systematic series of compounds based on this structure and to solve the problems of rational design of biologically active substances using computer prediction methods.

The **aim** is a targeted synthesis of biologically active substances in a series of derivatives of [1,2,4]triazolo[4,3-*a*]pyrazine and the study of the properties of the synthesized compounds with a view to finding an effective pharmacological agents.

Materials and methods. Methods of organic synthesis; physical and physicochemical methods of analysis of organic compounds (^{1}H and ^{13}C NMR spectroscopy, elemental analysis), the study of biological properties using standard techniques; analysis of the results obtained and their generalization, statistical methods for processing experimental data.

Results and discussion. The scheme of interaction of N^{1}-aryl/benzyl-3-hydrazinopyrazine-2(1*H*)-ones **1***{1-4}* with aromatic and heterocyclic carboxylic acids. To activate the carboxyl group, we proposed using of *N*,*N*′-carbonyldiimidazole (CDI) in anhydrous DMF with a 1:1 reagent ratio.



1*{1-4}* **2***{1-10}*

R1 = Ph; 4-FPh; 4-diFPh; 4-ClPhCH$_2$;
R2 = 3-ClPh; 3,4-diMePh; 3-Pyr; 3,4-diOEtPhCH$_2$

Microbiological screening of compounds of the [1,2,4]triazolo[4,3-*a*]pyrazine-8(7*H*)-one series allowed the identify of derivatives with antimicrobial and antifungal activity.

Conclusions. The proposed approach to the synthesis of [1,2,4]triazolo[4,3-*a*]-pyrazine-8(7*H*)-one derivatives allows obtaining arrays of compounds with antimicrobial activity for the needs of medical chemistry.

FSP3: SIMPLE AND VALUABLE

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Introduction. The discovery and development process of innovative drug requires a shocking amount of money and time due in part to the high attrition rate of drug candidates in development. The most prominent cause of the failures was associated with poor pharmacokinetic and ADME (absorption, distribution, metabolism and elimination) properties. Thus, these features should be measured at the early stages of drug design using structural physicochemical parameters of molecules including computational calculations.

Most of modern discovery hits extremely suffer from a lack of three-dimensional shape. Oppositely, natural products have "advanced" 3D-shapes and demonstrate exquisite action on very specific biotargets. Molecule nonplanarity could be characterized by "fraction of sp^3-hybridized carbons (Fsp3)", i.e. number of sp^3-hybridized/total carbon counts.

Aim. The main purpose of this research work is to attract attention to such structural parameter as Fsp3 *via* analysis of available data about nature and importance for the early stages of drug discovery.

Materials and methods. As an example, the structural calculations of Fsp3 for the marketed nonsteroidal anti-inflammatory drugs (NSAIDs) known as acetic and propionic acid derivatives and comparative analysis of data obtained were carried out. All NSAIDs chosen for analysis were divided into 2 groups: acetic acid derivatives (diclofenac, indometacin, ketorolac, sulindac, tolmetin, etodolac) and propionic acid derivatives (ibuprofen, naproxen, ketoprofen, fenoprofen, flurbiprofen, tiaprofenic acid). All computational calculations (Fsp3) of molecules selected were performed using a *Chemicalize* free online service by *ChemAxon*.

Results and discussion. Average values of Fsp3 for acetic and propionic acid NSAIDs were calculated: Fsp3=0.208±0.056 for acetic acid derivatives and Fsp3=0.202±0.054 for propionic acid derivatives. As we can see, calculated means of Fsp3 for these groups are the same but very low according to the modern opinions of medicinal chemistry. As a result, it is possible to suppose that increasing of Fsp3 of candidates during further search of novel COX-inhibitors in the series of acetic and propionic acid derivatives could make many of the ADME properties better.

Conclusions. Fsp3 is easy computable and very useful structural parameter of molecule. Researchers should use this characteristic broader at the early stages of drug design to improve ADME profile of possible candidates.

SYNTHESIS OF NOVEL ISOINDOLINE-1,3-DIONE N-DERIVATIVES AS PROMISING ANTICANCER AGENTS

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Introduction. Cyclic imides derivatives are widely used in modern medical practice as effective drugs. These compounds exhibit the versatile biological activities namely: anticonvulsant, anxiolytic, antidepressant, antineoplastic and more. It is important, that mentioned above compounds are promising objects for chemical modification. Thus, the new functional groups that modify the expression of pharmacological activity can be introduced in structure of cyclic imides.

Aim. Our research is devoted to the synthesis and anticancer activity evaluation of novel cyclic imides, that contain isoindoline-1,3-dione and 1,2,4-triazine moieties.

Materials and methods. The features of the reaction between initial 6-R-3-(2-aminophenyl)-1,2,4-triazin-5-ones (I) and phthalic anhydride in a glacial acetic acid were studied. The structure and purity of synthesized compounds were confirmed by the complex of physicochemical methods (^{1}H, ^{13}C NMR, IR, LC-MS, MS, X-ray study). Anticancer activity according to NCI DTP protocol were study for the four of synthesized compounds. Mentioned above activity was studied in vitro on 60 human cancer cell lines at 10.00 μM concentration.

Results and discussion. It was shown, that mentioned reaction led to the formation of 2-(2-(6-R-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)phenyl)isoindoline-1,3-diones with high yields. As we consider, reactions proceeded as multistep process wherein products of N-acylation played role of the intermediate. The direction of subsequent cyclisation caused by proximity of formed carboxylic group and amide fragment. The results of the biological activity screening showed that synthesized compounds exhibited moderate anticancer activity. Thus synthesized compounds inhibited the growth of kidney cancer (on 22%) and non-small lung cancer.

Conclusions. Interaction of 6-R-3-(2-aminophenyl)-1,2,4-triazin-5-ones with phthalic anhydride proceed as "classical" acylation followed by cyclization. The products of this reaction are the new derivatives, that contain isoindoline-1,3-dione and 1,2,4-triazine moieties. The structures of the synthesized compounds were confirmed by complex of instrumental methods. The obtained 2-(2-(6-R-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)phenyl)isoindoline-1,3-diones (II) reveal antitumor activity against kidney cancer, breast cancer, and non-small cell lung cancer.

MECHANISM OF QUINOLONE ACTION AND RESISTANCE. NEW 3-ALKYLQUINOLONYL CARBOXYLIC ACIDS AS POTENTIAL ANTIMICROBIAL AGENTS

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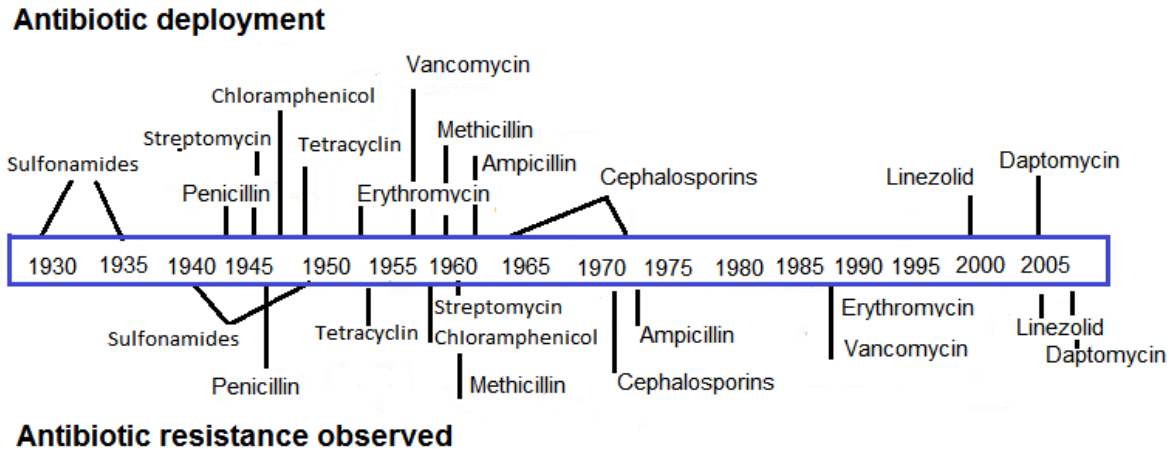
The discovery of antibiotics was one of the most significant events in the history of medicine which had led to significantly increasing of the humans' life expectancy. However, from the first application of penicillin in practical medicine, humanity was faced with the serious problem as emerging antimicrobial resistance (AMR). In consequence, after the first time employment of any new antibiotics were identified cases of clinically significant resistance to this drugs, which was always developed by microorganisms in a relatively short period of time.



Quinolones are one of the most commonly prescribed classes of antibacterials in the world and are used to treat a variety of bacterial infections in humans. Because of the wide use (and overuse) of these drugs, the number of quinolone-resistant bacterial strains has been growing steadily since the 1990s. The general mechanism of action employed by the fluoroquinolone class is inhibition of type II topoisomerases DNA gyrase or topoisomerase IV (topoIV).Taking into account the latest data of the key role of magnesium in the cation complex forming quinolone-topoisomerase-DNA we carried out molecular modeling (force field MMFF94) for 3-(2-methyl-4-oxo-1,4-dihydroquinoline-3-yl)propanoic acid with cation $Mg2^{+}$. The possibility of forming a strong complex between them has been showed.

The results of the antimicrobial activity screening have shown that two compounds - 1,3-diethoxy-2-[(2-methyl-4-oxo-1,4-dihydroquinolin-3-yl)methyl]-1,3-dioxopropan-2-ylcarbamic acid and 3-(2-methyl-4-oxo-1,4-dihydroquinolin-3-yl) propanoic acid have moderate broad-spectrum activity.

SYNTHESIS OF THE 6-(1*H*-BENZIMIDAZOL-2-YL)-3,5-DIMETHYL-2-OXO(THIOXO)-2,3-DIHYDROTHIENO[2,3-*d*]PYRIMIDIN-4(1*H*)-ONES WITH POTENT BIOLOGICAL ACTIVITY

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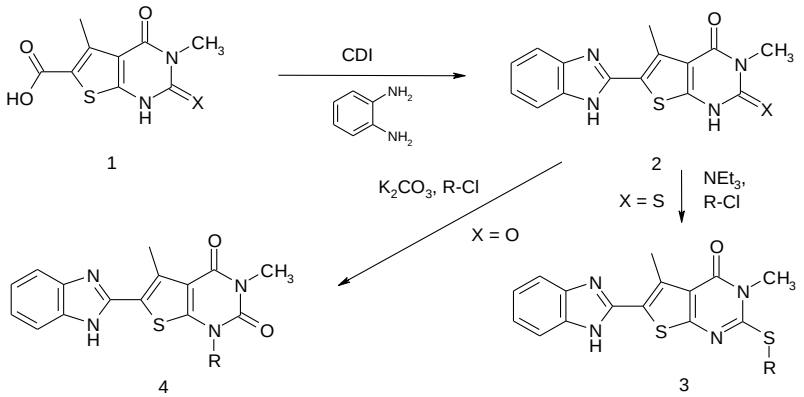
Introduction. The previously reported data about the pharmacological activity of 6-(1*H*-benzimidazol-2-yl)thieno[2,3-*d*]pyrimidin-4(1*H*)-ones confirmed their antimicrobial properties; the experimental data about their anti-inflammatory screening has been also reported.

Aim. Therefore preparation of the analogues containing benzimidazole system at position 6 of thieno[2,3-*d*]pyrimidin-4(1*H*)-one combined with the presence of oxo- or thio- groups at position 2 could be a promising way for preparation of the novel biologically active compounds.

Materials and methods. The methods of organic synthesis, instrumental methods of organic compounds analysis.

Results and discussion. We have developed the procedure for preparation of the novel 6-(1*H*-benzimidazol-2-yl)-3,5-dimethyl-2-oxo(thioxo)-2,3-dihydrothieno[2,3-*d*]pyrimidin-4(1*H*)-ones using the 1,1'-carbonyldiimidazole (CDI) promoted reaction of 3,5-dimethyl-4-oxo-2-(oxo)thioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidine-6-carboxylic acids with *o*-phenylenediamine.



To enlarge the number of candidates for the screening of biological activity we alkylated the compounds 2. The structure of the obtained compounds was confirmed by mass-spectral and NMR data. The regioselectivity of alkylation for compounds 2 (X=O) as well as the structure of 4 was assigned by the HMBC correlation method.

Conclusions. An effective procedure for synthesis of the potently biologically active 6-(1*H*-benzimidazol-2-yl)-3,5-dimethyl-2-oxo(thioxo)-2,3-dihydrothieno[2,3-*d*]pyrimidin-4(1*H*)-ones has been developed; the regioselectivity of their alkylation was confirmed by HMBC method.

THE SEARCH FOR NOVEL PSYCHO- AND NEUROTROPICALLY ACTIVE COMPOUNDS IN THE SERIES OF AMINOMETHYLATED 2-METHYL-1*H*-QUINOLIN-4-ONES

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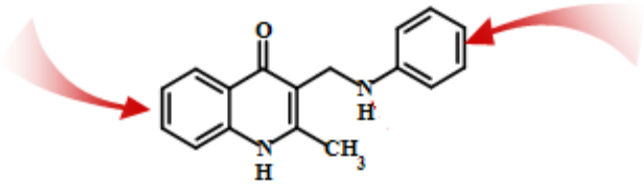
Introduction. Notwithstanding the abundance of modern medicines, the goal to develop an "ideal drug" for mental disorders treatment has not been reached yet and is still of great current interest.

Aim. The mail purpose of present study was implementation of the *in vivo* screening profiling of psycho- and neurotropic properties of novel 3-(N-R,R′-aminomethyl)-2-methyl-1*H*-quinolin-4-ones.

Materials and methods. The "points of diversity" of the "mother" molecule – 2-methyl-3-(phenylaminomethyl)-1*H*-quinolin-4-one, a promising antidepressant with polymodal effect on CNS, were defined:



The target 3-(N-R,R′-aminomethyl)-2-methyl-1*H*-quinolin-4-ones was synthesized from 2-methyl-1H-quinolin-4-ones *via* aminomethylation and further interaction of the Mannich bases obtained with the corresponding amines. The structure of the compounds obtained was confirmed by ^{1}H NMR spectroscopic method. The open field test, elevated plus maze, rotarod test, tail suspension test, passive avoidance test and acute normobaric hypoxia with hypercapnia were used for *in vivo* profiling of psycho- and neurotropic properties of this series of derivatives.

Results and discussion. It became absolutely clear that derivatives with the phenylaminomethyl fragment have pronounced mnemotropic effects against scopolamine-induced amnesia. 3-[[(4-Methoxyphenyl)amino]methyl]-2-methyl-1*H*-quinolin-4-one exhibiting a specific sedative effect and a considerable anti-amnesic activity deserves a deeper and more detailed pharmacological study. Taking into account the modest scope of experiment the great conclusions concerning SAR regularities can not be made.

Conclusions. It may be concluded that 3-(N-R,R′-aminomethyl)-2-methyl-1*H*-quinolin-4-ones are, undoubtedly, interesting objects for the further research as psychoactive substances.

Section 2.

STUDY OF MEDICINAL PLANTS AND CREATION OF HERBAL MEDICINAL PRODUCTS

CARBOHYDRATE COMPOSITION OF *PHOENIX DACTYLIFERA* L. FRUITS FROM IRAQ FLORA

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Introduction. In the Muslim countries the dates fruits have been popular since ancient times. Dates have been famous for their healing properties. It was believed that the fruits of date palms give strength, endurance, increase life expectancy. About 80 percent of the world trade in dates is in Iraq. In Iraq, among the 420 varieties of dates, there are varieties that are not found in other countries - Halavi, Khadravi and Saiger. Given the availability of raw materials, as well as the insufficient level of study of the chemical composition of dates, collected in Iraq, a comparative phytochemical study of their chemical composition is promising for expanding the information on BAC of fruits of *Phoenix dactylifera* L.

Aim. The aim of this work is the comparative study of carbohydrate composition and polysaccharides quantitative content in varieties of dates - Halavi, Khadravi and Saiger.

Materials and methods. The object of the study was the fruits of dates. Extraction of polysaccharides from the raw material was carried out with water. For this, 100 g of raw material was poured into two liters of hot water, the extraction was carried out for 30 minutes. Extraction was carried out thrice. The resulting extract was combined and evaporated, water-soluble polysaccharides were precipitated with 96% ethanol. The polysaccharides were separated by centrifugation, dried and weighed. The qualitative composition of polysaccharides was determined by chromatographic method (paper chromatography) after acid hydrolysis by 10% solution of sulfate acid with heating. Chromatography was carried out in solvent system butanol-acetic acid-water (4: 1: 2). As reference samples were used L-arabinose, D-xylose, D-glucose, D-fructose. The resulting chromatograms were dried, processing with aniline phthalate and dried. The quantitative content of polysaccharides was determined gravimetrically. The resulting polysaccharides are crystalline, shiny, yellow-brown substances.

Results and discussion. As a result of the study, pentoses (L-arabinose, D-xylose) were stained red, hexoses (D-glucose, D-fructose) - brown.

Conclusions. It has been established that all investigated varieties are contain glucose and fructose, arabinose is contained in the "Khadravi" variety, xylose is found in the "Saiger" variety. The quantitative content of water-soluble polysaccharide complex (%) was: variety "Halavi" 40.7%, variety "Khadravi" - 39.9%, variety "Saiger" - 41.04%.

STUDY THE CONTENT OF ASCORBIC ACID IN HERB OF *URTICA URENS* L.

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Introduction. For a long time we are using plants for the treatment and prevention of various diseases. And nowadays phytotherapy is an actual direction of correction of various diseases. Recently, the popularity of herbal preparations has increased, which is due to the fact that due to a complex of biologically active substances (BAS), resistance to them is less often formed. Particular attention in the choice of objects of research should be given to plants having adequate sources of raw materials. One of such plants is nettle stinging (Urtica urens L), which grows on the territory of Ukraine. This plant has found application in folk medicine and homeopathy for the treatment of nasal, hemorrhoidal and uterine bleeding. In order to expand the information on BASs of species of the genus *Urtica* L., a phytochemical study of the herb *Urtica urens* L. is of scientific interest.

The **aim of our study** was to investigate the content of ascorbic acid in *Urtica urens* L. herb collected in different region of Ukraine.

Materials and methods. The object of the study was the dried herb of *Urtica urens* L. collected in 2016 year. To identify the ascorbic acid was used the chromatographic method. Extraction of ascorbic acid from the raw material was carried out with distilled water. For this, the raw material was placed in a flat bottom flask, poured with water at room temperature in a feed-extractant ratio of 1:10, mixed and insisted for 20 minutes. The filtrate was applied to a capillary plate Silufol chromatographic grade, dried and chromatographed in the solvent system ethyl acetate-glacial acetic acid (8: 2). The resulting chromatogram was dried in a fume hood and treated with 0.04% aqueous solution of 2,6-dichlorphenolindophenolate sodium. Chromatography was performed using a standard sample of ascorbic acid. The quantitative content of ascorbic acid was determined by the titrimetric method. 20 g of raw material were ground, placed in a flask, water purified in a feedstock-extractant ratio of 1:15 was added, insisted for 20 minutes. After the contents are filtered. 1 ml of the filtrate was placed in a conical flask, 1 ml of a 2% solution of hydrochloric acid and 13 ml of purified water was added. Titrant is a solution of 2,6-dichlorphenolindophenolate sodium (0.001 mol / l). The quantitative association of ascorbic acid was determined by the formula:

$$x = \frac{V * 0{,}000088 * 300 * 100 * 100}{\mathrm{m} * (100 - \mathrm{W})}$$

are: V - the volume of a solution of sodium 2,6-dichlorphenolindophenolate (0.001 mol / l), used for titration, ml;

m - the weight of the sample, g;

W - loss in mass when drying raw materials, %;

1 ml of sodium solution of 2,6-dichlorophenolindophenolate (0.001 mol / l) corresponds to 0.000088 g of ascorbic acid.

Results and discussion. After processing the chromatogram with a chromogenic reagent, white spots were found on a blue background, which in color and Rf values coincided with the standard sample. The results of the quantitative content of ascorbic acid are given in Table 1. The statistical processing of the data was carried out using the MS Excel program using the basic statistical indicators.

Table 1

The quantitative content of ascorbic acid in herb of *Urtica urens* L.

m	n	X_i	X_{cp}	S^2	S_{cp}	P	t(P, n)	Interval	ε, %
1	2	3	4	5	6	7	8	9	10
Raw materials collected in the Kharkov region									
5	4	0,1012 0,1001 0,1011 0,1001 0,1000	0,10	0,000510031	0,0125	0,95	2,78	0,10±0,0404	1,03
Raw materials collected in the Kiev region									
5	4	0,0800 0,0840 0,0910 0,0790 0,0810	0,08	0,000023500	0,0115	0,95	2,78	0,083±0,006	1,25
Raw materials collected in Ivano-Frankivsk region									
5	4	0,1201 0,1204 0,1193 0,1202 0,1199	0,12	0,000000177	0,0002	0,95	2,78	0,12±0,0005	1,02

Conclusions. Based on the results of the studies, ascorbic acid was identified in all samples. The quantitative content of ascorbic acid in raw materials harvested in the Kharkiv region was 0.10%, Kiev region - 0.083%, Ivano-Frankivsk region - 0.12%.

CHROMATOGRAPHIC RESEARCH OF VERONICA INCANA L. HERB

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Introduction. The studies of biologically active substances (BAS) of species of the genus Veronica L. have been carried on the Department of Pharmacognosy, that there are over 30 species in the Ukraine flora. *Veronica incana* L. is in scientific interest, that it has sufficient base of herbal drug and can be a source of BAS. It is a perennial plant, to 60 cm in height, with white-gray woolly trichomes. The leaves are opposite, ovate or oblong-oval with pointed tip, bright blue flowers, that gathered in dense raceme. It is growing on rocky limestone slopes in deciduous forests. It is grown as an ornamental plant. In folk medicine infusions of leaves are using as anti-inflammatory, antitoxic, antispasmodic and astringent remedy.

Aim. The aim of our research to study of main groups of BAS from *Veronica incana* L. herb by used of chromatographic method.

Materials and methods. The object of the study was air-dried herb of *Veronica incana* L. (*Plantaginaceae*), that had been collected in the flowering stage (July) in summer 2016. The study was conducted by thin layer chromatography (TLC) and paper chromatography. Extract had been obtained by 70 % ethanol, used for chromatography plates “Sorbfil”, “Silufol” and chromatographic paper “Filtrac 12”, the solvent system: ethyl acetate – formic acid – water (10 : 2 : 3) and 15 % acetic acid. The observations were carried out, both in daylight and in UV -light at 350 – 360 nm. Substances have been identified by characteristics of fluorescence in UV-light after processing of chromogenic reagents (ammonia vapors, diazotized sulfanilic acid, 10% alcohol solution of sodium hydroxide), spots color and the Rf value.

Results and discussion. Studies have been revealed the presence of such groups of BAS: flavonoids, saponins, tannins, iridoids and coumarins. In the result of the chromatographic study of the *Veronica incana* L. herb extract 10 compounds had been found. According to the results a value of Rf and features coloration of spots before and after reaction with chromogenic reagents in daylight and fluorescence in UV-light 6 compounds have been belonged to flavonoids, 4 compounds – to hydrocynnamic acids. After acid hydrolysis aglycones apigenin, luteolin and quercetin chromatographically have been determined.

Conclusions. Our results shown, that further in-depth study of *V. incana* L. as a source of BAS can be considered promising for the pharmacy.

DEVELOPMENT AND EVALUATION OF ANTICEPTICS FROM MEDICINAL PLANTS

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Introduction. Antiseptics and disinfectants are an essential part of infection control practices and aid in the prevention of many infectious diseases. A wide variety of active chemical agents are found in these products. Most of these chemicals or biocides are lipid soluble. For this reason antiseptics can pass from skin into blood as a result of long time usage and consequently even few amounts of it may disturb or affect hormonal status of organism. And usage of these broad spectrum xenobiotic antiseptic solutions especially by children, may alter hormonal status and effect to the growth and improvement of children negatively. These shortcomings of modern antiseptics generate the need to develop more environment friendly antiseptics.

Aim. To choose among local medicinal plants with higher antiseptic properties and with toxicological effect to organism, and to develop method of making antiseptic solutions from them.

Materials and methods. Dried "Herba Artemisia Absinthi" and "Prosopis Farcta" used as raw material which was collected near to Ashgabat city. It has been grinded separately to the of 50-200 μm and dissolved in distilled water at the concentration of 10.0 gr/20.0 ml. After 3 days extract of each plant was collected and evaluated its features. Extract of "Herba Artemisia Absinthi" has a pleasant smell and bluish-yellow color and extract of "Prosopis Farcta" has also good odor with greenish-brown color. If 1-2 drops of 96% ethanol added to latter solution, color changed to dark green. Short term high dose and long term effects of extracts studied on rats, rabbits and mice. Antiseptic property was studied on artificial wounds of rabbits and rats. Wound was washed with antiseptic solutions that we made until healing of wound completely.

Results and discussion. In this study method of preparing aqueous antiseptic solutions from "Herba Artemisia Absinthi" and "Prosopis Farcta" was developed. Experiment conducted on animals showed that there was no toxicological effects of antiseptic solutions LD_{50} value was very high by using different rout of administration. It was determined that these antiseptic solutions showed great antibacterial property by keeping wound clean until complete healing with primary intention of wound. Also it accelerates healing of wound. It is obviously known that water extracts of plants will not pass from skin and it will have no side effect. Pleasant smell of these solutions is also will be positive side of antiseptic solutions which will be developed from these plants.

Conclusion. 1. Water extracts of "Herba Artemisia Absinthi" and "Prosopis Farcta" has great antiseptic properties with no toxicological effect. 2. New method of preparing water extracts of medicinal plants was developed.

SULFUR IMPORTANCE IN THE MANUFACTURE OF ENVIRONMENTALLY PURE PRODUCT FROM MEDICINAL PLANTS

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Introduction. As many researchers note in their scientific papers, in obtaining an environmentally pure product with a low amount of nitrates, a great positive effect is exerted by sulfur. However, all irrigated lands of the Republic of Uzbekistan need sulfur, which is due to a change in the composition of the range of fertilizers produced and the reduction of mineral fertilizers containing sulfur. Also, the dynamics of the amount of sulfur and its effect on vegetation in the soil of irrigated oases has been very little studied (Taddesi, 1988).

Aim. Our research is aimed at obtaining an environmentally pure product from prickly artichoke by using sulfur-containing fertilizers.

Materials and methods. In order to achieve the stated goal, experiments were carried out at the experimental site of the Pharmaceutical Institute, during which the change in the amount of sulfur in the tissues of the artichoke plant was studied. The effect of protein nitrogen as well as nitrogen and nitrate nitrogen was studied outside the protein composition in plant leaves.

Results and discussion. As the results of studies have shown, the amount of sulfur decreases sharply in the budding and flowering phase of the plant. The greatest amount of sulfur is observed when the soil is fertilized at 50-60 kg / ha (i.e., with the ratio of nitrogen and sulfur at 1: 0.25-0.30). It should also be noted that when the plant ripens, the quantities of quantitative indicators are somewhat reduced, which is explained by the re-utilization of sulfur from the leaves into the fruits of the plant. These data indicate a deficit, a lack of sulfur in the tissues of the observed plants, which leads to the accumulation of a large number of nitrates in plant tissues. This, in turn, causes a number of violations in obtaining an ecological clean product.

As the results of the analysis show, in connection with an increase in the sulfur rate, the total amount of nitrogen in the leaves of the plant increases. In leaves, the amount of protein nitrogen increases, and the amount outside protein nitrogen decreases significantly, while its quantity decreases in the leaves of the plant.

Conclusions. So, when the ratio of nitrogen to sulfur (N:C) 1:0.25, i.e. at optimum variants (when C 50 kg / ha), the amount of nitrate nitrogen of the leaves of the prickly artichoke in the soil is reduced by 2 times, which is precisely what makes it possible to obtain an environmentally pure product.

THE WAY OF APPLYING NITROGEN FERTILIZERS IN THE MAINTENANCE CYNARA SCOLYMUS CONTRIBUTING TO THE REDUCTION OF ENVIRONMENTAL POLLUTION

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Introduction. It Should be noted that the development of methods of efficient use of nitrogen fertilizers for the plants, including the prickly artichoke has not only scientific, but also practical importance, as it provides in plants of globe artichokes harvest of high quality as well as reducing environmental pollution.

Transformation of nitrogen fertilizers on irrigated typical gray soils, and using plants depending on the mode of nitrogen nutrition has not been studied.

Aim. In this regard, we have aimed to develop methods of application of nitrogen fertilizers contribute to the reduction of environmental pollution and ecologically clean raw materials from the globe artichokes.

Materials and methods: In this regard, we in 2011-2016 was conducted both vegetation and field experiments on a typical grey desert soils.

Samarkand and Tashkent regions of Uzbekistan. The area of each plot of 480 m2. The arrangement of plants 60x50x1 with 36680 density of bushes per hectare. Repeated the vegetation experiments, 10 -, and field-4x. Gasket vessels conducted in the autumn of soil taken from a field experiment (0-50 cm horizon), taking into account its genetic horizons.

Soil moisture in the vessels was maintained at 75% of capillary capacity.

Results and discussion. Based On the results of our research on the balance and transformation of nitrogen fertilizers in the system soil-plant, it can be argued that on typical gray soils with high organic matter content and wide C:N ratio in the initial period of plant development more demanding of nitrogen than on light gray soils.

Studies have shown that, with the onset of seed maturation provision of plant nitrogen grown in the Samarkand region is higher than on typical gray soils of Tashkent region, due to the release of previously absorbed nitrogen to soil microorganisms.

Research results found that the content of nitrogen compounds fertilizers in plant tissues varies with soil differences.

From the beginning of vegetation budding to the mass amount of

immobilization of nitrogen from fertilizers on typical gray soils (or Samarkand region, the transition of inorganic nitrogen into organic form in the body of microorganisms) is more intense than the typical gray soils of Tashkent region.

Annual rate g/vessel				2-3 true leaves			Budding		
N	P	K	Manure	Gross	Organic	Inorganic	Gross	Organic	Inorganic
Tashkent region									
6	5	2	-	1868	976	892	1376	1298	78
6	5	2	400	2014	972	1032	1736	1390	346
Samarkand region									
6	5	2	-	2432	1278	1154	1784	1572	212
6	5	2	400	2484	1396	1088	1892	1454	438

With manure still more reduced content of inorganic nitrogen fertilizers not used by plants nitrogen fertilizers (the end of its growing season) on typical gray soils of Tashkent region, particularly the spreading of manure more than on typical gray soils of Samarkand region than in the soils of the Tashkent region, which is associated with different contents in these soils the weight of organic residues, and the ratio of C:N.

In connection with the immobilization of the nitrogen contents of plant-available inorganic compounds in its early phases of development and budding of the plants is reduced, especially in the conditions of Tashkent region.

This makes it necessary to study the effectiveness of nitrogen fertilizer taking into account the biological characteristics of nitrogen transformation and soil conditions.

Conclusions. the Result of our research revealed that Cynara scolymus L. grown in Tashkent region with the introduction of a complete fertilizer especially manure, contributes to greater formation of seeds and the formation of greater biomass. The amount of biomass more on typical gray soils of Samarkand region than on typical gray soils of Tashkent region.

HYDROXYCINNAMIC ACIDS OF SOME SPECIES OF GENUS THYMUS

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Introduction. Hydroxycinnamic acids are one of the most widespread classes of natural phenolic compounds contained in medicinal plant and herbal drugs. Among them, in plants of the genus Thymus, caffeic and rosemarinic acids are most often spread. Hydroxycinnamic acids show high antioxidant activity, have also anti-inflammatory, antiviral, immunostimulating effect.

Goal. To study the qualitative and quantitative composition of hydroxycinnamic acids of Thymus serpyllum, Th. crenulatus, Th. marshallianus, Th. pulegioides, Th. dimorphus, family Lamiaceae.

Materials and methods. The qualitative composition of hydroxyrcinnamic acids was analyzed using chromatography on paper and in thin layers of the sorbent. For this purpose, chromatographic paper Filtrak № 1 and 5, chromatographic plates "Silufol" and "Sorbfil" were used. The analysis was carried out in a solvent system: chloroform-methanol-water-24: 14: 3; butanol-acetic acid-water-4: 1: 2; 2 and 15% acetic acid. After chromatography, the chromatograms were analyzed in UV light before and after treatment with specific reagents (ammonia vapor, sodium hydroxide solution). The composition and acid content of hydroxyrcinnamic acids in the Thymus sample was determined by HPLC on a Shimadzu LC 20 Prominence chromatograph and spectrophometrically on an Evolution 60S.

Results. With the help of various types of chromatography, the presence of caffeic and rosmarinic acids in the investigated species of Thymus has been determined. The HPLC method was used to determine the content of caffeic and rosmarinic acids in the medicinal plant and herbal drugs. It was found that the content of rosmarinic acid ranges from 2343.40 mg / kg to 14351.74 mg / kg, caffeic acid from 74.41 mg / kg to 93.86 mg / kg. A procedure for the spectrophotometric determination of the total hydroxycinnamric acid acids with the reference into rosmarinic acid in Thymus spesies plants has been developed. The amount of hydroxycinnamic acids varies from 3.27% to 19.28%.

Conclusions. The results of the analysis of the content of hydroxycinnamic acids in Thymus species indicate the prospect of creating preparations with antiviral activity based on different Thymus species herbal drugs.

STUDY OF THE CARBOHYDRATES OF SAFFLOWER

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Introduction. Safflower (the safflower, American saffron, wild saffron, sultanica, dyeing Thistle, krokos (lat. Carthamus tinctorius L.) is an annual plant of the family Asteraceae. On our country there are created several varieties of this plant: solar, steppe, agile, affectionate.

Aim. The aim of this work is the study of free and compound carbohydrates in a new medicinal herbal materials.

Materials and methods. Chromatographic separation was performed using gas chromatography-mass spectrometry system Agilent 6890N / 5973inert (Agilent technologies, USA). Column capillary HP-5ms (30m × 0,25 mm × 0,25 mkm, Agilent technologies, USA). Evaporator temperature is 250 ℃, interface temperature 280 ℃ . Separation was carried out in programming mode temperature - the initial temperature of 160 ℃ was heated for 8 min., gradient from 5 ℃ / min to 240 ℃. The final temperature was kept for 6 min. Sample volume of 1 μl was injected in the split mode flow 1:50. Detection was performed in SCAN mode in the range (38-400 m / z). The flow rate of carrier gas through the column at 1.2 ml / min . Identification was performed by retention time of standards of monosaccharide and using the library of mass spectra NIST 02.

Results and discussion. For the extraction of carbohydrates were used 80% ethyl alcohol, then was got derivatives of monosaccharides in the extracts of flowers and roots of safflower.

At the same time preparing the sample without hydrolysis of inulin (without adding enzyme), which determined the content of free sugars. During previous researches it was established that the raw material also contains a disaccharide sucrose, which upon hydrolysis also liberates fructose.

The empirical conversion factor for fructose relative to inulin and sucrose (factor of conversion of inulin into fructose and sucrose into fructose) was determined by sequential processing of samples, various amounts of enzyme using ramnose as internal standard and determine the amount allocated to fructose.

Conclusions. For the first time investigated the carbohydrate composition of safflower grown in Ukraine. The studies identified carbohydrates the flowers and root of Carthamus tinctorius. For the first time in the flowers and roots of the safflower were identified: arabinose, glucose, fructose, sucrose.

METHODOLOGICAL ASPECTS OF THE DRUGS DEVELOPMENT – AS AN INITIAL STAGE OF THE NEW HERBAL REMEDY CREATION

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Introduction. Development of medicinal products based on medicinal plants with a multidirectional pharmacological effect is one of the directions of creating medicines from herbal substances. The initial stage of pharmaceutical development of a drug product involves the formation of a notion of scientific research sequence, identification of objectives, validation of working assumption and consideration of the achievements of scientists dealing with the issues in this field or working with similar objects.

Aim. To identify methodological approaches to the development of a solid dosage form, namely capsules with a dense extract of burnet rhizome and roots for use in gastroenterology.

Materials and methods. To achieve the goal, analysis and synthesis, methods of scientific induction and deduction have been used as research methods.

Results and discussion. When creating capsules with a thick burnet extract, it is important to find out the place of the preparations based on herbal substances in pharmacotherapy of inflammatory diseases of the gastrointestinal tract, to study the sources that form the idea of the latest advances in the field of encapsulated herbal preparations, to substantiate the rationality of creating a new therapeutic agent and its dosage form, which is possible after the marketing analysis of the drugs used in the treatment of the above mentioned pathology.

The next part of scientific research is supposed to involve procurement and comprehensive study of the herbal substance of burnet: from the determination of technological parameters of the herbal substance and the impact of pharmaceutical factors in the development of extraction technology to physical and chemical research, the development of a project of quality control methods and the study of the new extract stability.

The primary aspects in the preparation of medicinal products include determination of the content of the active plant substance by screening pharmacological and microbiological studies, selection of auxiliary substances and substantiation for the technology of capsules with a thick extract, further study of their standardization and stability, studies of antiulcer properties to justify the applicability of the therapeutic agent in gastroenterology in the treatment of inflammatory diseases of the digestive tract.

Conclusions. Implementation of the above mentioned stages of scientific research will make it possible to substantiate the formula of the capsules with a thick burnet extract, and its creation will expand the range of drugs for the treatment of inflammatory diseases of the gastrointestinal tract.

THE EFFECT OF THE MIXTURES WITH BIOLOGICALLY ACTIVE SUBSTANCES FROM FRAXINUS EXCELSIOR AND PHLOMIS PUNGENS ON THE RESISTANCE TO HYPOXIA IN WHITE RATS COMPARED TO THE ACTION OF α-TOCOPHEROL AND MEXIDOL

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Introduction. Any pathological process in the body is more aggressive in the presence of hypoxia, or hypoxias themselves play a role in the pathogenesis of diseases. Ischemic diseases of the heart and brain, impaired supply of oxygen to the body organs, and even some infectious diseases occur as a result of hypoxia. Therefore, protection of the body from hypoxia and its undesirable effects is an urgent problem of practical medicine and is of great social importance.

Taking all of this into account the **aim** of our research was to study the antihypoxic action of the biologically active mixtures obtained from Fraxinus excelsior (European ash) and Phlomis pungens (Jerusalem sage) and compare their action with α-tocopherol and mexidol.

Materials and Methods. When conducting our study the methods of acute hypobaric hypoxia were used. The model of acute hypobaric hypoxia was created using white rats in an airless pressure chamber. The pressure was measured by an altimeter, the rate of hoisting – by a variometer. The animals were hoisted at an altitude of 11.000 m and at the rate of 25 m/s (198.7-185 mmHg). This position was held for 10 min. Then the animals were returned to their previous position for 5 min. To eliminate hypercapnia the CO_2 absorber (30-35% alkali) was placed to the chamber. To create the same conditions of hypoxia simultaneously 3 animals of each group (experimental and control) were placed to the chamber. There was the own control group for each experimental group. The life span of animals and the number of surviving rats were calculated. To compare the antihypoxic resistance of biologically active mixtures obtained from Fraxinus excelsior and Phlomis pungens with α-tocopherol and mexidol these substances were injected into the abdominal cavity of the animals 40 min before the experiments. The control group of animals was injected the same amount of physiological salt solution. The data obtained during the experiments were statistically processed in accordance with the current re- quirements.

Results and Discussion. The resistance of biologically active mixtures obtained from Fraxinus excelsior and Phlomis pungens to hypoxia was studied compared to α-tocopherol and mexidol in male and female white rats on the background of hypobaric hypoxia. The similar experiments were also conducted on intact white rats. The rats

were injected abdominally with the biologically active mixture from Fraxinus excelsior in the dose of 300 mg/kg, the biologically active mixture from Phlomis pungens in the dose of 400 mg/kg and α-tocopherol and mexidol in the effective doses of 200 mg/kg.

The biologically active mixtures obtained from both plants showed the antihypoxic action in female and male white rats. Thus, the biologically active mixture from Fraxinus excelsior in the dose of 300 mg/kg injected abdominally increased the resistance to hypoxia in both male and female rats. The results of the control group of male rats were 9.19±0.31 min, with introduction of the biologically active mixture from Fraxinus excelsior (300 mg/kg) the results increased to 12.20±0.04 min. Therefore, when using the biologically active mixture from Fraxinus excelsior in male rats the resistance to hypoxia statistically increased by 32.8%. The antihypoxic effect of the biologically active mixture from Fraxinus excelsior was also observed in female rats. The results of the control group were 8.59±0.16 min, while on the back-ground of the biologically active mixture from Fraxinus excelsior (300 mg/kg) they were 11.23±0.05.

The results obtained have shown that the biologically active mixture of Fraxinus excelsior in the dose of 300 mg/kg increases the resistance of male rats by 32.8%, and female rats by 30.7% to hypoxia.

The similar powerful antihypoxic effect was observed with abdominal introduction of the biologically ac- tive mixture of Phlomis pungens in the dose of 400 mg/kg. he results of the control group were 9.19±0.31 min in male rats, while when using the biologically active mix- ture from Phlomis pungens (400 mg/kg) they were 10.64±0.33 min. This means that the biologically active mix- ture from Phlomis pungens in the dose of 400 mg/kg statistically increased the resistance to hypoxia by 15.8% ($p<0.01$) in male white rats. When introducing the biolo- gically active mixture from Phlomis pungens in the dose of 400 mg/kg to female rats the results were 9.30±0.03 min, and the values of the control group were 8.59±0.16 min. Thus, the resistance to hypoxia of female white rats re- ceiving the mixture from Phlomis pungens (400 mg/kg) statistically increased by 8.3%.

To check the efficiency of the results obtained the mixtures studied were compared to the action of the natural antioxidant α-tocopherol and the synthetic antioxi- dant mexidol. The research demonstrated that the abdomi- nal injection of α-tocopherol in the dose of 200 mg/kg increased the resistance to hypoxia in the group of white male rats compared to the control. The results of the control group were 9.19±0.31 min, while the introduction of α-tocopherol (200 mg/kg) increased the results to 10.40±0.33 min. Thus, α-tocopherol statistically in- creased the resistance to hypoxia of male white rats by 13.2%. The antihypoxic effect was also observed in ex- periments with female rats. The results in the control group of female rats were 8.59±0.16 min, while when in- troducing α-tocopherol they increased to 9.30±0.03 min.

PHARMACOGNOSTIC STUDY OF PLANT MATERIALS FROM THE MUSACEAE FAMILY

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Introduction. Demand on phytomedicines grows constantly. It is associated with a wide spectrum of pharmacological action, insignificant side effects, compared with synthetic analogues. One of relevant tasks of modern pharmacy is the search of new valuable sources of medicinal plant material. Bananas are one of the oldest food crops for tropical countries and an important food plant for main export. There are more than 40 types of banana varieties, however is widely used for export and food purposes the artificially created variety Musa paradisiaca. The banana contains a great number of biologically active compounds, such as vitamins of C, B, K, P, Fe, methionine, lysine and tryptophan. **Some** banana varieties are cultivated in Ukraine. This group of the plants includes mainly inedible ornamental varieties with very beautiful colors. They can be grown wild or they are grown by advices of beauty. Inedible bananas are also used for the production of different textile products, pillows, for motor-car seats and nets. These banana variaties include textile banana, Japanese banana, Darjecling banana etc.

Aim. Morphological and anatomical study of paradise banana fruit.

Materials and methods. The object of the study were pericarp of paradise banana fruit. The plant material was collected in spring 2017.

Results and discussion. Morphological analysis and identification of diagnostic features of the anatomical structure of pericarp Paradise banana fruit was carried out. It was found that in terms of morphological diagnostic value of the pericarp the color, texture, external and internal surface of the pericarp, innervation type, vascular bundles were of the great importance; for stem-length, surface and color. From the anatomical point of view the major diagnostic features of the pericarp as a plant material were the nature of the epidermal cuticle, structural features of epidermal cells, as well as the structural features and placement of the conducting system.

Conclusions. The analysis of morphological and anatomical structure of the pericarp of paradise banana fruit is the first step in the pharmacognostical study of raw materials of Musaceae family.

MORPHOLOGICAL AND ANATOMICAL RESEARCH HERB OF MAYWEED

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Introduction. Due to the rich chemical composition chamomile officinal extensively used in folk and official medicine. Chamomile officinal shows cholagogic, antispasmodic, stimulates the appetite, relieves muscle spasms of the gastrointestinal tract, analgesic, sedative properties. Chamomile flowers is used for gastritis, hepatitis, cholecystitis, colitis, cystitis, increased gastric acidity, stomach and duodenal ulcers, the malignant tumors, craw, for the treatment of of septic wounds and ulcers, lotion for conjunctivitis, dermatitis, burns. The infusion of chamomile inflorescences in oil used for grinding rheumatism and gout. Most preparations consisting of chamomile:"Recutan" –has a local antiinflammatory and wound-healing effect,"Rotocan" - has a local anti-inflammatory, used in dental practice, liniment "Ayurom"- used as a local anti-inflammatory and anesthetic drug arthritis, radiculitis, for the prophylaxis of pressure ulcers.The most common types are chamomile (german) *Chamomilla recutita (L.)Rauschert*, roman chamomile, also named noble chamomile *Chamaemelum nobile (L.) All.* , *Anthemis nobilis L.* (used almost similar as a chamomile, but within the CIS the. Roman chamomile is found only in the Crimea, Europe their areas are intersects); Chamomile aroma of *Matricaria matricariodes Porter*; chamomile Odorless *Matricaria inodora L.* (In folk medicine is also used almost similar as a chamomile, unfortunately,it is wrong.) Anthodia of this type of chamomile have whole receptacles and bigger anthodia than chamomile- up to 12 mm. The mayweed *Anthemis cotula L*. has a film-coated receptacle.

Aim. To conduct a morphological and anatomical research herb of an *Anthemis arvensis L*.

Materials and Methods. Raw material harvested in Kharkov region in June 2016. Micropreparations were prepared of a fresh herb, fixed in a mixture of alcohol-water-glycerin (1:1:1) according to conventional methods. The research was performed using microscopes MBR-1 and MBI-6 LOMO with an increase of 100, 120, 400 and 600. Obtained data were photographed on camera "*Kodak-400*." Photos were processed using the computer program "*Photoshop CS5*".

Results. Identified diagnostic signs of the morphological and anatomical structure of the *Anthemis arvensis* herb.

Conclusions. The research of the morphological and anatomical of *Anthemis arvensis* herb was conducted.

THE STUDY OF CARBOXYLIC ACIDS IN OPOPHYTUM HERB AND FLOWERS

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Introduction. *Opophytum forskalii* (syn. *Mesembryanthemum forskalii*), or samh, is a species from Aizoaceae family which unites drought-tolerant succulent plants. The plants from *Opophytum*, or *Mesembryanthemum* genus are known under the name ice plants due to the glittering cells present on their surface.

The representatives of *Mesembryanthemum* genus are known to accumulate flavonoids, phenolic acids, fatty acids. They are widely used as cosmetic agents to avoid skin dehydration and ageing, as well as antioxidants, antidiabetic, anti-inflammatory, antibacterial remedies. Samh, or *Opophytum forskalii*, grows wildly in Al-jouf (northern part of Saudi Arabia) and is extensively used by natives as flour for bread, cookies or is just mixed with dates. Recent research has shown it to possess moderate hypoglycaemic activity, though the data on its chemical composition is insufficient.

Aim. The purpose of the current experiment was to determine the qualitative composition and quantitative content of organic acids in Opophytum herb and flowers.

Materials and methods. The plant material was collected in Al-jouf region of Saudi Arabia in 2016. Organic acids were studied by GC-MS method using the Agilent Technologies 6890 chromatograph with MS detector 5973. Internal standard – tridecane; capillary chromatographic column DB-5 with internal diameter 0,25 mm and length 30 m; speed of the gas-carrier (helium) – 1,2 ml/min; evaporator temperature - 250°C; the thermostate temperature was programmed from 50°C to 320°C with the speed 4 degrees per minute. The mass-spectra libraries NIST05 and WILEY 2007 were used for the identification of the components.

Results and discussion. The experiment carried out allowed detecting 26 carboxylic acids in both types of the plant material studied. *Opophytum forskalii* herb and flowers were found to accumulate quite large amounts of oxalic, malic and citric acids. There were 10 fatty acids detected among the total number of organic acids in both types of Opophytum plant material. Unsaturated fatty acids prevailed among the total number of fatty acids in both herb and flowers.

Conclusions. The obtained data will be used at working out the standardization parameters and quality control methods for *Opophytum forskalii* herb and flowers in future.

THE INFLUENCE OF MINERAL NUTRITION ON THE PRODUCTION OF ECOLOGICALLY PURE BIOLOGICALLY ACTIVE SUBSTANCES OF GLOBE ARTICHOKES

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Introduction. The core of the current challenges of environmental science and medicinal plant of the 21st century is to develop methods of rational and correct use of fertilizers in the cultivation of agricultural, medicinal and other crops, and ways to reduce the environmental pollution by mineral fertilizers. As well as the production of ecologically clean medicinal vegetative raw material with application of mineral fertilizers. It is known that nitrogen, phosphorus and potassium nutrition are essential in the cultivation of agricultural, medicinal and other crops. In this regard, they are the main focus in their farming.

Aim. Given the above consideration, we aimed to study the effect of different forms of nitrogen fertilizers, as well as the degree of availability of soil phosphorus to the crop of globe artichokes and the rutin content in its raw materials.

Materials and methods: Experimental work was carried out in 2012-2016 at the experimental station of the Tashkent Pharmaceutical Institute, and the agricultural scientific and educational experimental station of Tashkent State Agrarian University.

In the above-ground part of plants the rutin content was determined in accordance with SPh (State Pharmacopoeia) XI edition. Mineral fertilizers are used in the following forms: nitrogen is in the form of ammonium nitrate, urea and ammonium sulphate

Results and discussion. The results of the conducted researches it is established that with an increase in the availability of soil phosphorus, regardless of the form of nitrogen fertilizers, the content of biologically active substances in medicinal plant raw materials of globe artichokes growing. However, it should be noted that the increase in the content of biologically active substances in raw globe artichokes depending on the degree of availability of soil phosphorus in the range of "medium" and "high" are not significant depending on the quantity of this element of nutrition in the soil.

This suggests that a further increase in the availability of soil phosphorus

from "medium" to "high" does not lead to a noticeable increase in the content of rutin in raw globe artichokes. As the results of our studies of the diversity of applied nitrogen fertilizers in the soil application of urea and ammonium sulphate more triggers the synthesis of biologically active substances in medicinal plant raw materials of globe artichokes, than at introduction of ammonium nitrate. The researchers note that the synthetic processes and the outflow of these compounds from leaves to other organs of the plant organism are associated with redox potential. For example, the increased oxidative activity accelerates the outflow of substances from leaves to other organs and Vice versa, which leads to increase of intensity of synthetic processes. Therefore, with the increase in the availability of soil phosphorus increased displacement redox potential of the cells of the leaves of the globe artichokes to predominance of reduction reactions over oxidation. Perhaps, this explains the direct correlation between values of pH (acidity of cell SAP), Eh (redox potential), and rH2 (level of oxidation-reduction reactions) on the one hand and the content of rutin in raw globe artichokes on the other, which occurs under the influence of mineral fertilizers (nitrogen, phosphorus and potassium). Conducted researches it is established that with increasing doses applied to the soil sulfur content of rutin is increased.

However, when making ammonium sulphate in doses of 150 and 200 kg/ha, content of rutin authentic, tangible differences between them is not detected. In this regard, from an environmental and economic point of view, we consider it appropriate to apply the sulphur-containing nitrogen fertilizer ammonium sulphate in doses of 150 kg/ha.

Conclusions:

1. Cultivation of globe artichokes with an average availability of soil phosphorus on the background of ammonium sulfate, which is the best form of nitrogen fertilizer, which enhances biosynthesis of rutin in medicinal herbs, globe artichokes.

2. In order to increase the content of rutin in raw material (the aerial part of prickly artichoke) and increasing its biomass advisable to make the soil the ammonium sulfate in the dose of 150 kg/ha.

REDUCTION OF ENVIRONMENTAL POLLUTION BY REGULATING THE WATER REGIME OF GLOBE ARTICHOKES

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Introduction: It is known that each period of development of globe artichokes is in different from each other and at different times. It is also known that early maturing types, protected from rapid aging, which decreases the yield in a small amount of assimilate nutrients and at the same time, use them sparingly, not wasting resources. A number of studies have shown that the level of mineral nutrition and supply plants with water connected. These processes, in turn, are important in the regulation of the yield of the plant.

Aim: Given the above, we aimed to study the possibility of regulation of reduction of environmental pollution by regulating the water regime of globe artichokes.

Materials and methods: Studies were conducted by vegetation experiments in a tenfold repetition in terms of the typical gray soils on research and training experimental station of Tashkent State agrarian University. Soil moisture in pots was maintained at 50 and 75% of the full plaguemaster soil. Annual rate of fertilizer following : Nitrogen 5, Phosphorus 4, Potassium 1.5 grams per vessel.

The results obtained: The results showed that in the first half of the growing season globe Artichokes absorb a lot of nitrogen fertilizer. Since the flowering period is observed the opposite effect. This situation can be explained by the relatively long period of vegetation of globe Artichokes. These data confirm the results of the assimilation of nitrogen fertilizer. At the end of the growing season for globe artichokes in soil moisture under conditions of 50% of the total moisture, the coefficient of digestibility of nitrogen fertilizer was low . Under optimal soil humidity conditions at 75% of the total moisture content was observed the opposite phenomenon. Under conditions of low humidity environment, that is, in terms of 50% of the total volume of humidity. Under conditions of low humidity environment, the amount of unaccounted-for nitrogen fertilizer in the soil where grown globe artichokes. But under conditions of optimal humidity environment was observed in low number does not take into account the loss of nitrogen, than under low soil moisture. The results of the research identified low digestibility of nitrogen fertilizer the globe artichokes under conditions of low humidity environment.

Conclusions: As the results of the vegetation experiments at 75% soil moisture of its total plaguemaster plant globe Artichokes absorbs more nitrogen, which contributes to the reduction of environmental pollution by various waste nitrogen fertilizers.

RESEARCH ESSENTIAL OIL TANACÉTUM BALSAMÍTA

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In recent years, not only in Ukraine but all over the world faced the problem of treatment of the most common dermatosis as psoriasis. Sick people of all ages, often young. Psoriasis is a disease which live life. Frequent application of drugs, lead to resistance and lack of therapeutic effect. Therefore there is a need to find new medicines to improve the course of disease and increased remission. For the treatment of psoriasis in folk medicine use water, alcohol and oil extracts from leaves and grass Tanacétum balsamíta. The aim was to investigate the chemical composition of essential oils of herbs Tanacétum balsamíta, harvested during flowering collectible area botanical garden of NUPh. To achieve this, we have harvested aerial parts Tanacétum balsamíta length of 15-20 cm., dried by the rules drying essential oil raw materials and sent for analysis. Definition of quality and quantitative components of essential oils in the grass Tanacétum balsamíta performed by chromatography-mass spectrometry in the gas mass spectrometer Apex. The identity of the components was performed using a library of mass spectra NISTO2. L. Were identified peak area and retention time. The study found more than 40 volatile compounds identified 21 of them. Of the monocyclic monoterpenes identified D-Limonene; Eucalyptol and their esters. Bicyclic monoterpenes are: Thujon, Trans Pinocarveol, Pinen, Thujol, Myrtenal. Of the bicyclic sesquiterpenes derivatives found Naphthalen. Aromatic compounds are - 2-Cyclohexen-1-one, 2-methyl-5- (1-methylethenyl). In terpenoids found in the grass volatile compounds that belong to carboxylic acids - Pentanoic acid, Butenoic acid. Mostly composed of volatile compounds Thujon (17,37%) and 2-Cyclohexen-1-one, 2-methyl-5- (1-methylethenyl) (50,26%). These classes of compounds exhibit significant antibacterial activity, expressed anti-inflammatory properties. As a result of the study of the Tanacétum balsamita grass harvested during flowering, 19 terpene compounds found in the essential oil were found. Component and quantitative terpenoids can cause antibacterial, antiseptic, anti-inflammatory activity. The predominant among compounds derived terpenes are bicyclic monoterpenes and aromatic compounds. These data can be used to further standardize the raw Tanacéti balsamíta herba.

PHARMACOGNOSTIC STUDY OF RAW MATERIALS OF SOME PLANTS OF GERANIACEAE FAMILY

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Introduction. The demand for herbal medicines in recent times is constantly growing. This is due to a broad spectrum of pharmacological effect, and few side effects compared to synthetic analogues. Our attention is drawn to the plants of Geraniaceae family – Geranium genus, which are widely cultivated in Ukraine and widely used in folk medicine. Geranium or cranesbill is genus of the Geraniaceae family. It is best known for more than 400 species of herbs and subshrubs of the genus, scattered around the world, and also in the tropical zone – in the mountains. The most famous houseplant is Zonal Geranium, which also are grow in the wild.

Leaves petiolate, palmatipartite or palmatilobate, cut to share or blades of different sizes and shapes, rarely pinnate. Peduncles with one – three flowers. Flowers are regular, large and beautiful, five-leaves from open cups and five similar nearly round petals of the corolla, which is also open almost in the plane; their color is white, magenta, blue and purple of different shades. Flowers are with ten stamens, all are usually with anthers. The fruit is a capsule with sepals remaining intact on the fruit. Forest Geranium contains vitamin C, essential oil, significant amounts of tannins, carotene, starch, pectin, gum. Geranium has an antiseptic effect, anticatarrhal action, helps with cardiovascular diseases, as well infusion is used in kidney stones.

Aim. Pharmacognostic study of raw materials of some plants of the Geraniaceae family. The study of underground organs of Forest Geranium with the determination of the main diagnostic characters, morphological and anatomical structure of whole and crushed plant material.

Materials and methods. The object of the study were the roots of Zonal Geranium which harvested in October-November 2016.

Results and discussion. The root of the Zonal Geranium has cylindrical shape, the surface is wrinkled, color is light brown. Integumentary tissue is represented by multi-layered cork. The conducting system is represented by two open collateral bundles, in which a layer of cambium is well marked. In the heart of The rays of primary xylem are visible in the middle. Two medullary rays are very well observed. Druses are present in both cork and core parenchyma.

Conclusions. The result of the research established the main anatomical and diagnostic features of the underground organs of the Zonal Geranium. The obtained data allow us to identify raw materials and to make a conclusion about the prospects of the study of the geranium root to create new drugs based on it.

DETERMINATION OF SOME NUMERICAL INDICATORS OF BARK BIRCH

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Introduction. Plant of genus Betula L. – propagation in the world widely, is a typical boreal plants, widespread in all temperate, extratropical regions of the northern hemisphere. It is deciduous, medium or small height, low trees or shrubs that even a trail. The bark can be white, yellow, brown or black, which exfoliate into thin strips (birchbark). The birch – the lightest of wood species. In our country the most common plants of the genus Betula L. are betula pendula Roth. and betula pubescens . The betula pendula studied better. In our country officially raw materials are gemmas. Other raw materials – leaves, wood, bark and stems are used in folk medicine. The bark and stems are used in tumors as vulnerary and anti-inflammatory. In addition, these raw materials are wood-cutting departure and woodworking industry. The complex processing of raw materials and the use of waste are very importent, its supports providing raw material without damaging fund of flora.

Aim. Determine the numerical indicators from different parts of the cortex preparations.

Materials and methods. The quantitative composition of tanning material was determin by kompleksonometriyi per halotanin content of catechins amount determined by spectrophotometry in the calculation of (+) - catechin.

Results and discussion. defined the loss in weight on drying, total ash, extractive substances, oxygenized phenolic compounds, in the bark of birch from different parts of the workpiece (6 regions of Ukraine). Also in the cortex defined quantitative tannins, and the amount of catechins. All indicators measured were more or less variable. The research allowed to find out the upper or lower limits corresponding figure. Thus, the loss on drying to the bark of birch was not more than 10.0%, total ash – not more than 10.0%, extractives content – not less than 22.0%, the amount of oxygenized phenolic compounds – not less than 12.0%, tanning substances – not less than 2.0%, the amount of catechins – at least 3.0%.

Conclusions. The results will be considered in future research birch bark.

PROSPECTS FOR PHARMACOGNOSTIC RESEARCH OF TANACETUM PARTHENIUM

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Introduction. In search of new medicinal substances scientists turn to natural sources more and more. Medicinal plant raw material is inexhaustible resource of biologically active substances. Nowadays research on cultivated and wild plant for development of medicinal drugs with different spectrum of pharmacological activity is a topical task of pharmacy. Representatives of the Pyrethrum genus are of particular interest. This genus counts about 100 species, which belong to 14 sections and spread all over Europe. 56 species grow on the territory of Ukraine and CIS countries. Among these species Tanacetum parthenium is used in medicine. This species is included in monographies of European, British, American, German, French Pharmacopoeia and State Pharmacopoeia of Ukraine of second edition. Tanacetum parthenium is widely used abroad as drugs from migraine and inflammatory diseases of the joints, but there are no drugs on its basis in Ukrainian market, so research on this species is a task of current interest of pharmaceutical science.

Aim. To analyze and summarize information about chemical composition and spectrum of biological activity of Tanacetum parthenium from different sources of literature.

Materials and methods. Descriptive, comparative and systematic search.

Results and discussion. Tanacetum parthenium contains mono- and bicyclic sesquiterpenes, and especially parthenolid as the main one, which accounts for 85% of all sesquiterpenes. There are also flavonoids, based on kaempferol, quercetin, apigenin, luteolin, chrysoeriol; essential oils, mainly camphor, camphene, p-cymene, and bornyl acetate; melatonin mainly in leaves; coumarin isofraxidine and its ester in the composition. Parthenolid determines a whole range of pharmacological effects, such as anti-inflammatory, cytotoxic, analgetic, spasmolytic, hypoglycemic, antihypertensive and so on. So wide spectrum promotes application of this species in the treatment of neurological, inflammatory and cancer diseases.

Conclusions. The results of the studies carried out prove that Tanacetum parthenium is a promising plant for futher studies as a source of biologically active substances and creation of drugs on their basis.

RESEARCH ON THE SYRINGIN CONTENT IN THE FLOWERS OF COMMON LILAC OF BUFFON VARIETY

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Introduction. Nowadays medicinal plants which contain biologically active substances of phenylpropanoidal nature are widely studied. The representatives of Syringa genus are known to be a promising raw material for obtaining phenylpropanoids, and especially syringin (eleutheroside B) as the main one. Bark is the only part of the plants of the Syringa genus, which is used in officinal medicine, so research on the syringin content in the flowers of common lilac of Buffon variety is a task of current interest of pharmaceutical science.

Aim. The aim of the research was quantitative determination of syringin in the flowers of common lilac of Buffon variety.

Materials and methods. Quantitative content of eleutheroside B was determined by spectrophotometer Mecasys Optizen POP (Korea). Extraction of eleutheroside B was carried out by the following procedure. 1.0 g of the crushed flowers were put to a flask with capacity of 100 ml and fractional extraction with 20 ml 70%, 95% of ethanol and mixture chloroform-ethanol (5:1) was carried out. Extracts were combined, filtered and evaporated. Than 10 ml of water were added to the evaporated residue in the flask and purification of water phase by the triple extraction with 10 ml of tetrachloromethane was made. The purified fraction was placed in a separation funnel, syringin was extracted by the mixture chloroform-ethanol (5:1). The extract was filtered through a paper filter with 1.0 g of sodium sulfate anhydrous into a measuring flask with capacity of 100 ml, where the mixture chloroform-ethanol (5:1) was added till the mark. Quantitative determination was made using specific absorption value of syringin at the wavelength 278 nm, taking mixture chloroform-ethanol (5:1) as a reference solution. The content of eleutheroside B (X, %) was calculated using the formula: $X = A \cdot 100 \cdot 50 \cdot 100 / A_{1cm}^{1\%} 20 \cdot m \cdot (100 - W)$, where A – absorbance of the solution studied; $A_{1cm}^{1\%}$ – – specific absorption value of syringin at 278 nm; m – – weight of the plant material, g; W – weight loss on the plant material drying, %.

Results and discussion. Content of syringin in the flowers of common lilac of Buffon variety in terms on absolutely dry plant material was 1.5±0.01 %.

Conclusions. The results of the studies carried out are encouraging to use eleutheroside B (syringin) as a marker for analysis of extracts of common lilac flowers of Buffon variety.

VALUE OF USING OF CARBAMIDE – FORMALDEHYDE FERTILIZER IN DECREASING OF ENVIRONMENTAL POLLUTION

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Introduction: Further increase in the yield of agricultural and medicinal crops, including artichoke prickly and others, requires an increase in the doses of nitrogen fertilizers. According to the estimates of experts about 50-60% of increasing of a harvest is due to use of mineral fertilizers. However with increasing in norms of introduction of nitrogen fertilizers their efficiency progressively decreases, and the increasing amount of unused nitrogen poses a potential threat for the environment, turning into a factor of pollution of the hydrosphere and troposphere.

Research objective: We have aimed to study use by artichoke prickly nitrogen from urea and carbamide and formaldehyde fertilizers (KFU-Kazan Federal University), its transformation in the soil and their value in decreasing of environmental pollution.

Materials and methods of a research: efficiency of use of urea and the carbamide and formaldehyde fertilizers (KFU) on the typical not salted gray soil of Tashkent and a light medium salted gray soil of Syr Darya areas was studied.

Vegetative and field experiments were made: Repeatability of the above-stated experiences – fourfold. The area of an allotment is 600 square meters on medium salted light gray soil and 400 square meters on a typical non- saline gray soil. The scheme of a placement of an artichoke prickly is 90x50x1. Watering carried out according to the scheme 4-6-4, 50 of % of annual norm of nitrogen brought before crops, other part during mass budding. KFU with an urea ratio to formaldehyde 1,6:1 and 2,5:1 was tested. Content of nitrogen in KFU is 40-42%.

The received results: By results of the researches conducted by us it was established what quantitative indices of content of ammoniac and nitrate nitrogen depends on a development phase. Higher rates of these compounds of nitrogen are dated for phases of budding and blossoming, and then they decrease, reaching a minimum in a phase of maturing of seeds of the plant studied by us, an artichoke prickly. During maturing of seeds of plants the amount of residual nitrogen considerably prevails at introduction under plants urea, than KFU. These data demonstrate that the nitrification of the KFU ammoniac nitrogen is much less, than urea nitrogen. As a result of it, leaching of nitrates, especially in the conditions of the salted soils happens to a close bedding of ground waters to a large extent at urea

introduction, than KFU. Thanks to bigger contents in the soil of ammoniac nitrogen at introduction of KFU, residual nitrogen (unused a plant) decreases in relation to urea that eventually the efficiency of nitrogen on plants increases and losses decrease. The total of the residual inorganic nitrogen composing from nitrates and ammonia is much higher when using under the studied urea plant, than KFU. On the basis of these data, it can be assumed that nitrogen losses from urea as a result of denitrification and leaching occur to a greater extent when used under artichoke for prickly urea than for KFU. This indicates a certain advantage of the use of KFU than urea in reducing environmental pollution harmful to the body of the remains of mineral fertilizers. Similar data on the content of ammonia and nitrate nitrogen in the soil were obtained under field experiments based on a typical non-saline sierozem.

Consequently, the use of carbamide-formaldehyde fertilizer is especially important in conditions of saline soils with close groundwater occurrence, where it is possible to expect significant nitrogen losses as a result of nitrate leaching into groundwater. In addition, the higher content of nitrates in the soil with the introduction of standard mineral fertilizers leads to significant nitrogen losses, the sizes of which reach considerable values. As a result, a number of environmental pollution problems arise, since the greatest danger is the high content of nitrates in the soil.

At the same time, nitrates accumulate not only in soil - ground, groundwater, but also above the permissible norm they accumulate in medicinal plant raw materials and, consequently, enter the human and animal organism. In this respect, the use of KFU plant under the conditions of saline light gray soils with a close groundwater occurrence is especially acceptable in ecological terms than the standard mineral fertilizers.

Conclusion: The use of prickly carbamide-formaldehyde fertilizers for artichoke contributes to the reduction of environmental pollution by nitrates on a typical non-saline sierozem, especially in conditions of saline light sierozem with a near occurrence of groundwater than the introduction of ammonia-nitrate forms of nitrogen. Carbamide-formaldehyde nitrogen fertilizers increase the efficiency of nitrogen on plants and reduce unproductive nitrogen losses from the soil.

PHARMACOGNOSTIC INVESTIGATION OF ERIGERON ANNUUS

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Introduction. The study of medicinal plants nowadays with the aim of creating phytopreparations on their basis is an actual problem for modern domestic pharmacy. When introducing these plants into medical practice, it is necessary to conduct a whole range of studies aimed at identifying the relationship between biologically active substances in the plant and their possible pharmacological activity. There is an increasing trend of finding new fully rich in biologically active substances of herbs in modern science and medicine. Erigeron annuus is a native pioneer species that often colonizes disturbed areas such as pastures, abandoned fields, vacant lots, roadsides, railways, and waste areas. In these habitats it competes, often successfully, with introduced invasive weeds. Sufficiently limited use of the investigated species of Erigeron anuus in a folk medicine and their lack of application in the official medicine testifies to a small phytochemical study of the plants under consideration.

Aim. The research of new sources of herbal raw materials in experimental determination of biologically active compounds in previously unexplored by anyone at sufficient level such a weed as Erigeron annuus.

Materials and methods. The object of pharmacognostic research will be the grass of Erigeron annuus, which is related to the family of Asteraceae. There will be also methods, which include such as like phytochemical study with morphological and anatomical analysis, excretion of biologically active compounds and determination of their chemical structure, development of technology for extracting dry extract from the grass, standardization and study of its pharmacological activity.

Results and discussion. Thanks to the researched sources of the literature with insufficient information about the grass of Erigeron annuus, there is much work to study and explore.

Conclusions. Significantly new and previously unknown plants, actually even weeds, which can include all necessary biologically active compounds can be a great opening in pharmacy. So they could be used in medicine at all. That is why, of course, Erigeron annuus must be fully considered and experimentally investigated at a sufficient level.

PROCESS OPTIMIZATION OF EXTRACTION METHODS FOR BETA-CAROTENE FROM THE FLOWERS OF *CALENDULA OFFICINALIS* L.

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Introduction. *Calendula officinalis L*. is a medicinal plant that accumulates large amounts of carotenoids in its inflorescences.

Aim. Our study was dedicated to modification of beta-carotene extraction methods from *Calendula officinalis L.* flowers. We analysed two different extraction methods, that we use for *Calendula officinalis L.* flores collected from three different regions of Lithuania.

Materials and methods. In the first extraction method beta-carotene was extracted from 0.2 g frozen and dried inflorescences with a mixture of water containing ethanol and ascorbic acid as an antioxidant. The extract was saponified with 50 % KOH and dissolved in hexane. For the removal of soaps and alkalies, the solution was washed four times with distilated water. The samples were kept under the nitrogen, until further utilization. The second extraction method was optimized without saponification process and as an antioxidant was used butylhidroxitoluene (BHT). This method has disadvantages such as: long extraction time, low exposure. In Literature there are knowledge that beta carotene may have extracted without saponification. During researches we have modified the method without saponification. As a solvent we choose hexane, and extracted for three times 30, 15 and 15 min in ultrasonic bath. Another problem is the flowers homogenization process because in previous studies fresh flowers were homogenized with a float or grinding machine, so the homogenization degree for extracting maximum quantity of beta- carotene was too low to reach the best results. So the homogenization process was conducted with liquid nitrogen and homogenized with grinding machine. The other aspect of extraction method optimization was using wide – neck glasses with the cork because of high volatility of solvent. The samples were investigated with HPLC method.

Results. The results of quantitative determination of total beta-carotene contents show that extraction method with saponification the amount of beta-carotene was 3.097 mcg/ml and in the other extraction method, where samples have been affected with liquid nitrogen, amount of beta – carotene was 11.1 mcg/ml.

Conclusion. Extraction method without saponification was more selective than other extraction method approximately three times.

A STUDY OF ORGANIC ACIDS OBTAINED FROM DAHLIA NYMPHAEALES HERBA VARIETY KEN'S FLAME

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Introduction. Along with carbohydrates and phenolic compounds include organic acids, the most common substances contained in plants. They are involved in many life processes of plants, respiration, biosynthesis of pigments, fat, lignin, aromatic acids, amino acids and others. Qualitative and quantitative analysis of organic acids in different plant organs is changing factor. Organic acids influence involved in human metabolism, activating the secretion of bile and pancreatic juice, regulate the activity of salivary glands. In a comprehensive study materials advisable to investigate the composition of organic acids.

Aim. The purpose of our research studying of qualitative structure and the quantitative content of organic acids of Dahlia herba variety Ken's Flame.

Materials and methods. For the experiment we used herbs of Dahlia Ken's Flame cultivar dried to air-dry state. Beforehand studying of qualitative composition of organic acids carried out by means of paper chromatography with use of systems of solvents: I –butanol- formic acid-water (5:0.5:2), ethylacetate-formic acid-water (3:1:1) with standards of organic acids. Processing of chromatograms carried out 2% bromocresol green (yellow spots on a green background) and 0.04 % bromocresol blue (yellow spots on a dark blue background). The quantitative content of substances defined with the help chromatography-mass spectrometry was applied on a Agilent Technologies 6890.

Results and discussion. As a result of preliminary studying of organic acids on chromatograms 4 spots are revealed, 3 are identified as oxalic (I system – Rf 0,12; II system – Rf 0,80), malic (I system – Rf 0,65; II system – Rf 0,71) and citric (I system – Rf 0,55; II system – Rf 0,62) acids. As a result of research for the first time in herba Dahlias Nymphaeales variety of Ken's Flame 13 organic acids among which in the greatest numbers collected are revealed malic acid (4604,16 mg/kg) and citric acid (3341,53 mg/kg). Malonic acid was contained in an amount of 722,14 mg/kg, oxalic acid – 619,30 mg/kg. Also defined fumaric acid and vanillic acid were determined, their content was the equal (173,96 mg/kg та 177,33 mg/kg appropriately). In smaller quantities are founded 3-heksenic (30,18 mg/kg), phenyl acetic (29,98 mg/kg), benzoic (19,33 mg/kg), salicylic (18,93 mg/kg), lilac (19,23 mg/kg) acids.

Conclusions. Results of studying of organic acids in herba Dahlias variety of Ken's Flame confirm prospects of use of this type of raw materials for development of new medicinal forms with particular pharmacological effect.

RESEARCH IN VOLATILE COMPOUNDS OF LIPOPHILIC COMPLEX OF THE HERB *GALIUM VERNUM*

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Introduction. Reseachers worldwide have long taken interest in the genus *Galium* L. family *Rubiaceae* Juss., *Galium vernum* Scop. being among them. This perennial herbaceous plant grows on sun-drenched clearings coniferous woodland. It is widely spread in the West of Ukraine.

Earlier studies established that anthraquinones are mostly accumulated in the underground parts of the plant, whereas flavonoids were mostly found in aerial parts.

Aim. The aim of this study consisted in the research in volatile compounds of the lipophilic complex of the herb *Galium vernum*.

Materials and methods. The subject of the study was the herb *Galium vernum* harversted in the Ivano-Frankivsk oblast in the flowering phase in the summer of 2016. The lipophilic fraction was obtained by means of exhaustive extraction of the herbal raw material with chloroform in the Soxhlet apparatus, whereupon the mixture was filtered and the filtrate was subsequently vacuum-evaporated with the use of the rotary evaporator and dried up at 40°C.

The study in the volatile compounds of the lipophilic complex the herb *Galium vernum* was carried out with the aid of hydrodistillation. The analysis was performed with the use of the chromatograph Agilent Technology 6890N and with the mass spectrometric detector 5973N. The content of the compounds was calculated with the internal standard taken into account (tridecane, 50 mg in hexane).

Results and discussion. The content of the volatile compounds in lipophilic complex of *Galium vernum* herb was quantified as 3.86 %, with 44 compounds identified. The dominant components in the mixture are linoleic acid (12632.9 mg/kg), coumarin dafnetine (8009.2 mg/kg) and palmitic acid (6030.8 mg/kg). Among the terpenoids, the identified compounds include dihydroactinidiolide, loliolide, 3 isomers of neofitadiene, phytol and squalene. Among the aromatic compounds, the following substances were identified: 2 isomers of dafnetine, cinnamic aldehyde, benzyl alcohol, β-pheniletilic alcohol, propiophenone, methylacetophenone, 4-vinylphenol, 2-methoxy-4-vinylphenol, acetovanillone and vanillinic acid. Among the steroids, identified were campesterol and γ-sitosterol.

Conclusions. The results obtained suggest the necessity of further research in the herb *Galium vernum*.

MICROSCOPIC ANALISIS OF LEAVES AND STEMS OF LOPHANTHUS TSCHIMGANICUS LIPSKY

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Introduction. In folk medicine a genus of lofant anise – Lophanthus anisatus Benth., lofant chinese – Lophanthus chinensis Benth. are used for reducing high blood pressure, inflammatory diseases of the gastrointestinal tract, to improve the immune system etc.

Lofant chimgan is abundant in the mountains of Tyan-Shan and Urals (Piskam, Ugam, Chatkal). It grows wild on stony and gravel soils, in middle of the mountain.

Aim. To study anatomic structure of Lophanthus tschimganicus Lipsky.

Material and methods. It has been studied anatomical structure of Lofant chimgan – Lophanthus tschimganicus Lipsky. During the study the microdiagnostic indications of leaves and stems of this lofant's species were determined. This data help to identify lofant's raw material.

The object of the study served during the blooming dried plant, taken from the Tashkent region. Anatomical character ofstem and leaf determined by State Pharmacopeia XI. For taking microphotography usedmicroscope"nlcd-307b"(China).

The members of the plant fixed 70% ethanol, mitigatedglycerine solution, watchedunder the microscope by dropping chloral hydrate solution.

Results and discussion. It was identified characteristic properties offamily and specific properties of stems and leaves under a microscope.

The leaves are covered with a lot of inner and outer side withcilia. On the upper side of the leaves located glandular cilia. Leaf epidermis is multi-layered, round, where exist small size pores. Pores wrappedwith two epidermises (property of family). There are has glands with essential oil, which located disorderly andspecificstar-shaped.

Stem four-sided, has chlorenchyme. Stem is coveredwith epidermis.It was observed that sclerenchyma is situated under cortex then phloem is inside of them. Stem has xylem elements and tracheid libriform, center is corked

Conclusions. It has been studied anatomical structure of leaf and stem species Lofant chimgan and identified specific properties of raw material.

BIOLOGICALLY ACTIVE SUBSTANCES OF SECONDARY RAW MATERIALS IN ALCOHOL PRODUCTION

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One of actual directions of modern pharmacy is the rational use of plant raw materials in the development of medicines. Constant reduction of space, the complexity of the cultivation of plants, the systematic inability of workpieces of wild plants determine the future use of secondary raw materials, of great interest, among which is grain distillery grain grain. Grain contains all the valuable substances of the grain (except the starch) and the waste products of the yeast, on the other hand, in Russia it has a huge resource base: 10 million tons per year.

The aim of the study is to study the pharmaceutical use of grain distillery grain as a new source of biologically active substances (BAS).

Materials and methods. The object consisted of wheat, corn, barley, millet grain production distilleries in Stavropol region. To study the physico-chemical characteristics of grain used methods: potentiometry, gravimetry, elemental analysis. The content of protein and amino acids was studied by the methods of Kjeldahl, spectrophotometry, HPLC, gel-chromatography; carbohydrates – TLC, spectrophotometry, gravimetry; fatty acid composition – GLC, gravimetry; flavonoids - TLC, spectrophotometry; vitamin – titrimetry.

The obtained results and conclusions. The grain represents a polydisperse system of yellow-brown color with specific odor characteristic of yeast. The physical and chemical characteristics of grain is acidic in nature (3.7-4.4), low density (1.006 g/ml), low dry matter content (4.6-6.9%) and ash (1.4-1.8%). Organic matter of solid and liquid phase of the vinasse presented by carbon (41.6-50.7%, 3.2-3.9% respectively), nitrogen (3.1-6.2%, 0.12-0.15%) and hydrogen (6.3-7.6%, 0.6-0.7%). The elemental composition of vinasse is characterized by active accumulation of biogenic elements (up to 0.8%) and low content of heavy metals (0.004%).

The concentration of proteins and amino acids, depending on the plant source grain and method of analysis were as follows: in the liquid phase 20.4-46.4%, in the solid phase – 2-2.5%. Of the 14 detected prevalent amino acids glutamic acid (3-12%). Of particular value are the 8 essential amino acids (44% of

all amino acids). Found heterogeneity of protein fractions by molecular weight in wheat, corn and millet grain is dominated by proteins with an average molecular mass (47.7-67.7%), barley grain – proteins with high molecular weight (57.9%). The heterogeneity of the protein fractions revealed according to their solubility in water and salt solutions: all types of grains is dominated by insoluble proteins (69-75%), mainly that prolamins (39-41%).

Carbohydrate composition at grain contains maltose, glucose, arabinose, galakturonic acid, no starch, dextrins. In the greatest quantitative content of reducing sugars it is possible to allocate the bard corn (17.5%), the content ureido – wheat the grain (5%). It is noteworthy that in the liquid phase of the grain content of reducing sugars (13.1-17.5%) in 7 times more than in the solid phase. Reducing sugar is mostly comprised of optically active carbohydrates: 3.9-5.5% in the liquid phase, 0.8-1.3% - in the solid phase. The contents uronides in the solid phase of the grain (3.4-5.3%) 4 times more than in the liquid phase, which can be attributed to their preferential localization in the cell walls. In addition, the solid phases grain contains cellulose (0.5-0.9%).

The highest content of fatty oil is installed in the corn grain (11%); other types of grains it 1-3% below. The resulting oil treat semi-drying oils. It is established that all components of the oil are myristic (0.3-12.4%), pentadecane (0.1-1.4%), stearic (0.7-2.9%) and linoleic (35.7-45.9%) acids. Noted the high content of essential fatty acids ("vitamin F"): linoleic (36-46%) and linolenic (2-4%), and, in addition, palmitic (19-27%) and oleic acid (14-20%) acids.

In grain discovered the different groups of flavonoids (flavonols, flavones, flavonglycosides) with a total content of 0.4-0.9%. In wheat, corn and barley grain establishes the content of tocopherols (3.4-7.7 mg%), wheat and corn grain – ascorbic acid (6.2-11.4 mg%).

Thus, in the liquid phase of the grain revealed the accumulation of: proteins, amino acids, reducing sugars, nutrients, ascorbic acid; in solid phase – galacturonic, higher fatty acids, flavonoids, tocopherols, which creates the prospect of development of herbal remedies.

COMPOSITION DEVELOPMENT AND ANALYSIS OF GASTRIC HERBAL COLLECTION

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Introduction. The diseases of the gastrointestinal tract differ in wide prevalence, recurrent course, temporary disability and has a great medical and social importance. Nearly half of patients with gastroenterological diseases that are looking for a medical help, have such functional types of disorders where it's not always appropriate to prescribe only synthetic medications. At the same time therapeutic options prescribed by physicians are much greater with the complex use of medications of herbal nature (or herbal medications).

Chronic gastritis is a common digestive system's disease to which worldwide about 20-30% of the adult population suffer. Among all the diseases of the stomach, chronic gastritis accounts for 80-85%. Doctors often deal with chronic H. pylori gastritis which is about 90% of all chronic gastritis. This gastritis associated not only with chelicobacterial infection but also genetically linked with the peptic ulcer disease. The prevalence of peptic ulcer disease among adults worldwide from 5 to 15%. The reasons that contribute to the occurrence of chronic gastritis include using of rough, badly chopped food (the poor condition of the masticatory apparatus), spicy, hot food that injure the gastric mucosa; irregular meals operate badly too. Food allergies can lead to eosinophilic gastritis. Prolonged alcohol abuse leads to disruption of mucous discharge and processes of circulation and regeneration of gastric mucosa and further to its atrophy. The inflammatory process in the gastric mucosa may develop under the influence of various drugs (nonsteroidal anti-inflammatory drugs, sulfanilamide drugs, iodine, etc.). Duodenal ulcers occur 4 times more common than gastric ulcer. Given that peptic ulcer disease is a serious social problem of modern medicine due to high level of morbidity, conderable prevalence often prolonged course and frequent recurrences of temporary and sometimes longstanding disability, the relevance of studying this subject is undeniable.

The advantage of herbal medications in the therapy of gastrointestinal tract's diseases is a complex effects spectrum of biologically active substances of medicinal plants. Therefore, the search and development of new effective phytomedications for the therapy of the gastrointestinal tract's diseases is the actual purpose of pharmaceutical science.

Aim. The aim of our work was to develop composition and to make the analysis of gastric herbal collection.

Materials and methods. Using qualitative reactions and chromatographic methods of analysis in gastric preparation we have found a variety of biologically active substances. The quantitative content of biologically active substances in determined herbal collection was defined by titrimetric, gravimetric methods of analysis and steam distillation. Macro- and microscopic methods of analysis have been established morphological and anatomical characteristics of the collection's medicinal plants. Weight and gravimetric methods were defined numeric parameters in gastric preparation.

Results and discussion. We have developed a gastric herbal collection with the following components:

Rp.: Glycyrrhiza radices
Chamomillae floris
Lini seminae
Menthae piperitae foliae
Valerianae rhizomatae cum radicibus 20,0
30,0
30,0
10,0
10,0
Misce ut fiat species.

Due to qualitative reaction in gastric collection were identified bound and free sugars, polysaccharides, coumarin, flavonoids, tannins and saponins.

The quantitative content of biologically active substances in gastric preparation was determined. The content of polysaccharides is 11.7%, hydroxycinnamic acids 2.34%, flavonoids 1.61%, the amount of polyphenol compounds 7,56% essential oil 0.44%, ascorbic acid 0.16% and the amount of free organic acids (1.17%). To establish identities of the components for gastric preparation we have studied their morphological and anatomical characteristics. To standardize gastric preparation we have defined numeric parameters, namely the weight loss after drying (12.49%), total as content (3.8%), insoluble ash in 10% hydrochloric acid solution (0.65%) and extractives withdrawn with water (20.32%).

Conclusions. We have analyzed the literature, developed composition and conducted pharmacognostical analysis of gastric collection. The quantitative content was determined. The results will be used to develop the relevant sections of the project of quality control methods for gastric preparation.

INVESTIGATION OF THE PHARMACOLOGICAL ACTIVITY OF POLYSACCHARIDE COMPLEX OBTAINED FROM LEDUM PALUSTRE

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Introduction. Herbal medicines have more advantages than their synthetic counterparts. Low toxicity, the gradual achievement of pharmacological effects, complex action are some of them. That's why, obtaining and investigation of plants biologically active substances are the actual task of modern pharmacy.

One of the perspective plant materials is *Ledum palustre* shoots (*Cormus Ledi palustri*), which have long been used in folk medicine as an antispasmodic, diuretic, diaphoretic, disinfectant, anti-inflammatory, sedative and antitussive remedy. The wide spectrum of plant biological activities is due to the presence of terpene compounds, flavonoids, tannins, organic acids, polysaccharides and other substances in the plant material .

Terpene compounds of Labrador tea are the most studied. They are component of essential oil, and medicine "Ledin" with antitussive effect was developed on their basis. While the polysaccharide complex of this plant is almost not studied.

So **the aim** of our research was the investigation of the polysaccharide complex (PSC) obtained from *Ledum palustre* shoots and determination its pharmacological activities.

Materials and methods

Object of our research was PSC obtained from *Ledum palustre* shoots. 200 g of chopped raw material, with particle size less than 2 mm, was put in the volumetric flask capacity 2 liters, 1000 ml of water was added and the flask was heated on water bath for 30 minutes with a reflux condenser. Extraction was repeated three times with a new portion of extractant. Water extracts were collected separately in containers, centrifuged and filled to the mark in volumetric flask capacity 1000 ml by water. 25 ml of each water extract was taken for analysis. Extracts were united and evaporated to the volume 100 ml in the vacuum-circulation apparatus at 100 °C. 300 ml of ethyl alcohol was added to the concentrated solution. Precipitation of polysaccharides formed, it was allowed to stand for one hour, centrifuged, washed with 30 ml of 96% ethyl alcohol and dried at room temperature to dryness.

Phytochemical research of PSC was carried out by paper chromatography, gravimetry and spectrophotometry.

Antitussive activity of *Ledum palustre* PSC were analyzed on cough model induced a 10% solution of citric acid. All substances were studied at doses of 10 mg /

kg, 20 mg/kg, 50 mg/kg, 75 mg/kg, 100 mg/kg.

The study of PSC antitussive activity was performed at the pharmacotherapy department of the National University of Pharmacy with the head of prof. Kireev I.V.

The antitussive effect was evaluated as follows: the antitussive activity of the Ledum palustre PSC and the reference preparations was compared with the control. The results were calculated by the formula:

$$\text{Antitussive effect}=[(C_к-C_д)/ C_к]\times 100\%, \text{ where}$$

$C_к$ - the number of cough responses in the control group;

$C_д$ - number cough reactions in the experimental group.

Results and discussion

PSC was obtained from *Ledum palustre* shoots, the yield was 2.60±0.07% in terms of absolutely dry raw materials.

It was determined dynamic of polysaccharides yields from *Ledum palustre* shoots, which was 0.97±0.03% during the first extraction, 1.24±0.03% during the second extraction, 0.39±0.01% during the third extraction by Gravimetry. D-glucose, D-Galactose, L- rhamnose and L-arabinose were identified in the hydrolyzate of PSC by the method of paper chromatography.

The amount of monosaccharides in glucose equivalent in PSC was determined by spectrophotometry. After statistical analysis of the results the content was determined as 43.25±0.80%.

Results of study of PSC and drug reference anti-inflammatory activity are given in Table 1.

Table 1. The effectiveness of PSC Ledum palustre using ethyl acetate as compared to control , %

Dose	Number cough shocks in the control group	Number cough shocks in the experimental group	Antitussive activity
10 mg / kg	18,00±0,7	3,2±0,8	82%
20 mg / kg	18,00±0,7	5,8±0,8	68%
50 mg / kg	18,00±0,7	2,8±0,8	84%
75 mg / kg	18,00±0,7	2,4±0,5	87%
100 mg / kg	18,00±0,7	3,8±0,8	79%

From the data we can conclude Ledum palustre PSC has the maximum activity observed at 75 mg / kg.

INVESTIGATION OF THE PERSPECTIVE TYPE OF MEDICINAL RAW MATERIAL IMMUNOMODULATING ACTION

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Introduction. The search for new sources of medicinal plant raw materials has been and remains one of the priorities of pharmacy. The use of plant products is primarily due to their high biological activity and complex effects on the human body. The immune system is a collection of organs, tissues and cells, the work of which is directed directly at protecting the body from various diseases. To date, a number of different plants are known that affect the maintenance of the human immune system. Basically, these are representatives of the families Araliaceae, Asteraceae, Liliaceae, Crassulaceae.

In addition to immunomodulating action, aloe juice from freshly picked leaves, preserved with 95% ethanol and chlorobutanol hydrate, has a laxative, anti-inflammatory and bactericidal effect. They are used inside (in gastroenterology) and externally for the treatment of purulent wounds, burns, skin diseases.

Liquid extract Eleutherococcus is used as a stimulant of the central nervous system. Ginseng preparations are effective in diabetes, chronic hypo- and anacid gastritis.

Therefore, medicinal plants have long been used in folk and scientific medicine, such as Echinacea purpurea Echinacea purpurea, Aloe arborescent Aloe arborescens, Eleutherococcus senticosus, Ginseng, Aralia mandshurica are widely used in a number of diseases.

Aim. To search for raw materials of flora plants in Ukraine, which can be used to maintain and restore the immune system of a person.

Materials and methods. The objects of our research were the raw materials of representatives of the families Asteraceae and Crassulaceae.

Results and discussion. In carrying out preliminary studies of the chemical composition of plant raw materials, it was found that the objects contain phenolic substances, in particular flavonoids, phenol-alcohols, as well as polysaccharides, zinc and silicon. These compounds are responsible for the immunostimulatory action of plants.

Conclusions. The obtained data testify to the prospect of in-depth study of plants of the genera Onopordum, Crassula as sources of raw materials positively influencing the human immune system.

MICROSCOPICAL FEATURES OF LETTUCE LEAVES OF "LOLLO BIONDO" VARIETY

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Introduction. Phytotherapy is a top-priority direction of modern healthcare which is extensively used in prophylaxis of acute and chronic disorders and improvement of the quality of life. Thus the search of new available sources of biologically active compounds is always of great interest.

Our attention was drawn to lettuce which is cultivated in a great number of varieties with different nutritive value. One of the most widely used lettuce varieties is "Lollo Biondo" which has large crunchy green leaves. Lettuce is known to contain high amounts of antioxidants such as phenolic acids and flavonoids, sesquiterpene lactones which might have moderate analgesic properties, and other groups of biologically active compounds that are essential for normal functioning of human body. Since identification of different lettuce varieties is challenging, it is important to carry out microscopical analysis of its plant material.

Aim. The purpose of the current study was to determine the microscopic features of fresh lettuce leaves of "Lollo Biondo" variety.

Materials and methods. The microscopical features were studied using Digital camera for microscope DCM 300" (USB 2,0) with resolution 3M pixels. The micropreparations were made from the margin of the leaf, its middle part and on the cross section.

Results and discussion. According to its anatomical structure the leaf is dorsiventral. The upper epidermis consists of small cells with thin sinuous or straight cell walls. The lower epidermal cells are smaller with sinuous cell walls. The epiremal cells along the veins are elongated with straight cell walls. The epidermal cells at the margins consist of small cells with wavy cell walls on the lower surface, while upper epidermal cells are mainly elongated. The leaf is amphistomatic. The stomatal apparatus is of anomocyte and anisocyte type, with anisocyte stomata prevailing on the upper epidermis, while the lower epiderm contains mainly anomocyte stomata surrounded by 4-5 cells. Vessel bundles contain spiral tracheids. The surface of younger leaves might contain trichomes – simple and glandular hairs.

Conclusions. The obtained data will be used at working out the standardization parameters and quality control methods for lettuce leaves of "Lollo Biondo" variety in future.

ESSENTIAL COMPOUNDS OF *NERIUM OLEANDER FLOWERS* L.

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Introduction. Nerium oleander -shrub or small tree from family Apocynaceae. All parts of this plant are contain the toxic elements: cardiac glycosides, saponins, digitoxigenin, oleandrin, oleondroside, nerioside. Because of this, the use of raw materials of this plant in medicine and pharmacy is limited. Analyzing the degree of research on the chemical composition of this plant, it can be concluded that some classes of biologically active substances (BAS) have not been studied. To expand the information on the chemical composition of *Nerium oleander* L. flowers, it is relevant to study the essential compounds of this raw material.

Aim. The aim of our study was to investigate the component content of essential compounds of *Nerium oleander* L. flowers.

Materials and methods. The object of study was the flowers of *Nerium oleander* L. collected in September 2016 in Botanic garden of National university of Karazin V.N. Considering that the raw materials are poisonous, collected of flowers was carried in gloves. For experiment used dry raw material. Raw material dried under cover in a dry, well-ventilated place. The raw materials were stored in paper bags. The qualitative and quantitative content of compounds established by Gas Chromatographic-Mass Spectrometric method in chromatograph 5973N/6890N MSD/DS Agilent Technologies, mass spectrometer detector 5973N. A weighed sample of raw material (0.5 g) was placed in a 20 ml vial and was added the internal standard. As an internal standard used the tridecane (50 mkg on a sample), followed by calculation the resulting concentration of the internal standard, which is then used for the calculations. In the process of distillation volatile compounds are adsorbed on the internal surface of the reflux condenser. Adsorbed substances is washed off after cooling the slow addition of 3 ml of pentane in a dry vial for 10 ml. For quantitative calculations used the method of internal standard.

Results and discussion. Were identified 17 essential compounds: aromatic (benzaldehyde); terpenoids (caryophyllene, caryophyllene oxide, linalool, nerol, squalen); aldehydes, ketones, higher alcohols and hydrocarbons (dodecanale, tetradecanale, tricosane, pentacosane, hexacosane, nonacosane. In most high concentration (mg/kg) are content linalool (14,3), benzaldehyde (12,5), caryophyllene (12,8) and caryophyllene oxide (15,3).

Conclusions. The qualitative composition and quantitative content of volatile substances of *Nerium oleander* L. flowers is established.

PERSPECTIVENESS OF THE USE OF SOME REPRESENTATIVES OF THE GENUS IRIS L.

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Introduction. In the modern pharmaceutical industry naturopathic and homeopathic medicines occupi an important place, which is due to their effectiveness and mild effect in comparison with synthetic analogues. In Ukraine about 250 species are recognized as medicinal plants, 150 of them are recognized by scientific medicine. The prospects for studying medicinal plants are great.

Aim. Review of scientific literature on the composition and practical use of plants of the genus Iris L. To establish the most promising directions of the study of representatives of the genus Iris L. with the goal of creating a new medicinal product.

Materials and methods. Subjects of the study were Iris hungarica Waldst et Kit. and five varieties: Bright White Waldst et Kit., Indian pow wow Waldst et Kit., Galleon Gold Waldst et Kit., Mini Dynamo Waldst et Kit., Little dream Waldst et Kit. We studied the literature sources, data of electronic resources, also publications of other authors.

Results and discussion. According to literature, plants of the genus Iris L. number more than 300 species. The arial is regions of the temperate and subtropical climate – the countries of The Europe, Asia, North America. They grow on the slopes, glades, river valleys. Irises have been long introduced into the culture due to their decorative qualities. In folk medicine irises use as a diaphoretic, astringent, diuretic, laxative, expectorant mean. Also there are data on the anti – inflammatory and analgesic qualities of representatives of this genus.

The chemical composition of irises is represented by organic, phenolcarbonic, hydroxycinnamic acids, tannins, saponins, xanthones, polysaccharides, flavonoids, isoflavonoids.

Iris hungarica is the perennial herbaceous plant 15 – 40 cm height, the stem with direct line – xiphoid or sickle curved leaves up to 45 cm long, narrowed at the ends. In the winter the leaves die off, appear after stems in the spring. The

stems are thin up to 50 cm tall, the branching. Perianth is blue – violet color, back – ovoid form, has sixtyseporated limb. The orange – yellow "beards" are situated at the slightly bent outer parts. The basis of flowers are covered by swollen leathery leaves. The underground organs are presented by thick branched rhizome of about 2 cm in thickness with branches grows. The fruit is the cylindrical box. It grows in the forest – steppe zone, mainly in shrubs, meadows, slopes, glades. Blooms from May to June. Iris hungarica belongs to a group of bearded irises, which has a large selection. Five the most common varieties of Iris were selected for study.

Variety Bright White Waldst et Kit. – plants have a height of about 15 cm, white flowers are on the peduncle in length about 30 cm. Leaves are linear, basal. The plant does not like waterlogging, needs the sun.

Variety Indian pow wow Waldst et Kit. – plants 30 – 45 cm height, the leaves are linear. Flowers have a bronze – brown color. Photophilous plants.

Variety Galleon Gold Waldst et Kit. – plant up to 30 cm tall, has 2 – 3 flowers on the peduncle. Leaves are gray. The flowers are yellow with a lilac – purple beard.

Variety Mini Dynamo Waldst et Kit. – a flower spike 30 – 35 cm long, has 1 – 2 flowers purple color with a blue beard.

Variety of Little dream Waldst et Kit. – the flower spike is more than 30 cm with 2 – 3 flowers, which are located above the leaves. Flowers have diameter about 10 cm, are lilac with a light – blue beard.

Conclusions. We conducted a literature review of all available sources in the field of application, chemical composition, morphological features of irises. It was established that further study of the data of representatives of the genus Iris L. will consist in establishing a quantitative and qualitative composition. The results of further research will help to establish the possibility of using iris varieties as an alternative raw material for the isolation of individual substances and the creation medicines of based on them.

QUANTITATIVE DETERMINATION OF CARBOHYDRATES IN RADIX HARPAGOPHYTUM PROCOMBENS DC

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With each year the treatment with herbal medicines is gaining increasing popularity. This makes it important to identify and study the properties of biologically active substances (BAS) of plant raw materials and drugs based on them. Harpagophytum procumbens DC. of the Pedaliaceae family is used in official medicine for the treatment of the musculoskeletal system, due to the presence of anti-inflammatory and analgesic properties.

With **aim** of more detailed study of BAS Harpagophytum procumbens DC., it was determined the total content of polysaccharides and their individual fractions. Determination the content of free and total monosaccharides in the studied raw materials.

Materials and methods of research. The total content of polysaccharides was determined by the well-known reproducible gravimetric method. The content of individual fractions of polysaccharides: water-soluble polysaccharides (WSPS), pectin substances (PR), hemicellulose A (GC A), and hemicellulose B (GC B) was determined in the rest that remainder after obtaining lipophilic fractions.

The study of the qualitative composition and quantitative content of free and total monosaccharides was performed by gas-liquid chromatography-mass spectroscopy (GC/MS).

The **results** of the study. The studies found that the total amount of polysaccharides from the raw radix of Harpagophytum procumbens DC is 12.01±0.11% of the absolutely dry raw material. The contents of individual fractions of polysaccharides: WSPS – 5.66±0.12%; PR – 12.14±0.10%; GC A 0.15±0.13%; GC B – 3.50±0.13%.

As a result of the study, a qualitative composition of free monosaccharides was established, which is represented by sucrose – 45.20±0.02 mg/g; glucose – 3.80±0.02 mg/g; galactose – 1.91±0.03 mg/g; fructose – 1.74±0.02 mg/g from absolutely dry raw materials. The components of bound (common) monosaccharides are - galactose –77.98±0.03 mg/g; glucose – 64.12 ± 0.05 mg/g; rhamnose – 4.38±0.04 mg/g from absolutely dry raw materials.

Conclusions. According to the conducted studies it was found that the total amount of polysaccharides in the studies raw material is 12.01±0.11%. The predominant component of free monosaccharides is sucrose with a quantitative content of 45.20±0.02 mg/g from absolutely dry raw materials.

MONITORING OF THE EXTRACTION OF PECTINS FROM THE HERB OF *GALIUM VERUM* L.

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Introduction. Lady's bedstraw, *Galium verum* L., of the family *Rubiaceae* Juss. is widely used in folk medicine as a choleretic, bactericide or anti-inflammatory remedy. As a certified medication it is used as a component in the *Tazalok* composite herbal preparation.

Previous studies established presence of hydroxycinnemic acids, flavonoids, coumarins, iridoids, and ether oil components. The present study has been focused on the water-soluble polysaccharides in the herb *Galium verum.*

Aim. The aim of the present study consisted in research in the peculiarities of the extraction of pectin compounds from the herb *Galium verum.*

Materials and methods. The subject under study was the herb of *Galium verum* harvested in the Kharkiv region of Ukraine in the flowering phase in June 2015.

The extraction was performed on 63.46 g air-dried oil cake of the herb *Galium verum* obtained from the water-soluble polysaccharides extraction, drained with 480 ml of a 0.33 % aqueous solution of oxalic acid, followed by heating in a boiling water bath for 1 hour (pH = 3), whereupon 790 ml purified water and 1 ml of a 25 % aqua-ammonia solution was added and heated for another hour (pH = 6).

The solution obtained was filtered and evaporated under vacuum down to 30 ml, whereupon the pectin substances were precipitated with a 96 % ethanol in the ratio 1 : 3. The precipitate was separated by means of centrifugation for 10 minutes at 3000 rpm then rinsed with a 96 % ethanol, re-centrifuged and dried up.

The extraction was performed twice again, every time with the addition of 1270 ml purified water. The residue was weighed up, dried and weighed up again.

Results and discussion. The results established the presence of pectin substances (%) in the 3 extractions at I – 3.88, II – 2.41, and III – 0.81. The yield of dried pectins from the raw was quantified as 2.12 %.

Conclusions. The present study established that the herb Lady's bedstraw contains 7.1 % pectin substances, which suggests the necessity of further research in the carbohydrate content of the *Galium verum.*

QUNTATIVE FINDING ORGANIC ACIDES IN SERIES OF FRUITS VIBURNI OPULUS

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Introduction: *Viburnum opulus (L).* representative of family *Caprifoliaceae* – is a common shrub of the native flora. The official species of raw is the bark Which shows a pronounced hemostatic effect.Fruits of Viburni have a wide range of applications in folk and official medicine. Available in fruits organic acids are showing tonic, antiseptic, disintoxication and antioxidant properties, regulating the acidity. Also involved in in the processes of digestion, renewal the skin and smoothing of wrinkles, regulate glucose levels in blood. The excellent composition of fruits makes it expedient to use viburni tea during the following diseases: tonsillitis, pneumonia, bronchitis, including those caused by nicotine addiction, chronic cough. Also the most common types of *Viburni*: Viburnum glabratum *(*Kunth*)*, Viburnum molle*(*MICHX.*)*, Viburnum utile*(*HEMSL). Viburnum dilatatum*(*THUNB.), Viburnum alnifolium*(*MARSHALL).

Aim. Quantative finding organic acides in series of fruits *Viburnum opulus***.**

Materials and Methods: We have researched 7 series of fruits, that harvested during 2016 in Kharkiv, Lugansk, Poltava, Lviv, Kyiv, Kirovograd and Zhitomir regions. The content of sum organic acides, counting on malic acid, were defined by titrimetric method.

Results: We had been founded the content of sum of organic acids in 7 series of fruits *Viburnum opulus*, which varied nearly doubled, depending on a series of raw and was within 1,41%-2,95% in terms of absolutely dry raw materials. Defined the content of this group of compounds in each series: the harvesting in Kharkiv region 2,14±0,03 %, Lugansk region 1,41±0,01%, Poltava region 1,86±0.02 %, Kyiv region 1,68± 0,01%, Kirovograd region 1,94±0,01%, Zhitomir region 2,47±0,02%, Lviv region 2,95±0,01%. As a result of research we have identified the lower bound of quintative finding organic acides in.series of fruits *Viburnum opulus***,**it was not lower 1,4%.

Conclusions: We had conducted quntative finding organic acides in 7 series of fruits *Viburnum opulus*. Found that the lower bound of content this group of compounds was 1,41±0,01% (Lugansk region) and the higher 2,95±0,01% (Lviv region).

DETERMINATION OF MORPHOLOGICAL AND ANATOMICAL FEATURES OF THE PLANTS OF AGAVACEAE FAMILY

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Introduction. Nowadays herbal drugs are very popular since they contain ecologically pure active substances that are extracted from medicinal plants. By their pharmacological properties they are similar to those of synthetic origin. However, they are characterized by naturalness. Natural substances present in herbal drugs are close to the human organism. Thus the features which should be taken into account during the clinical trial appear.

In this aspect, our attention was attracted by plants from the Agavaceae family, Chlorophytum capense and Chlorophytum comosum. In ethnoscience they have been used since ancient times as anti-inflammatory and anti-microbial agents, and Chlorophytum absorbs formaldehyde, carbon monoxide, liberates phytoncides, has significant bactericidal effect, disinfects and cleans the air.

Aim. To conduct the study of morphological and anatomical features of Chlorophytum comosum plant material.

Materials and methods. The object of the study was the leaves of Chlorophytum comosum, procured in September and October 2016.

Results and discussion. During morphological study such diagnostic features were established: leaves are narrow, linear, form basal rosette. Average length is 40-50 cm, but can reach up to 60-70 cm, 1.5-2 cm wide, and often they are green with a cream stripe along the central vein.

During the anatomical research the features of the structure of basic epidermal cells, features of stomata and their type were established. Leaves are of isolateral type of structure, the chlorenchymacells are located loosely, with intercellular spaces filled with air.

The type of stomatae apparatus, placement of conductive elements were of diagnostic value.

Conclusions. As a result of studies the complex of external and internal structural features of leaves Chlorophytum comosum were established which makes it a promising source of medicinal plant material and drugs based on it.

STUDY OF PERSPECTIVE DRUG VEGETABLE RAW MATERIALS *MEDICAGO SATIVA*

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Introduction. An important feature of medicinal plants is that they are faster and more actively involved in the biochemical processes of the human body than chemical agents that are foreign to the body. The advantage on the side of medicinal plants is also because they, unlike synthetic drugs, rarely cause complications, especially allergic reactions. Medicinal plants, normalizing the functions of individual organs and systems, positively affect the metabolism in the body. That's why they can be used for long-term treatment.

Therefore, it is considered important to study the different medicinal plants of their composition, properties and effects on the human body. *Medicago sativa* is very well known as fodder grass, but few people now know that our ancestors used the widely enough healing properties of Alfalfa. *Medicago sativa* operates in different directions and can be used to treat a large number of diseases. *Medicago sativa* - "Queen of Herbs" - alfalfa is one of the richest in mineral substances products. Mineral substances in *Medicago sativa* are in the most balanced state, which facilitates their assimilation.

Aim. To study the chemical composition of the herb of Lucerne blue *Medicago sativa*.

Materials and methods. The object of our research is the grass of Lucerne blue *Medicago sativa*, harvested in 3 regions of Ukraine.

Results and discussion. We extracted the extracts with the help of extractants of different polarity, then with the help of qualitative reactions, qualitative chromatography in a thin layer of sorbent, in a number of solvent systems, in the development of specific reagents it was shown that the grass of alfalfa blue can be a source of chlorophyll and carotenoids, protein and flavonoids.

Conclusions. The data obtained by us on studying the chemical composition of the herb of alfalfa blue, taking into account the wide prevalence of this plant and the aspects of its use in folk medicine, confirm the prospects for further study of the medicinal plant material as an actual activity direction.

TECHNOLOGY OF PREPARATION OF THE EXTRACT FROM LEAVES OF ARTISHOK PRICKLY AND PRODUCTION OF NANOPARTICLES ON THEIR BASIS

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Introduction. Of great interest is the study of plant objects that are used as food and at the same time can contain biologically active substances showing hepatoprotective and choleretic activity. Among such objects it is necessary to include artichoke prickly (Cynara scolymus L.) which belong to the family of Astroids (Asleraceae). Cynara scolymus L. is used as a food and medicinal plant especially in Europe, South America and other countries of the world. Its nutritional value is explained by the presence in their tissues of such biologically active substances as polyphenolic compounds, polysaccharides, organic acids, etc.

Besides these in recent years, researchers are increasingly attracting researchers to create nanoparticles based on nanoparticles (nanoparticles - the sizes of drug particles in nanoscale, i.e a billionth of a meter) that will be delivered directly to the diseased human body by blood flow, which will increase the efficiency of its use and reduce side effects.

Aim. In connection with these studies of artichoke prickly and the possibility of obtaining nanoparticles and drugs on their basis is an urgent problem for pharmaceutical science and practice.

Materials and methods. To obtain a nanoparticle from an artichoke prickly, an extract was prepared from leaves of artichoke prickly, which was grown on the experimental site of the Tashkent Pharmaceutical Institute and at the experimental station of the Tashkent State Agrarian University. Collected fresh leaves of Cynara scolymus L. for 100 g. Purified, and crushed with a scissor to a size d = 2-3mm, divided into 2 parts of 50 g. The first part with the help of a pistil and mortar pressed and crushed until a mushy state was formed. The resulting mass was divided into 2 parts. Transferred to the vials by adding in the ratio 1: 1 (25g: 25 g.) 40% and 70% ethyl alcohol. Extraction cannot be carried out with pure alcohol, because it can remove unwanted substances and only partially dissolve the desired substances. Tightly closed the lid and left for storage for 16 days. Periodically, the bottles were shaken. The second part was left to dry (first by airing, then into a drying cabinet at a temperature of 50-60 ° C). After 3 days drying from the raw materials completely dried. Dry feed was divided into two parts and a consistency of 1:10 (5:50 grams)

was added 40% and 70% ethyl alcohol. Labeled and left at room temperature in a dark place for a certain time (24 hours) for swelling. After 3-day maceration (maceration - a method of recovering of the active nutrients (rutin, quercetin, luteolin, etc.)), by infusion in a liquid, the resulting extract is pressed, and measured raw absorption ratio (volume of extractant absorbed identity raw masses during it. swelling to more efficient extraction process, forecasting and valuation extract quality in this case to an extract with 40% ethanol -2.7sm^3 / g. Based on the results and for the 70% -3 cm ^{3} / g prepared new. extracts were respectively added to 5 g of feed 52.7 g of 40% alcohol and 5 g to 53 g of raw material of 70% alcohol. The resulting extract left for 3 days at room temperature.

Results and discussion. An important feature is its raw commodity humidity at which the leaves are stored in a dry place without damage, as well as the contents of ash, ash - insoluble in hydrochloric acid. Experimental data have shown that cultivated in Central Asia humidity dry extract obtained from the leaves of the medicinal plants Cynara scolymus L. was 8-12 ± 0.5%, and the ash content of 7-10 ± 0.5%, ash insoluble in hydrochloric acid 2,0 - 2.2 ± 0.1%, organic impurities 0.6-0.7 ± 0.04%, mineral impurity 0.6 ± 0.03%. The norm of organic and mineral impurities is considered expedient when their content in the samples is not more than 1%. The extractive substances content in Cynara scolymus L. leaves was: for the extract with 40% ethyl alcohol 24.5 ± 0.5%, and for 40% ethyl alcohol was 23.7 ± 0.5%.

Phytochemical research of leaves of artichoke prickly, cultivated in Uzbekistan, was carried out with the goal of creating an effective nano-drug product with effective pharmacological action. The qualitative analysis of flavonoids found in leaves of artichoke prickly has shown that for the extract obtained with 40% ethyl alcohol is: rutin-0.76, quercetin-0.88, luteolin-0.91, cinaroside-0.83, scuterarin-0.90, hyperoside-0.78. The dry extract of Cynara scolymus L. obtained from 40% ethyl alcohol was 18%, and for 70% ethyl alcohol, 23%. From the dry extract by grinding method on a ball mill, nanoparticles of artichoke prickly are obtained, the sizes of which are from 150 to 280 nm.

Conclusions. Thus, Cynara scolymus L. cultivated in the conditions of the Republic of Uzbekistan, corresponds to the standard indices required for the creation of nano-drugs. In their leaves and extracts found such biologically active substances as phenolic compounds, tannins, vitamins, amino acids, fatty acids, and carbohydrates.

STUDY OF THE MAJOR GROUPS OF BIOLOGICALLY ACTIVE SUBSTANCES OF COMPLEX PRODUCT BASED ON PLANT EXTRACTS

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Introduction. Bearberry – a pharmacopeia plant, it is known as a source of phenolic glycoside arbutin. For Pharmacy this plant is interesting by the content of methylarbutin, pyrozyd (6 acetylarbutin) coffeilarbutin. Complex of phenolic compounds such as hydroxypirone derivatives, flavonoids and polyphenols is detects antiseptic, diuretic and anti-inflammatory properties of raw materials. Considering the demand of raw materials necessary for the production of medicines in France, Slovakia and Poland, the bearberry widely introduced into the culture. We are obtained the complex product, it content the dry extracts of *Arctostaphylos uva-ursi* leaves, herb of *Potentilla alba* and herb of *Melilotus albus.* Currently we study of antioxidant activity of this complex.

Aim. The aim of this study was chromatographic determination of phenolic compounds of extracts of leaves *Arctostaphylos uva-ursi* (L.) Spreng. (*Ericaceae*), herb of *Potentilla alba* L. *(Rosaceae)*, herb of *Melilotus albus* (L.) Pall. (*Fabaceae, Leguminosae*).

Materials and methods. The objects of the study were explored kinds of raw materials and extracts obtained from them.The analysis was conducted by the method of paper chromatography. Substances are identified according the characteristics of fluorescence in UV – light, color of spots after processing of chromogenic reagent and the value of Rf.

Results and discussion. In result of the chromatographic study were identified: in *Uva-ursi* leaves extract – 12 phenols compounds, in herb of *Potentilla alba* – 8, in herb of *Melilotus albus* – 8, among them are flavonoids, hydroxycinnamic and phenolcarbonic acids. Determination of arbutin in the complex product was performed by the method of direct spectrophotometry at 280 nm using a specific absorption index of arbutin ($E^{1\%}_{1см}$=77). Quantitative content is 1,15□0,02%. The content of water-soluble polysaccharides were determined by gravimetric method, the content is 7,80□0,02%. The content of tannins is 4,6□0,02%.

Conclusions. Our results are proved that further in-depth study of the *Arctostaphylos uva-ursi* leaves as a source of biologically active substances can be considered like promising for the pharmacy.

STUDY THE DYNAMICS OF THE ARBUTIN'S CONTENT IN *ARCTOSTAPHYLOS UVA-URSI* L. LEAVES

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Introduction. *Arctostaphylos uva-ursi*, also known as bearberry or manzanita, is a small procumbent woody groundcover shrub, widely distributed in Europe, Asia and North America. It is a pharmacopeia plant, which has long been known as a source of hydroquinone derivatives arbutin and methylarbutin. It is described that this plant contains also flavonoids, tannins and phenol carboxylic acids. From the leaves of this shrub diuretic and anti-inflammatory drugs are obtained. Substances with bearberry leaves ordinary exhibit antibacterial, anti-inflammatory, antioxidant, diuretic effect and can be used for the treatment of mild urinary tract infections.

Aim. The aim of the study was to investigate the content of arbutin and the dry residue in *Arctostaphylos uva-ursi* leaves.

Materials and methods. The object of the study was the dried and crushed leaves of *Arctostaphylos uva-ursi.* The sample was placed in a flask. Extraction was carried out with water, when heated in a water bath for 30 minutes. The resulting solutions were evaporated on a rotary evaporator and adjusted to 50 ml with distilled water. Polysaccharide is precipitated with ethanol. The resulting solutions were used for the determination of dry residue and arbutin. Determination of content of arbutin was performed by spectrophotometry method. Determination of the dry residue conducted by gravimetric method.

Results and discussion. As a result of phytochemical analysis of extracts of *Arctostaphylos uva-ursi* leaves the dynamics of the content of arbutin and in the dry residue content of the obtained extracts were revealed. In determining the arbutin was received 5 fractions, in which the content of arbutin amounted 4.05%, 1.26%, 0.026%, 0.012% and 0.006%, respectively (Fig. 1). The dry residue in these fractions amounted 7,79%, 2,56%, 1,61%, 0,45% and 0,07% respectively (Fig. 2).

Conclusions. In the course of our research it was found that the production of arbutin advisable in the first two fractions, starting with the third fraction, the content of the substance is insignificant. Our results are prove that further in-depth study of the *Arctostaphylos uva-ursi* leaves as a source of biologically active substances can be considered shows potential for the pharmacy.

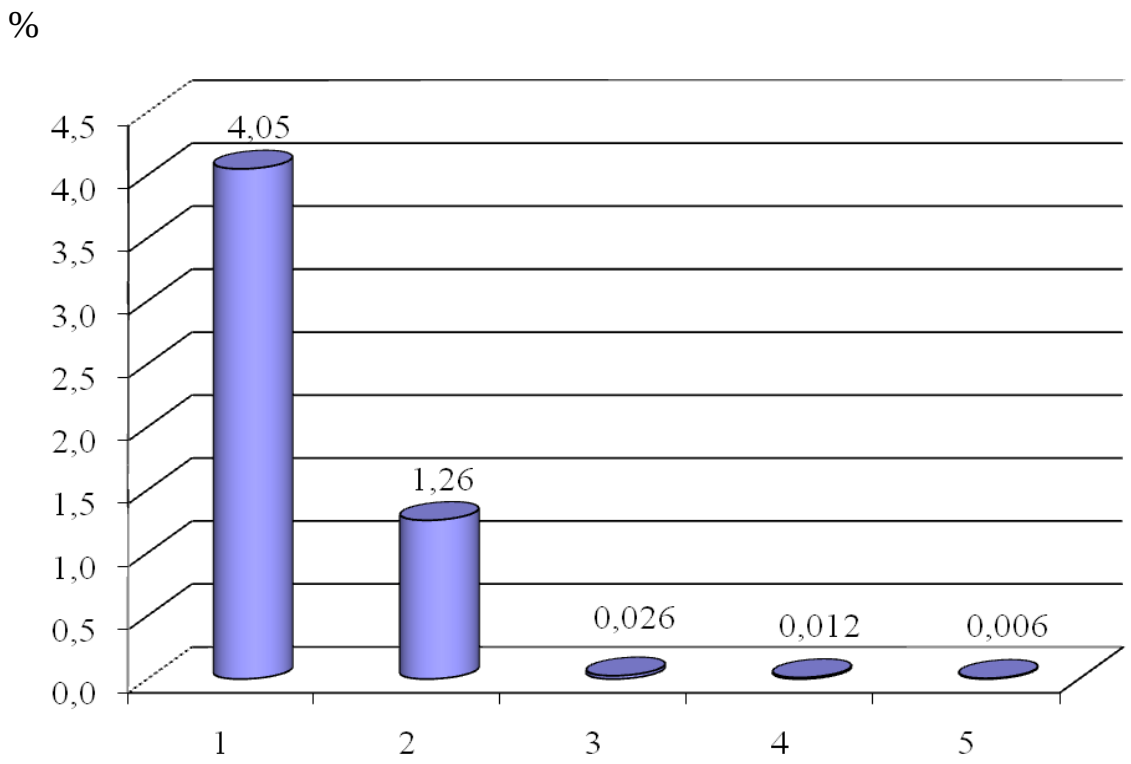

Fig. 1. Dynamics of the content of arbutin in the raw material during the extraction

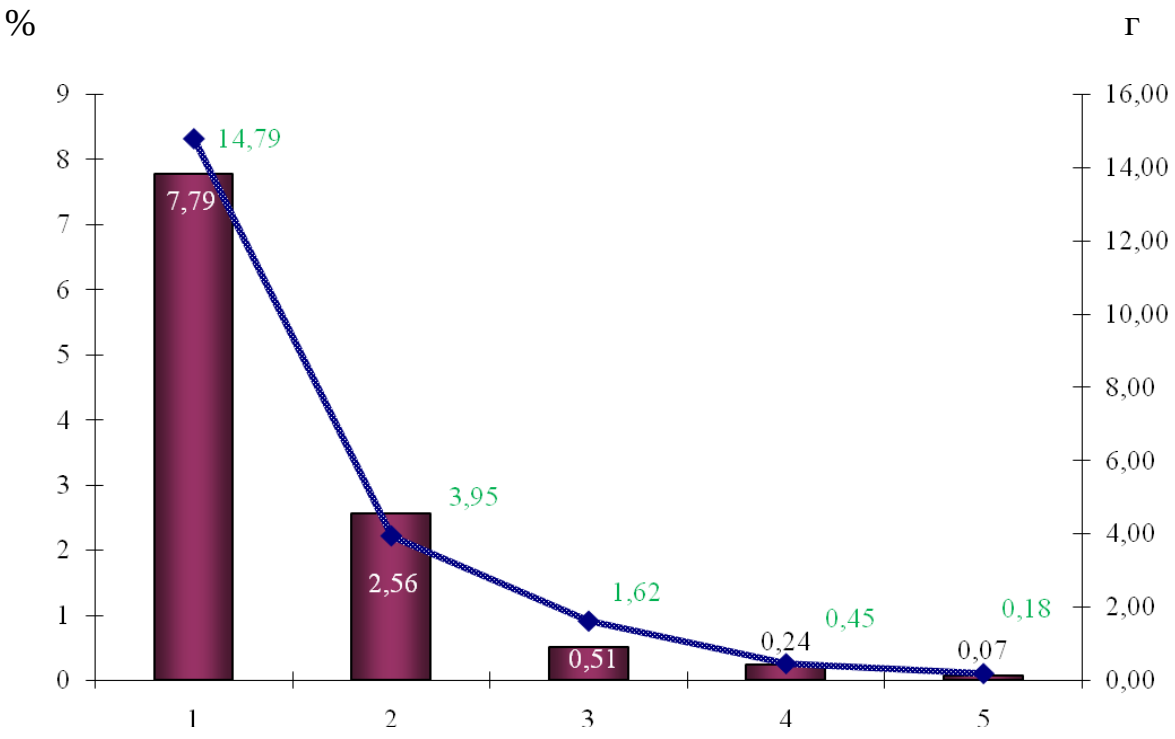

Fig. 2. Dynamics of dry residue during extraction

THE CONTENT OF PROCYANIDINS IN FRUITS OF MOUNTAIN ASH

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Introduction. Mountain ash (Sorbus aucuparia L.) from the Rosaceae family is spread all over Ukraine, grows in the underbrush of coniferous and mixed forests, among shrubs, on the woodside; it is widely cultivated. Main active substances are vitamins (carotenoids, ascorbic acid), organic acids (malic, citric, oxalic, sorbic), phenolic compounds (phenol carboxylic acids, catechins, anthocyanins, leucoanthocyanidins, flavonols, tannins) and carbohydrates. They cause multivitamin, diuretic, choleretic, anti-inflammatory, laxative, hemostatic and antioxidant effects of fruits.

Aim. The determination of content of procyanidins in fruits of mountain ash.

Materials and methods. The object of the study were the fruits of the mountain ash, which were harvested in September 2016 in the Botanical Garden of the National University of Pharmacy. The raw material was identified based on herbaria stored at the herbarium fund of the Pharmacognosy Department, NUPH. The content of procyanidins in fruits of mountain ash was determined by the method of absorption spectrophotometry according to the procedure described in the monograph of the State Pharmacopoeia of Ukraine 2.1 "Rosae fructus" on a spectrophotometer "Specord 200" at a wavelength of 555 nm.

Results and discussion. The content of procyanidins in fruits of Mountain ash, which was determined by the method of absorption spectrophotometry, is 0.13±0.001% (calculated as cyanidin chloride). Statistical processing of the results of the quantitative determination was performed by the method of variance analysis according to the requirements of the State Pharmacopoeia of Ukraine under the program Microsoft Excel 7,0 using the «Statistica» software package.

Conclusions. The content of procyanidins was determined by the method of absorption spectrophotometry in fruits of mountain ash. The obtained results will be considered in the development of the monograph on "Sorbi fructus" in State Pharmacopoeia of Ukraine.

Fruits and leaves of mountain ash is a perspective raw material for further pharmacognostic research and the creation on their basis of medicines of various pharmacological actions.

IMPORTANT TO KEEP THE USE OF MINERAL FERTILIZERS ENVIRONMENT

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Introduction: It is known that nitrogen is the most important part of the nutrient. For example, nitrogen, substances necessary for the life of the plant protein, amino acids, nucleic acids, enzymes, chlorophyll, and other components of the substances. The researchers estimated that medicinal use of nitrogen fertilizers and agricultural productivity increases of 50-60% and more. In recent years, the production of nitrogen fertilizers and agricultural crops is developing at a rapid pace. At present, the use of nitrogen fertilizers in the country to use a high amount of consecutive bring a lot of unpleasant situations. Experiments have shown that a large amount of land required for the application of nitrogen fertilizers, humus material reduction, will reduce its performance characteristics, as well as causing a reduction in the amount of organic forms of nitrogen present in the soil. This is, of course, lead to a fall in the efficiency of nitrogen fertilizer. In addition, the application of large amounts of nitrogen fertilizers and plant them by the "development" in the form of nitrate and nitrite nitrogen in the soil due to a growing medicinal substances of vegetable and melon crops will increase, resulting in the formation of human and animal diseases, lead to pollution of the external environment .

Purpose: Thus, the application of nitrogen fertilizers in the wrong hand, can lead to unpleasant circumstances. Therefore, the development of effective methods of applying them is important. In addition, the development of new and effective forms of nitrogen fertilizer of great practical importance (freshman and others, 1989; Yarovenko, 1969).

External storage environment tidy advanced agriculture with less negative impact on the external environment, reducing nutrients in the form of nitrate and nitrite nitrogen fertilizers, agricultural use of medicinal plants and delayed corporate taxation. One of them is a urea formaldehyde fertilizer carbamide and phosphorus fertilizer

Materials and methods: 1. Barbed artichoke: a) the Samarkand State University's area of expertise; b) the experience of the Tashkent Pharmaceutical Institute of Land (typical soils);

Results: It should be noted that the use of carbamide and phosphorus plant delayed less humus in the soil and hence a high level of fertility of the soil. carbamide and phosphorus fertilizer plant delayed the use of nitrogen in the soil microorganisms

will go through the body and the structure of the organic substance in the soil, which maintains a flow of nitrogen washed.

Most importantly, the impact carbamide and phosphorus fertilizer departure tax gaseous nitrogen is reduced by 15-20 percent. As laid carbamide and phosphorus fertilizer ammonium nitrate form of nitrogen in the soil than in version (20-25%) will be reduced. Urea or through the washing of the tax increase in the nitrate form of nitrogen gas to reduce the flight mode. This means that the external environment will lead to the reduction of harmful nitrates and nitrites.

Impact on the effectiveness of the fertilizer urea formaldehyde soil conditions, it will depend on the terms and methods (Yarovenko and others, 1964; Madraimov and others, 1966; Yarovenko, 1969). Salinity, light conditions typical soils, if delayed cynara scolymus of hectare, carbamide and phosphorus fertilizer 220-230 pounds are used. 40% of the amount of fertilizer before planting, and the rest of the plant and making sure it 2-3 real leaflets budding better to print a depth of 12-14 cm, and the yield of 20-30% per hectare.

At the end of the period of growth of the plants used less than carbamide and phosphorus fertilizer inserted into urea nitrogen in the soil. If the movement is less than the amount of nitrogen in the soil or soil fertility is low, it issued at the time of flowering of dehydration and instead of carbamide and phosphorus fertilizer positive influence on clusters of grapes are mixed with ammonium nitrate or urea and 10-15% in addition to the per hectare yield.

Conclusions. Slow the effects of carbamide and phosphorus fertilizer typical soils, meadow saline soils, especially in light gray soils the best results. According to experiments conducted in saline conditions of light soils the amount of nitrogen applied per hectare and 150 kg while its 50% 15-20 days before planting, and the rest is given during the dehydration of barbed yield per hectare yield of 50-60% of the prickly artichokes urea compartment 845 centners per hectare carbamide and phosphorus fertilizer tax 912 quintals respectively. Carbamide and phosphorus fertilizer osmotic pressure of the soil due to the application of this method and the amount of nitrate nitrogen in the form of urea decreased significantly compared introduction. Thus, the saline conditions of light soils prickly artichokes 800-900 centners per hectare, half of the planned carbamide and phosphorus fertilizer satisfied with the pre-application during the remaining half split.

ESSENTIAL OIL HERBS TEUCRIUM POLIUM L.

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Introduction. The plants used in folk medicine, are of particular interest to expand the resource base. These plants include Teucrium polium L. - herbaceous perennial from the family Lamiaceae. In folk medicine, it is used in disorders of the gastrointestinal tract, edema, jaundice; eczema as healing wounds; in mycosis and abscesses; in diseases of the urinary and gynecological diseases. The official medicine in our country there are no data on the use of herbs Teucrium polium.

Previously, we found that herb Teucrium polium accumulate various biologically active substances: essential oils, flavonoids, phenolic acids, tannins, triterpene compounds, organic acids, iridoids. The quantitative content of essential oil in the raw samples was 0.22-0.28%. The essential oil of this plant has a broad spectrum of biological activity – antibacterial, antifungal, antiseptic, antiviral, anti-inflammatory.

That is why the study of the essential oil composition of the Teucrium polium, which grows in the North Caucasus is a specific scientific and practical interest.

Aim. Determination of essential oil component composition Teucrium polium, growing in the Stavropol Territory.

Materials and methods. The object of the study served as the herbs of the Teucrium polium. Collection of raw materials was carried out in the flowering phase in the Stavropol region in the Georgievskiy district and is dried in the shade at 20-25^{0}C. shrinkage ratio was 4:1. Yield 25% of raw materials. Raw sample (sample average) for the studies prepared by quartering. Humidity was determined by the method of the State Pharmacopoeia XIII. It was established experimentally that the loss on drying was 8.9%. The raw material is a mixture of whole or partially crushed stalks pieces, leaves and flowers.

For essential oils used exhaustive method of hydrosteamdistillation. An average sample of air-dried raw material to a value crushed particles passing through the sieve with openings of 2 mm in size in an amount of 1.0 kg were charged in an all-metal installation with Clevenger showerhead. Isolation of essential oil is carried out for 10 hours to complete its discharge, which was controlled experimentally. Quantitatively collected in Clevenger showerhead defended essential oil, was dried over anhydrous Na_2SO_4. The composition of the

essential oil components herbs Teucrium polium performed the next day after its receipt. The yield of essential oil was determined in terms of absolutely dry raw material.

Essential oil component composition defined chromatograph Agilent Technologies 7890 GC System (US) with a quadrupole mass spectrometer as a detector 5975S using a capillary column with the phase of 5% diphenyl-95% dimethyl siloxane with an inner diameter of 0.25 mm. The content of components were calculated by peak areas, was carried out to identify the individual components by comparing retention indices and linear full mass spectra with corresponding data of the individual components. coincidence rate was not less than 97%. At full coincidence of the mass spectra and retention indices of linear test compound known terpenoids and individual identification shall be deemed final.

Results and discussion. The experiment established that the essential oil is distilled Teucrium polium during 10 hours of continuous distillation, since the increase in time even stripping for 2-4 hours leads to no further separation of essential oil. The yield of essential oil on the results of 6 distillation was 0.20±0.11% of the sample is completely dry.

The method of gas chromatography-mass spectrometry in the essential oil of the herb Teucrium polium confirmed to contain 55 individual components, including 3 of unidentified substances. The main components of essential oils are: kadine trans-1,4-diene (13.32%), trans-β-farnesene (8.19%), τ-kadinol (6.63%), γ-himahalen (6.56%) germakren D (6.16%), β-turmeric (6.02%) cis-β-farnesene (5.98%), (1E, 4Z) -germakren B (5.11%) kadalen (3,67%), γ-elements (3,57%), τ-muurolol (2,82%), δ-cadinene (2.37%), di-epi-α-kedren-(1) (2.09%), bicyclogermakren (1.99%), α-bizabolen (1.41%), α-kopa (1.02%), himahalen epoxide (1.00%).

Conclusions. The exhaustive method of hydrosteamdistillation highlighted the essential oil from the herb Teucrium polium, growing in the Stavropol region in the Georgievskiy district.

The method of gas chromatography-mass spectrometry identified 52 components, the main ones are sesquiterpenes (kadine trans-1,4-diene, trans-β-farnesene, t-kadinol, γ -himahalen, germakren D, β-turmeric).

PHYTOCHEMICAL STUDY OF PURSLANE (PORTULACA OLERACEA. L)

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Introduction. Purslane is a common plant that grows on all continents and one of the most widespread weed in Ukraine. Portulaca oleracea is an annual succulent in the family of Portulacaceae. Purslane is rich in antioxidant vitamins α-tocopherol, ascorbic acid, and β-carotene, as well as polyphenols and glutathione, and the amino acids isoleucine, leucine, lysine, methionine, cystine, phenylalanine, tyrosine, threonine, and valine. It possesses a number of pharmacological effects such as antidiabetic, antioxidant, neuronal and anti-inflammatory, immunomodulatory, organo- and neuroprotective activity.

Aim. Obtaining lipophilic and hydrophilic fractions of the Portulaca herb and studying the phytochemical composition.

Materials and methods. The object of the research was the herb of the Portulaca oleracea L., collected in the Kharkov region (Ukraine) in July, 2016. The herb was dried at a temperature 50-60°C and was crushed into powder by the plant pulverizer. Lipophilic fraction was obtained by exhaustive extraction with dichloromethane in a soxhlet extractor. The method of repeated extraction with 80% ethanol and hot water was used. After extraction, the solvent was distilled off under vacuum. Thin layer chromatography (TLC) and paper chromatography (PC) in various solvent systems were used for the detection of substances.

Results and discussions. The lipophilic, ethanolic and aqueous fractions were obtained in a yield of 3.8, 15.0, 17.5%, respectively. Using common methods of phytochemical analysis, coumarins, chlorophylls and carotenoids were found in the lipophilic fraction. Flavonoids and hydroxycinnamic acids were discovered in the ethanol extract by TLC in solvent system *n*-butanol-acetic acid-water (4:1:2). Free amino acids, hydroxycinnamic acids and polysaccharides were found in the aqueous extract. Monosaccharide composition of polysaccharides was studied by PC after hydrolysis of polysaccharides with 5% sulfuric acid in the *n*-butanol-pyridine-water solvent system (6:4:3). The chromatogram was sprayed with aniline-phthalate reagent and heated at 100°-105°C for 10 min. Glucose, galactose, mannose, xylose, arabinose and rhamnose were detected.

Conclusions. The results of phytochemical studies of the purslane herb fractions is required to their further standardization and pharmacological research.

COMPONENT CONTENT OF VOLATILE COMPOUNDS OF *MENTHA AQUATICA* L.

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Introduction. Considering the wide disseminating and variety of chemical content of plants of family *Lamiaceae*, the actual is research of unpharmacopoeia plants, members of this family. Such plant is *Mentha aquatica* L. This plant is widespread on all territory of Ukraine. Grows along the banks of ponds and rivers. Since it is known that preparations of peppermint are widely used in medicine as an anti-inflammatory, antimicrobial, antioxidant and neuroprotective, the actual is pharmacognostic study *Mentha aquatica* L. in order to use this material as a complementary source of biologically active substances (BAS).

Aim. The aim of our study was to investigate the component content of volatile compounds of *Mentha aquatica* L. leaves.

Materials and methods. The object of study was the leaves of *Mentha aquatica* L. collected in July 2016. For experiment used dry raw material. For the investigation the qualitative composition and quantitative content of volatile compounds was used Gas Chromatographic-Mass Spectrometric method in chromatograph 5973N/6890N MSD/DS Agilent Technologies with a mass spectrometer detector 5973N. As an internal standard used the tridecane. In the process of distillation volatile compounds are adsorbed on the internal surface of the reflux condenser. Adsorbed substances is washed off after cooling the slow addition of 3 ml of pentane in a dry vial for 10 ml. Washout was concentrated by blowing (100 ml/min), high-purity nitrogen till the residual volume of extract 10 ml, it completely taken by chromatographic syringe. Conditions of analysis: chromatographic capillary column diameter 0,25 mm; carrier gas – helium; the temperature of thermostat 50 ^{0}C with programming 4^o/min. to 320 ^{0}C. The sample injection rate was 1.2 ml/min for 0.2 min; the capillary chromatographic column INNOWAX with the external diameter of 0.25 mm and the length of 30 m; carrier gas (helium) was 1.2 ml/min; the heater temperature was 250°C. For quantitative calculations used the method of internal standard.

Results and discussion. In leaves of *Mentha aquatica* L. were identified 20 volatile compounds of different chemical nature: terpenoids (α-pinene, limonene, caryophyllene, caryophyllene oxide), higher alcohols and hydrocarbons.

Conclusions. Since it is known that the identified substances have antimicrobial activity, the study shows the prospect of obtaining a lipophilic complex of leaves of *Mentha aquatica* L. and determining its antimicrobial activity.

RELEVANCE OF COSMETICS BASED ON IRIS

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Introduction. In our time cosmetics on plant basis become all more popular. Cosmetics for skin are the specially developed chemical medicines which apply to cleaning and protection of skin against an adverse effect of factors of the external environment, to her maintenance in good shape. Cosmetics for care of skin are divided on clearing, toning, feeding, moistening, protective, regenerating. Irises are an insufficiently known plant that has a row of advantages and features, one of that is ability to regenerate cell that prevents aging of skin. Iris (*I. germanica, I. pallida, I. florentina)* has gained great attention from the cosmetic and perfume industries due to their violet-like smell caused by irone-type compounds. Besides, *Irises* were reported to have various biological properties, including potent antiulcer, anticancer, antioxidant, piscicidal activities and other.

In the Crimea and Moldova cultivated irises and obtained from them the essential oil even the fifties. But production of oil does not exceed 30 kg/year. Technology was not justified and oil have ceased receive. An essential oil of iris rhizomes known as "*Orris butter*" consisting of myristic acid, with irone, ionone, methyl myristate. Isoflavonoids include irisolidone, irigenin and iridin. In volatile oil, chief constituents are cis-α- and cis-γ-irones.

Sixteen species of Iris genus inhabit the Ukraine. Some of them are promising for obtaining essential oils. Essential oil of the I. pallida, I. halophila, I. graminea, ect. of Ukraine populations was not previously studied, so it was very interesting to obtain essential oil and to study its component composition.

Materials and methods. We have studied the component composition of essential oil of the leaves and rhizomes of irises of Ukraine flora by chromatography-mass spectrometry method. Irises species harvested from the collections of botanical gardens of V. N. Karazin Kharkiv National University (Kharkiv, Ukraine; 2015). Essential oil was produced by steam distillation. The study was conducted on an Agilent Technologies 6890N chromatograph with 5973 mass-spectrometric detector. Constituents were identified using NIST05 and Wiley2007 mass-spectra libraries in combination with AMDIS and NIST programs for identification.

Results and discussion. Mostly as basis of cosmetic composition plant oils are used. Medicinal properties of irises rhizomes are caused by their chemical composition: they contain essential oil, that is used in perfumery, cosmetology, medicine; ascorbic acid, sugar, flavonoids, carotenoids, fat oils, tannins and glycosides.

Leaves of iris contains the vitamin C, which protects cells from a senilism, operating as an antioxidant, improves protective forces of organism. In a cosmetology use I. florentina, I. pallida and I. germanica. Irises promotes smoothing of skin, gives softness and velvet; prevents emergence of wrinkles; effectively fights against undesirable pigmentation. Properties of Iris florentina find application in production of cosmetics such as Nuxe, Sisley, Babor, Guerlain, Clarins, Lierac Regulance, Swiss.

Essential oil of the rhizomes of *I. florentina*, *I. pallida* and *I. germanica* use in aromatherapy in mixtures for a supervision upon a skin. Rhizomes of *I. japonica* accelerate healing of wounds. Essential oil of *I. germanica* contains more than 140 substances. The most significant of them: stearopten, eleopten, geraniol, benzaldehyde, linalool, ketones, irones, methylsalicylate, salicylic, olein acids.

Aromatherapy recommends using of iris oil for bronchial inflammation, coughing, as well as in mixtures for the care of the skin. Essential oil of iris normalize function of the brain, has a detoxifying, diuretic, expectorant, strengthens the immune system. It returns the resiliency of skin, stimulates the height of hair, improves a health and original appearance of hair. Irises oil has the expressed antiseptic and regenerating action, is immunomodulator.

The essential oil of *Irises* of Ukraine included terpenoids, their oxygenated derivatives (alcohols, ketones, aldehydes, esters), aromatic compounds, and triterpenoids. Triterpenoid squalene is distinguished from components according to contents: *I. pseudacorus* – in leaves 26% and in rhizome 21%; in leaves of *I. halophila* (22.84%); slightly less than in the leaves of *I. germanica* (17.01%) and *I. versicolor* (16.17%); in leaves of *I. graminea* (5.95%), *I. pallida* (6.12%) and *I. hungarica* (16.08%); the least content in the rhizomes of *I. hungarica* (0.96%) and *I. pallida* (0.69%), etc. Essential oils presented with terpenoid and aromatic compounds have antimicrobial, antioxidant and calming action

Squalene shows antimicrobial, moistening, immunostimulatory to the action; stimulates penetration of components deeply in an epidermis that creates a powerful positive effect; it is neutral and there are not contra-indications to application. Besides, in among components of irises oil sesquiterpenoids (geranylacetone, farnesylacetone, hexahydrofarnesylacetone, ect.) have been identified, are known exhibit an antimicrobial and cytotoxic activity. Fatty acids (palmitic, myristic, caprylic, lauric, ect.) their esters have antioxidant, antifungal, anti-inflammatory and immunomodulatory properties.

Conclusion: chemical composition of essential oil of irises gives an opportunity to apply them as a part of the antioxidant, anti-inflammatory, moisturizing cosmetics. Thus, the conducted analysis of the market of cosmetics, rich component structure, give good prerequisites for development new the phytocosmetic of means for skin, with regenerating, calming actions.

ANATOMICAL-DIAGNOSTIC FEATURES OF THE FLOWER OF CATNIP (*NEPETA CATARIA* L.)

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Introduction. *Nepeta cataria* Linn (Family *Lamiaceae*), commonly known as Catnip, is a herbaceous plant which has a wide geographic distribution, including Russia. This plant cultivated everywhere as an aromatic plant. In traditional medicine *Nepeta cataria* L. was used as a sedative, spasmolytic, antidepressive. Moreover, traditionally, the tea made of its leaves also used to relieve gastrointestinal and respiratory disorders such as colic, diarrhea, cough, asthma and bronchitis. Antimicrobial, immunomodulatory and antioxidant activities have been reported. The medicinal properties of *Nepeta cataria* L. are usually attributed to their essential oils, flavonoids and hydroxycinnamic acids. However, *Nepeta cataria* L. has not been listed in the State Pharmacopoeia of the Russian Federation because quality standards for *Nepeta cataria* L. are not available.

Aim. The purpose of this study was to describe the anatomic-diagnostic signs of the flower *Nepeta cataria* L. as parameter for identification of medicinal vegetable raw materials.

Materials and methods. This study was based upon examination of plants of *Nepeta cataria* L. cultivated at the Saint Petersburg State Chemical-Pharmaceutical Academy's Arboretum, Saint-Petersburg, Russia. Analyses of the flower were made in accordance with the requirements of monograph "Microscopic examination of herbal drugs and herbal drug preparations", the State Pharmacopoeia of the Russian Federation.

The flower was examined using fresh material, hand sectioned and viewed by binocular microscope Carl Zeiss Axio Lab.A1 with phototube AxioCam MRCS 5 and ZEN software. To improve the resulting image by Helicon focus software.

Results and discussion. The micomorphological analysis of the calyx showed longitudinally elongated epidermal cells with sinuous anticlinal walls and finely thickened striated cuticle (Fig. 3).

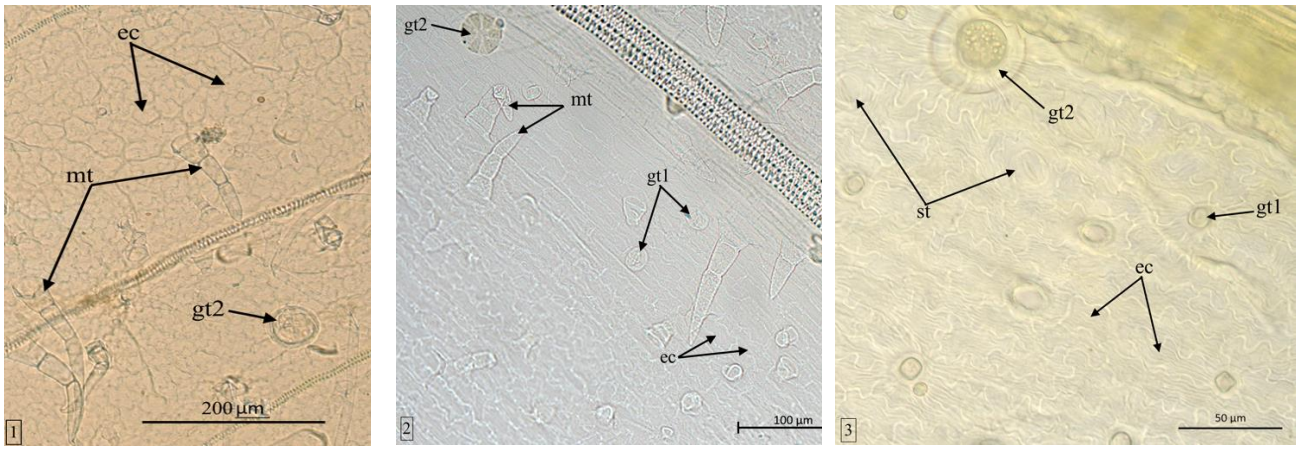
In the corolla tube in top the morphology of the epidermal cells presents no differences with regard to calyx epidermal cells, while the epidermis of the petal lobe analysis shows polygonal cells with wavy anticlinal walls. The epidermal cells of the petal lobe show wave shaped protrusions. The protrusions become less conspicuous when moving from the petal lobe towards the base of the corolla tube (Fig. 1, 2). The

stomata of the diacytic type are present on the epidermis of calyx (Fig. 3).

The analysis of trichomes and secretory tissues shows:

- multicellular hooked, straight or cranked trichomes, uniseriate, with pointed terminal cell and verrucose surface, the base of the trichomes is flattened, surrounded by 3–7 adjacent subsidiary cells (Fig. 1,2); glandular trichomes made up of a short stalk cell and a large globular head, composed of 4-6 cells separated by vertical walls (Fig. 1-3); glandular trichomes made up of a short stalk cell with a sub-spherpoidal or bi-cellular head, surrounded by 9–11 adjacent subsidiary cells (Fig. 2, 3); these trichomes and secretory structures are present on the epidermis of calyx and corolla tube.
- glandular trichomes made up of a subcylindrical stalk cell and multicellular head only on the epidermis of corolla tube.

These trichomes and secretory tissues are very rare in the epidermis of petal lobe.



Figures 1-3. Detail of the floral of *Nepeta cataria* L.

1: Detail of the surface of the petal lobe epidermis; 2: Detail of the surface of the corolla tube epidermis; 3: Detail of the surface of the calyx epidermis; ec=epidermal cell; st=stomata; gt1= glandular trichomes made up of a short stalk cell with a sub-spherpoidal or bi-cellular head; gt2= glandular trichomes made up of a short stalk cell and a large globular head, composed of 4-6 cells separated; mt= multicellular trichomes.

Conclusions. Conducted microscopic analysis of the flower of the Catnip (Nepeta cataria L.) which established anatomic-diagnostic signs, which is the element of standardization of medicinal vegetable raw materials. The main diagnostic criteria flower catnip common are the presence of stomata of the diacytic type, multicellular trichomes, glandular trichomes with a stalk cell and a large globular head composed of 4-6 cells, glandular trichomes with a stalk cell and or with a sub-spherpoidal or with bi-cellular head, glandular trichomes with a subcylindrical stalk cell and multicellular head.

The received results allow to identify authentically raw materials of the Catnip and will be further used in the development of normative documents on this type of medicinal vegetable raw materials.

DEFINING OPTIONS OF STANDARDIZATION LINGONBERRY LEAVES ACCORDANCE WITH THE METHODS AND REQUIREMENTS OF THE STATE PHARMACOPOEIA OF UKRAINE

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Introduction: kidney and urinary tract diseases occupy a leading place in the structure of diseases. Every third person in the world is prone to diseases of the genitourinary system. In Ukraine 10% of the population have signs of chronic diseases of the genitourinary system. Decoction of leaves lingonberry for the treatment of these diseases in traditional medicine. As Ukraine is committed to the European integration, the oll documentation for raw materials should be harmonized with the European Pharmacopoeia. As there isn't a monograph on the leaves lingonberry in the SPU, so development national monograph on this raw material is the actual task.

Purpose: The purpose of research is to determine the parameters of standardization of lingonberry leaves in accordance with the methods and requirements of the State Pharmacopoeia of Ukraine and carry out standardization of this raw materials

Materials and Methods: Lingonberry leaves purchased from a pharmacy is the object of the study, which is analyzed by SP XI requirements and the proposed project SPU monograph, which was developed on the basis of SPU monograph " bearberry leaves". Analyzing the leaves we used standardized techniques and unified technique of SPU.

Results and discussion: To determine the parameters of standardization lingonberry leaves we used monograph of SPU " bearberry leaves", which is the traditional substitute this raw material.

Standardization of leaves lingonberry is asked to carry out the description, macro- and microscopic characteristics, identification by TLC, to control the content of impurities, stems (up 5%) and other impurities (up 3%), leaves of others as color (up 10%); loss in weight on drying (up 10%), common ash (less than 5%); content of derivative of hydroquinone (not less than 3%).

Analyzed three sets of lingonberry leaves that were purchased at a pharmacy. All samples were answered proposed parameters.

Conclusions: The proposed parameters of standardization will be form for the basis of national monograph SPU "lingonberry leaves."

STANDARDIZATION OF THE MEDICINAL FORM CONTAINING PURSLANE EXTRACTS

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Purslane --- Portulaca oleracea. It is abundant plant in our country ,and it is widely used as food production,biological active agent, and medicinal form as Gipoklimic, in European countries, China and India**.** But in our territory wild purslane is thrown away and doesn't study its properties. Taking this into consideration we aimed to choose compound form of drug by subterian part of dry extract and standardization it.

Materials and methods: at the stage of blossoming and gives fruits the subterian dry extract is collected and extract is obtained by extracting crushed material with purified water. Total constitute of extract is 6.2% . The following medicines are prepared on the base of this extract.

Purslane extracts ----- 180 mg
Extract of licorice ---- 100 mg
Vitamin C ------ 30 mg

Due to the constitute medicinal form capsule is obtained.

To determine truth of the constitute: The weight of 0.1 g capsules 3 times with 10 ml of water is swayed volume of 30 ml of chloroform extracts were combined 1/4 thickened 3 times is worked out with 3 ml of 10% sulfuric acid Acidic combinations are combined total alkaloids specific qualitative reactions are taken (Silicon wolfram acid, Mosk reactive Drogendor reactive, Wagner reactive etc.) 0.1 g of the mass of the capsule in 10 ml of water is being swayed for 2 minutes, foam formation is specific to triterpen glycosides which are indicative of the presence of drugs containing acid gliserizin.

1) 0.1 g of the capsule mass is dissolved in 10 ml of water, 2.6 dixlorfenolindefenol sodium is dropped and red purple color solution becomes colorless (ascorbic acid)

To determine the amount of: The composition of purslane extract combination of alkaloids is identified by titration. For this, five capsules mass is dissolved in 30 ml of water 3 times with 20 ml of chloroform extraction Chloroform extractions are combined and thickened to 1/4 with 20 ml of 0.02 M sulfuric acid solution is swayed for 1 hour with a device. After the acidic separation of the layer of chloroform solution, is swayed with 20 ml of water then titrated with 0.02 M sodium alkaline solution (indicator metil purple)

Combination of alkaloids in capsule to norepinephrine is calculated to asses the amount on the basis of the following formula.

$$x = \frac{(V - \mathrm{Vo}) * \mathrm{T} * \mathrm{R} * \mathrm{P}}{a}$$

Hydrochloric acid in 1 ml of 0.02 MLI 0.0033 g is suitable to norepinephrine and medicine is amounted to 0.0009 ---- must be in a range of 0.001 g.

Glisrizin acid: 0.1g of the capsule with a weight of 20 ml of nitric acid (pH = 1.5) are heated with the acid in acetone. This process is repeated 3 times acetone combinations are combined 0.25% ammonia solution added until obtaining (pH = 9) (the universal indicator paper), the precipitate is filtered with filter paper was dissolved in purified water and is diluted 50 ml measuring flask with water (a solution) 2 ml A solution of 50 ml measuring flask of water.

This solution`s optical density is identified with spectrophotometer at 258 nm wave length of 1 cm cuvette. Amount of grams glisirizin acid in medicine is calculated using the following formula.

$$x = \frac{D * 822 * 25 * 100}{a - b * 11000 * 1000}$$

One capsule contains Glisirizin acid, the amount should not be less than 0.01 g.

Ascorbic acid: The weight of 0.05 g capsules is dissolved in 50 ml measuring flask of purified water is poured to the mark. (A solution). 10 ml (A solution) is titrated with 2.6 defenolindefenol sodium till it becomes light red color. One capsule of ascorbic acid, the amount is calculated by the following formula:

$$X = \frac{VK - TP * 50 * P}{a * 10}$$

1 ml of 0.01 M) 2.6 dixlorfenolindefenolsodium 0.000088 grams is suitable to ascorbic acid, its amount in medicine should not be less than 0.02 grams.

Conclusions:

1. it was worked out the purslane extract of complex components of the drug to determine the truth of biologically active compounds and methods.
2. Methods of worked out analysis may be used to determine the drug`s quality analysis.
3. The research is continuing to identify the private correctness, accuracy and suitableness due to validation of drug analysis method .

THE STUDY OF THE CONTENT OF EXTRACTIVES SUBSTANCES OF *V. TEUCRIUM* L. HERB, LEAVES AND FLOWERS

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Introduction. The unpharmacopoeia plant *Veronica teucrium* L. belongs to the *Plantaginaceae* family. The plant has the wide area of distribution on Ukraine territory and in the world flora, grows mainly in meadows and forest clearings. It is grown as an ornamental plant and has many ornamental varieties.

Infusions and tinctures of *V. teucrium* L. herb have been widely used in folk medicine and have been shown the expectorant, the anti-inflammatory and the antiseptic activities. However, the chemical composition of biologically active substances of *V. teucrium* L. is studied poorly. Medicines obtained from it is not available.

Therefore, the development of extracts obtained from *V. teucrium* L. and this standardization are the actual issue.

The aim of our research was study of the content of extractives substances of *V. teucrium* L. herb, leaves and flowers for the selection of the optimum extractant.

Materials and methods. The objects of study were the air-dried herb, that consisting of flowers, leaves, stems; dried flowers and leaves of *V. teucrium* L., that were collected at flowering phase in the summer 2015.

For the quantification of the content of extractives substances a 1 g (d=2 mm) of herbal drug was extracted by 10 ml of the extractant (1:10), with considering of the absorption coefficients. The absorption coefficient for flowers and leaves are 2, for herb – 2.5. Extracts were obtained by the maceration method with stirring for 2 days, tº = 20-23º C. As extractants were used the distilled water, the ethanol in different concentrations (20 %, 30 %, 40 %, 50 %, 60 %, 70 % and 96 %), and the 95 % methanol. The obtained extracts were filtered and were dried to the constant weight.

The content of extractives had been quantified by the gravimetric method. The study was performed for 5 times. The obtained data were processed statistically.

Results and discussion. In the result of study was found, that the content of extractives substances in *V. teucrium* L. herb extracted by the distilled water was 23.59 %, by the 20 % ethanol – 25.01 %, by the 30 % ethanol – 26.59 %, by the 40 % ethanol – 23.42 %, by the 50 % ethanol – 24.79 %, by the 60 % ethanol – 20.87 %, by the 70 % ethanol – 23.33 %, by the 96 % ethanol – 4.67 % and by the 95 % methanol – 9.29 % (Table 1).

Table 1

The content of extractives substances of *V. teucrium* L. herbal drug (%)

Extragent	Herb	Flowers	Leaves
Distilled water	23.59±0.01	26.69±0.01	25.24±0.01
20 % Ethanol	25.01±0.01	28.58±0.01	24.48±0.01
30 % Ethanol	26.59±0.01	27.23±0.01	23.11±0.01
40 % Ethanol	23.42±0.01	27.86±0.01	22.01±0.02
50 % Ethanol	24.79±0.01	30.30±0.01	22.84±0.02
60 % Ethanol	20.87±0.02	28.93±0.01	23.41±0.01
70 % Ethanol	23.33±0.01	16.63±0.02	22.87±0.01
96 % Ethanol	4.67±0.03	5.30±0.03	3.92±0.03
95 % Methanol	9.29±0.03	12.11±0.02	8.10±0.03

Note: n=5, p<0.95

In *V. teucrium* L. flowers a content of extractives substances extracted by the distilled water was 26.69 %, by the 20 % ethanol – 28.58 %, by the 30 % ethanol – 27.23 %, by the 40 % ethanol – 27.86 %, by the 50 % ethanol – 30.30 %, by the 60 % ethanol – 28.93 %, by the 70 % ethanol – 16.63 %, by the 96 % ethanol – 5.30 % and by the 95 % methanol – 12.11 %.

In *V. teucrium* L. leaves a content of extractives substances extracted by the distilled water was 25.24 %, by the 20 % ethanol – 24.48 %, by the 30 % ethanol – 23.11 %, by the 40 % ethanol – 22.01 %, by the 50 % ethanol – 22.84 %, by the 60 % ethanol – 23.41 %, by the 70 % ethanol – 22.87 %, by the 96 % ethanol – 3.92 % and by the 95 % methanol – 8.10 %.

In the result of study was found, that the 30 % ethanol was the optimum extractant for *V. teucrium* L. herb (26.59%), also the 20% ethanol and the 50% ethanol can be used for extraction.

For *V. teucrium* L. flowers the 50 % ethanol was the optimum extractant (30.30%), also the 20% ethanol and the 60% ethanol can be used.

For *V. teucrium* L. leaves the distilled water was the optimum extractant (25.24%), also the 20% ethanol and the 60% ethanol can be used as extragents for extraction.

Conclusions. The minor difference of the content of extractives substances, extracted by the ethanol in concentrations of the 30%, 50%, 60% and extracted by the 20% ethanol from *V. teucrium* L. herb, flowers and leaves, have been indicated the advisability of using the 20% ethanol as the optimum extractant.

The obtained experimental data can be used to the development the relevant of herbal drug (*V. teucrium* L.) quality control methods and of its extracts.

MEDICINAL PLANTS USED IN THE TREATMENT OF DISEASES OF THE UPPER RESPIRATORY TRACT

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Introduction. Herbal remedies popularity among the population of Ukraine today is high. For example, in the treatment of upper respiratory tract demand drugs based on ivy, cowslip, Icelandic moss, marshmallow. Unfortunately, in today's time of these drugs on our dominant pharmaceutical market is the proportion of foreign vehicles manufacturers. In this regard, the development of new means of pharmacological group deserves the attention of scientists.

When developing a new pharmaceutical complex herbal preparation important factor is the type of plant material used. Based on the physicochemical properties of one or another part of the plant and selected pharmaceutical form of future medicinal product. For example, the method of brewing herb tea is different from using bark or roots. Similarly, these features are taken into account in the design manufactures industrial technology. The method of extraction, solvent type significantly affect the properties and pharmacological properties of the resulting extract and directly related to the type of material. It is worth noting that the wrong type selected raw materials may lead to non-repeatability methods of quality control of the finished product, or incomplete transition to the desired bioactive compounds in the final dosage form of the drug.

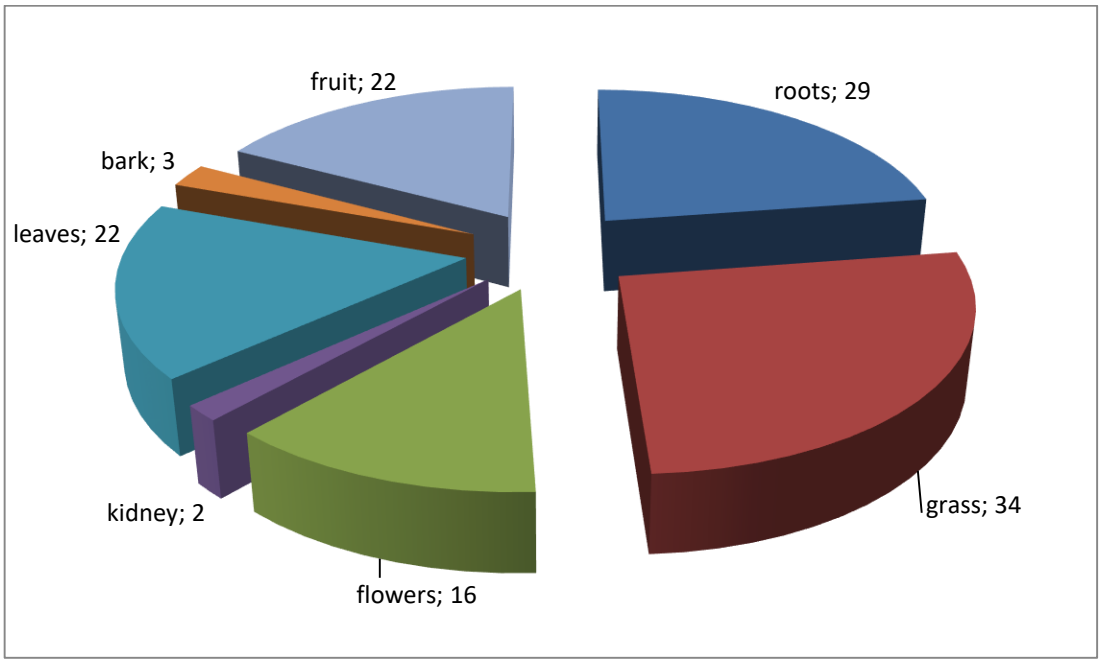
Aim. To analyze the literature regarding plant material, which is used to treat respiratory diseases. Identify the type of raw material, which is often used in traditional medicine.

Materials and methods. Our research conducted using literature that serves the experience of traditional medicine in the treatment of respiratory diseases. Done selection of plants used in this case analyzed what their morphological parts used for therapeutic purposes. Done statistical analysis of the results.

Results and discussion. As a result of the search, we selected 128 plants used in traditional medicine for the treatment of respiratory diseases. In the processed formulations, the following types of medicinal plants like grass, roots, fruits, leaves, flowers, bark and buds. The results shown in picture 1.

The most (34 plants), as seen from the chart, as a medicinal plant used grass - above-ground part of the plant, which includes stem (shoot) with leaves: *Achillea millefolium* L., *Artemisia vulgaris* L., *Equisetum arvense* L., *Hypericum perforatum*

L., *Phyllitis scolopendrium* (L.) Newm. and other.



Pic. 1. The use of medicinal plant individual plants (units)

Slightly less (29 plants) used underground parts of plants. This group also includes plants that use groundwater shoots modifications, namely tubers, rhizomes and bulbs. This category in particular include: *Archangelica officinalis* (Moench.) Hoffm., *Elytrigia repens* (L.) Nevski, *Daucus carota* L. ssp. sativus, *Geum urbanum* L., *Inula helenium* L., *Levisticum officinale* Koch. etc.

Often used in the formulations alone leaves of plants (22 plants): *Majorana hortensis* Moench., *Melissa officinalis* L., *Mentha piperita* L., *Ruta divaricata* Ten., *Salvia officinalis* L. and other.

No less often (also 22 plants) use fruits and seeds, including *Rubus saxatilis* L., *Viburnum opulus* L., *Hippophae rhamnoides* L., *Physalis alkekengi* L., *Carum carvi* L., *Pimpinella anisum* L.

Using flowers to plant a medicinal plant was found in 16 plants: *Calendula officinalis* L., *Arnica montana* L., *Sambucus nigra* L., *Tussilago farfara* L., *Thymus serpyllum* L. and other.

In some cases, there are plants, which in a medicinal plant can be used several morphological units (*Betula pendula* Roth. – buds, leaves, juice; *Pinus sylvestris* L.– buds, turpentine; *Taraxacum officinale* Wigg. – roots, flowers; *Filipendula ulmaria* (L.) Maxim.– blossoms, roots), bark (*Salix alba* L.), stem (*Cerasus vulgaris* L.).

Conclusions. The results show that most of traditional medicine in the treatment of respiratory diseases used type of raw grass. This raw material is easy with the provision and can be used in the form of tea, which in turn makes use of simple and affordable at home, and is most popular in manufacturing technology extracts for pharmaceutical companies.

DETERMINATION OF QUANTITATIVE CONTENT OF THE DIFFERENT GROUPS OF PHENOLIC COMPOUNDS IN THE SERIES *FRAXINUS EXCELSIOR* LEAVES

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Introduction. *Fraxinus excelsior* belongs to the olive family, which contains 30 genuses and approximately 600 species. This plant can be found in both in the wild and in a cultivated state in Ukraine. *Fraxinus excelsior* is widely used in traditional medicine due to rich chemical composition. All raw materials of this plant: leaves, bark, fruit, stems, wood and roots are used in traditional medicine. Groups of phenolic compounds, that included in leaves have tonic, neuroprotective, anti-depressant, anxiolytic, immunomodulating, hepatoprotective, antioxidant effects.

Aim. Establishing of quantitative content of the amount of the different groups of phenolic compounds in the series *Fraxinus excelsior* leaves.

Materials and Methods. There have been investigated 5 series of leaves, that we were harvesting during 2015-2016 years in the Kharkiv, Poltava, Vinnytsia, Zaporizhia and Lviv regions. The content of the phenolic compounds amount has been determined by spectrophotometric method in terms of a gallic acid, the content of the hydroxycinnamic acids amount has been determined by spectrophotometric method in terms of chlorogenic acid. To establish of quantitative content of the flavonoid glycosides amount has been used by spectrophotometric method that based on the usage of aluminum chloride in terms of a rutin. The content of the tannins has been determined by complexometric titration in terms gallotannin.

Results and discussion. There have been established the content of the of phenolic compounds amount in the series *Fraxinus excelsior* leaves, that is at least 6,50±0,29%,in terms of absolute dry raw materials. There have been established content of the hydroxycinnamic acids amount in 5 series *Fraxinus excelsior* leaves – at least 2,88±0,01%. All series leaves contained at least 0,87±0,01% of the amount of flavonoids. There have been established quantitative tannins in 5 series leaves was at least 0,18±0,01%.

Conclusions. There have been conducted quantitative determination of the contents of phenolic compounds: the phenolic compounds amount, the amount of hydroxycinnamic acids, the amount of flavonoids and tannins in 5 series *Fraxinus excelsior* leaves. There have been set lower limits content of each group. There have been choose standardization option of raw materials *Fraxinus excelsior* leaves, that we propose to standardize the content of phenolic compounds in amounts based on gallic acid.

THE DETERMINATION OF PRESENCE OF RUTIN AND QUERCETIN IN LEAVES OF SCHISANDRA CHINENSIS

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Research of leaves of Schisandra chinensis is topically for expansion of source of raw materials of medicinal degister, which contains adaptogens and optimizations of phytochemicals studies of this class of connections.

The search of the optimal system for realization of thin-layer chromatogram for Schisandra chinensis became aim of this work. Research object is tinctures of leaves, seeds and garden-stuffs of Schisandra chinensis. For setting the thin-layer chromatogram the systems of solvents of butanol - acetic acid – water (4:1:2) were used, 15% CH3COOH and ethylacetate – formic acid – water (88:6:6); chromatographics plates «Silufol» number 366, 254 and «ПТСХ – АФ – А – УФ»; revealing reagents FeCl2, 3% solute AlCl3 and saturated spirit solution FeSO4. Data in visible light and OOH - light fixed with the camera Nikon Coolpix 16.0 megapixels. Realiztion of thin-layer chromatogram showed that the plates «ПТСХ – АФ – А – УФ» and number 366 have the best division in the system BAW (4:1:2) and ethylacetate – formic acid – water (88:6:6). Then, the system BAW (4:1:2) were choosen for the search of phenic grounds, rutin and quercetin in a tincture from leaves of Schisandra chinensis. The biggest division was given by a chromatographic plate «ПТСХ – АФ – А – УФ». More clean and exact spots in OOH-light were educed on a plate «Silufol» number 366. Revealing reagents in this case were solutions of 3% AlCl3 and saturated spirit rasters FeSO4. 3% solute AlCl3 became the best revealing reagent, that in turn, in interaction with phenic grounds gave colors in OOH-light from brightly-green to lemon. But plates under the effect of this revealing reagent were subject to corrosion and did not save the primordial kind. Same with his action appeared the saturated spirit solute FeSO4. In interaction with phenic grounds it colored them in dark tones.

As the result of handled studie it is possible the pevelopment of identification from leaves of Schisandra chinensis in relation to chromatographic behavior of rutin and quercetin.

RESEARCH IN BIOLOGICAL ACTIVE SUBSTANCES OF THE BEARBERRY LEAVES EXTRACT, WHICH WAS OBTAINED WITH 50 % ETHANOL

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Introduction. The bearberry is a medicinal plant of the family *Ericaceae*, which is widely used in national and traditional medicine for treatment of the urinary system. Decoctions of bearberry leaves is used for cystitis, chronic nephritis, urethritis. This medical form has disadvantages such as: long preparation period, inconvenience and irregularity of dosage, short expiration date, absence of standardization before using. Therefore it is advisable to invent national standardization medicine on the base of biologically active substances of bearberry leaves.

Aim. Making a research of the chemical content of the dry extract from the of bearberry leaves, received with 50 % of ethanol was the aim of this work.

Materials and methods. The object of research was the dry extract of the bearberry leaves, which was received with 50 % of ethanol the ratio 1:10. The research was made in comparison with a decoction, which was received by the classical technology. The prior chemical research of the extract was conducted by normative methods thin-layer chromatography. The Quantitative analysis showed the content of arbutin, hydroxycinnamic acids, flavonoids and amount of phenolic compounds. It was made by using pharmacopoeia spectrophotometry methods.

Results and discussion. Simple phenols (arbutin), phenol carboxylic acids (gallic and ellagic acids), hydroxycinnamic acids (*p*-komarova and chlorogenic), flavonoids (luteolin, quercetin and kaempferol), tannins (gallo- and ellagotannins) were identified in the extract by the method of thin-layer chromatography.

Table

The quantitative analysis of phenolic compounds in the extracts from bearberry leaves

Group BAS	Assay, % (in terms of absolutely dry raw material)	
	The decoction	The dry extract
Arbutin	8,59 ± 0,05	7,56 ± 0,05
Hydroxycinnamic acids	1,58 ± 0,01	1,90 ± 0,04
Flavonoids	1,59 ± 0,04	2,15 ± 0,03
Phenolic compound	8,80 ± 0,05	13,80 ± 0,04

The content of total phenolic compound, flavonoids and hydroxycinnamic acids in the dry extract is more than in the decoction.

Conclusions. The research of chemical composition of the dry extract from the bearberry leaves, received with 50 % ethanol in comparison with the decoction shows that the received extract is a perspective material for the creation of a new medicine on the basement of hydroxycinnamic acids, flavonoids and phenolic compound of the bearberry leaves and the received data will be used for its standardization.

SCOTS PINE STUDY PROSPECTS

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Introduction. The Scots pine (Scotch pine) (*Pinus silvestris* L.) of the *Pinaceae* family is an evergreen coniferous tree. The plant reaches up to 40 m in height and up to 1.5 m in diameter. It is one of the most widespread plant species of forest and forest-steppe zones and is the main forest steppe species of Ukraine. Efficient use of needle-foliage, i.e. waste occurring in lumbering industry, is one of the most relevant problems of forest industry.

Aim. To conduct an analysis of literature data on dissemination, raw materials base, chemical composition, types of biological action of the Scots pine.

Materials and methods. Comparative method, systematized search, integration of information.

Results and discussion. According to the literature data, a pine is the main source of ether oil, rosin, turpentine, turpentine oil, tar. Buds, young shoots and needle-foliage, which contain ether oils, resins, carotenoids, ascorbic acid, phytoncids, pinicicrin bitter substance, flavonoids, phenolcarbonic acids, and tanning substances, are used in medicine. Ether oil contains pinene, carene, terpineole, limonene and other terpenoids.

Pine buds are registered raw material, are included in a range of pharmacopoeias, and are included in the State Pharmacopoeia of Ukraine.

Buds are used in the form of decoctions, infusions and tinctures for inhalation, as an expectorant, as a disinfectant in case of upper air passages diseases, and as a diuretic and an anti-inflammatory agent. Pine needles are included in the composition of I. Traskov antiasthmatic mixture. Vitamin drink is extracted from needle-foliage; it is included in the composition of chlorophyll carotene paste, which is used in case of skin diseases and burn injuries.

Ether oil is included in the composition of medicinal products for treatment of respiratory diseases, supporting-motor apparatus disorders, metabolism, and climacteric syndrome. Turpentine produces analgetic effect and is used in case of lumbago, neuralgia, and myositis. Tar produces disinfecting effect and is included in the composition of Vishnevsky ointment. Activated carbon is used to treat flatulence and in case of poisoning.

Conclusions. Scots pine has sufficient raw materials base and is a promising object for further study.

MICROSCOPIC DIAGNOSTICS OF UNDERGROUND ORGANS OF PRIMULA GENUS

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Introduction. Primula genus is one of most numerous in the world flora, and there are also thousands of artificially created ornamental forms, kinds, and hybrids. There are 9 species spread in the territory of Ukraine. As medicinal plant raw material (MPRM), which has expectorative, general strengthening, diaphoretic, and diuretic actions, rhizomes with roots of Primula veris L., P. officinalis (L.) Hill. are used. However, this species is getting rare, and requires preventive protection and rational use, which can be promoted by revealing and implementation of additional equivalent raw material. Similar to Primula veris, similar as for their chemical composition species are also used in medicine: Primula macrocalyx Bunge and Primula elatior (L.) Hill. As an official medical plant, Primula veris L. is indicated in British Herbal Pharmacopoeia. European Pharmacopoeia contains the following raw material: Rhizome and root of Primula veris L. or Primula elatior (L.) Hill. The State Pharmacopoeia of the USSR, edition XI, does not contain a respective monograph, which indicates to urgency of such monograph development of the State Pharmacopoeia of Ukraine. Identification section of the monograph that is based on microscopic analysis of the whole or milled raw material allows determination of MPRM reliability and detection of admixtures.

Aim. Study and comparison of microscopic structure of rhizomes and roots of 5 wild and cultivated Primula species, determination of common and diagnostic species characters, which can be used for determination of reliability and quality of the recommended initial raw material. The data obtained will promote increase of MPRM arsenal and preservation of natural resources.

Materials and methods. Rhizomes and roots of two wild Primula species: Primula veris L. and P. macrocalyx Bunge, harvested in Ternopil region and Crimea, and three ornamental Primula species: P. denticulata Smith., P. saxatilis Kom., and P. juliae Kusn., cultivated on the plots of M.M. Hryshko National Botanical Garden of the National Academy of Sciences, fixed in a mixture of alcohol-glycerol-water (1:1:1). The study of slices was carried out by commonly used methods. Microscopes MBS 9 and MS 10, as well as camera Samsung PL50 were used.

Results and discussion. On cross and longitudinal sections, the structure of rhizomes and roots has been analyzed; histochemical reactions have been carried out;

diagnostic signs of all types of raw material have been recorded via photographs. The data obtained indicate to the fact that underground organs of the species studied have sufficient quantity of individual and common generic signs. For rhizomes, the following characteristics are common: secondary structure, from fascicular to non-fascicular; thickened covers of external layers of exodermis impregnated with suberin; cortical and medullar parts are well developed, starch-containing, contain idioblasts with essential oil; sclerenchyma is pericyclic; phloem is obliterated. Common characteristics of roots are as follows: the structure is primary or transitive; mesoderm is well developed; endoderm cells are homogeneously thickened; central cylinder with miniscule phloem, without mechanical elements. Cumulative individual signs of rhizomes and roots of the species studied are as follows: Primula veris: starch grains are large, simple; content of idioblasts is colorless. Primula macrocalyx: starch grains are complex; content of idioblasts is colorless. Primula saxatilis: exodermis of rhizomes and roots is multi-layer, dark-brown, with secretory cavities and reservoirs; idioblasts of cortex, xylem, and core contain bright orange secretion; xylem contains mechanical fibers; parenchyma of cortex and core accumulates simple starch and aleurone grains; in the centre of secondary roots, there is nongenuine core. Primula denticulata: parenchyma of rhizome and root cortex practically has no starch grains, with rare single crystals of calcium oxalate of various forms; in parenchyma of all parts of rhizome, roots, and their embryos, there are multiple pigmented cells or their clusters with bright orange, light brown or almost red secretion. Primula juliae: cells of root exodermis are filled with bright orange secretion; parenchyma of rhizome and root cortex practically has no starch grains, with single crystals of calcium oxalate and frequent colored idioblasts; central part of roots consists of nongenuine core.

Conclusions. The studies conducted allowed to support, specify and complement data on anatomicohistological structure of the analyzed species of Primula genus. Comparative analysis has revealed distinctive features of cultivated primulas associated with content of significant quantity of secretory structures with essential oil. The data obtained allow supposition about prospects of ornamental primulas's use as initial plant raw material, which will promote increase of MPRM arsenal, preservation of natural resources, and diversity of wild rare plants. Over the long term, the peculiarities of structure determined may serve as diagnostic signs of MPRM.

THE DEFINITION OF MORPHOLOGICAL AND ANATOMICAL CHARACTERISTICS OF THE RAW MATERIAL OF THE ORCHIDACEAE FAMILY PLANTS

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Introduction. An important aspect of the development of modern pharmacy is to develop high quality, effective and low-toxic medicines. From this side of attracts the attention of medicinal plant material, especially plants, which have long been used in folk medicine.

Orchids are known primarily as beautiful ornamental plants and are favorite greenhouse plants. But unfortunately nowadays these plants are almost never used as a drug. The Orchid family is called the "aristocrats" among plants. For their beauty and uniqueness, many countries have chosen local orchids as their national symbols.

There have always been a stock of processed roots of this plants available since ancient times. Their healing properties were used in various occasions: they were considered a means of sexual activity stimulating; the roots were burned, driving away bad dreams. The first use of this plant is found as a therapeutic drug for various inflammatory processes on the skin, fever, rheumatism, neuralgia, etc.

Aim. To conduct the study of the morphological and anatomical structural features of the Phalaenopsis orchids plant material.

Materials and methods. The object of the study was the leaves of the Phalaenopsis orchid that were harvested in October 2016.

Results and discussion. A morphological study established the following diagnostic features: Phalaenopsis has monopodal branching stem, covered with usually 2-5 fleshy, leathery leaves which are bright green in color, has oblong-oval form. Leaves are sessile and entire, venation parallel. The top leaves often acuminate. Leaf length ranges from 25 to 50 cm and width 10 cm was Observed sheet outlet.

In the course of anatomical studies of the leaves installed the structural features of the underlying epidermal cells, features of stomata and their type.

Conclusions. The study established a set of features of external and internal structure of the leaves of an Orhidaceae family representative – Phalaenopsis as a promising source of medicinal raw material for making herbal remedies.

THE CHROMATOGRAPHY – MASS SPECTROMRTY STUDY OF SALIX ROSMARINIFOLIA L.

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Abstract. Introduction. Plants of the *Salix* genus (*Salicaceae* family) are the promising objects for study. They are the sources of highly active natural compounds used in folk medicine for a long time for the treatment of many diseases. The aim is to determine the component composition of volatile compounds and organic acids of the raw material of *Salix rosmarinifolia L*.

Introduction. One of the priorities of pharmacy is to expand the range of medicines due to introduction of new medicinal plants into medical practice. As it is known, herbal medicines are not inferior to synthetic analogs by their effectiveness; they have a favorable effect on the body with long-term application, and are used in the process of rehabilitation of all age groups. Plants of the *Salix* genus are the promising objects for study. They are the sources of highly active natural compounds used in folk medicine for a long time as anti-inflammatory, diuretic, antipyretic, disinfectant, haemostatic, astringent, sedative, wound healing, choleretic and antirheumatic drug for the treatment of many diseases. Some species of the genus are officinal in the European countries.

Materials and Methods. The objects of research were samples of *Salix rosmarinifolia L.* shoots collected in Kharkiv region of Ukraine in 2014–2015.

The chromatography - mass spectrometry study of the raw material was conducted on an Agilent Technologies 6890N chromatograph with a mass spectrometric detector 5973N at the National Institute of Grapes and Wine "Magarach" of the Ukrainian Academy of Agrarian Sciences by the method. To determine organic and phenolcarboxylic acids the internal standard (50 μg of tridecane dissolved in hexane) and 1.0 ml of the methylating agent (14% BCI3 in methanol Supelco 3-3033) were added to 0.05 g of the dried plant raw material in a 2 ml vial. The mixture was kept in a sealed vial for 8 h at the temperature of 65°C. During this period the exhaustive extraction of the plant material, hydrolysis and methylation of fatty acids took place. At the same time free organic and phenolcarboxylic acids were methylated. The reaction mixture was decanted from the precipitate of the plant material and diluted with 1 ml of distilled water. To extract methyl esters of organic acids 0.2 ml of methylene chloride was added, gently shaken for an hour, and the resulting extract of methyl esters of organic acids was chromatographed on an Agilent Technologies 6890N chromatograph with a mass spectrometric detector 5973N. The sample injection into the

chromatographic column was carried out in the splitless mode, and the rate of the sample injection was 1.2 ml/min for 0.2 min. The conditions of determination were as follows: the INNOWAX chromatographic capillary column with the length of 30 m and the internal diameter of 0.25 mm was used; the carrier gas was helium; the flow rate of the carrier gas was 1.2 ml/min; the temperature of the sample injection heater was 250°C; the thermostat temperature was programmed from 50°C to 250°C at the rate of 4°C/min; the detector temperature was 250 °C.

Discussion and conclusions. By the method of chromatography – mass spectrometry 30 volatile compounds have been identified in *Salix rosmarinifolia L.* shoots, among them eugenol, geraniol and squalene prevail. There are also 32 carboxylic acids, and among aromatic acids 2-methoxybenzoic and salicylic acids dominate by their content. The significant content of hydroxycinnamic acids derivatives is of considerable interest.

In *Salix rosmarinifolia L.* shoots 32 carboxylic acids have been identified by the method of chromatography - mass spectrometry, among them there are 11 fatty acids – 7 saturated and 4 unsaturated ones (oleic, linoleic, linolenoic, arachic acids). Among unsaturated acids essential polyunsaturated acids – linoleic (omega 3) and linolenoic (omega 6) acids significantly prevail by their content. These acids play an important role in the normal functioning of the human body. They are the main components of fatty oils of flax and soy, which are successfully used as antioxidant, hypolipidemic, membrane-stabilizing, antiaggregant drugs when treating atherosclerosis and various dermatological diseases. Among the saturated acids identified palmitic acid greatly dominate by its content. It is part of natural waxes. In *Salix rosmarinifolia L.* shoots 13 aliphatic acids (azelaic, caproic, oxalic, malonic, fumaric, succinic, heptadecanoic, malic, citric) and 8 aromatic acids (benzoic, phenylacetic, salicylic, vanillic, 2-methoxybenzoic, 4-hydroxybenzoic, syringic, ferulic) have been also identified. Among aliphatic acids oxalic and citric acids are noticeably prevalent by their content compared to other aliphatic acids. The composition and the content of aromatic acids identified in shoots have attracted the most scientific interest. These acids are presented by salicylic acid, benzoic acid, its derivatives and hydroxycinnamic acids. Among aromatic acids 2-methoxybenzoic (6568.13 mg/kg) and salicylic (2585.49 mg/kg) acids prevail by the content. To some extent it allows explaining the high pharmacological activity of drugs from willow. Benzoic acid is an aglycone of phenolic glycoside – populin containing in plants of the *Salicaceae* family. Populin in the body is hydrolyzed to benzoic acid, which exhibits antiseptic properties. Benzoic acid is used in medicine in skin diseases, as an external antiseptic and fungicidal agent, in trichophytosis and mycosis, and its sodium salt – as an expectorant. Esters of benzoic acid (from methyl to amyl ester) have a strong odor and are used in the perfume industry.

CHROMATOGRAPHIC RESEARCH OF *DIGITALIS PURPUREA* AND *DIGITALIS LANATA* FLOWERS

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Introduction. *Digitalis purpurea* and *Digitalis lanata* is pharmacopoeial plant that has been known as a source of cardiac glycosides a long time, of these leaves and herb are obtained cardiotonic drugs. It know that plants contain the choline, amino acids, steroid saponins and flavonoids.

The aim of this research was chromatographic study of phenolic compounds of *Digitalis purpurea* flowers and *Digitalis lanata* flowers

Materials and methods. The objects of the study were dried flowers of these species of family *Digitalis*, that have been harvested in summer 2016.

The analysis was conducted by thin layer chromatography and paper chromatography metods. Extracts was obrained by 90% ethanol. The chromatographic conditions: chromatography plates “Silufol”, chromatographic paper “Filtrac №12”, solvent systems – for aglycones: toluene –ether (1 : 1/saturated with 10% acetic acid); for glycosides: ethyl acetate – formic acid – glacial acetic acid – water (100 : 11 : 11 : 26); ethyl acetate – formic acid – water (10 : 2 : 3); chloroform – methanol – water (64 : 50 : 10) and 15% acetic acid. Chromatograms were studied in daylight and in UV-light. Substances have been identified by fluorescence characteristics in UV-light after processing, and by the Rf value and coloration with chromogenic reagents (UV-365 nm (without chemical treatment; for natural products – polyethylene glycol reagent; 10 % KOH in ethanol; anisaldehyde – sulphuric acid reagent; Kedde reagent: 5 ml of 3 % 3,5-dinitrobenzoic acid in ethanol, that prepared freshly with mixed of 5 ml of 2 M NaOH).

Results and discussion. In the result of the chromatographic study of extracts of *Digitalis purpurea* flowers and *Digitalis lanata* flowers had been found 8 and 12 phenolic compounds respectively. The caffeic acid and the luteolin-7-glucoside; after acid hydrolysis – luteolin, diosmetin, kaempferol and quercetin have been identified.

In flowers of two species iridoids, steroid saponins, cardiac glycosides, phenolcarbonic and hydroxycinnamic acid have been identified by chromatographic metod.

Conclusions. It was found, that flower of these species can be considered as a sources of flavonoids, saponins steroid etc. Our results indicate that further in-depth study of the *Digitalis purpurea* flowers and *Digitalis lanata* flowers as a source of biologically active substances can be considered shows potential for the pharmacy.

INVESTIGATION OF THE PERSPECTIVE TYPE OF MEDICINAL RAW MATERIAL APPLICABLE IN DYSMENORRHEA

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Introduction. The search for new sources of medicinal plant raw materials has been and remains one of the priorities of pharmacy. The scope of phytopreparations is diverse. In particular, phytotherapy is prescribed for various disorders of the menstrual cycle, in the treatment of premenstrual and climacteric syndromes, inflammatory diseases of the genital organs, mastopathy and mastalgia and other pathological conditions. To date, many different plants grow in Ukraine, which affect the reduction of pain and the normalization of the menstrual cycle in dysmenorrhea, whose pharmacological effect is due to the presence of such compounds: carotenoids, organic acids, essential oils, hamazulenes, sesquiterpenoids, flavonoids, coumarins. Chamomile flowers have anti-inflammatory, astringent and diaphoretic effects. Chamazulene chamomile has an antiallergic effect and speeds up the processes of tissue healing, and flavonoids relieve spasms of smooth muscles of internal organs. It has been experimentally proved that the broths of chamomile flowers also have a cholagogic effect. The main properties of phytopreparations from Calendula officinalis are anti-inflammatory, wound healing, spasmolytic and cholagogue. The distinctive sedative and hypotensive effect of galenical forms of Calendula flowers was experimentally established. The rhizome of Potentilla erecta, due to its haemostatic properties, is used to treat uterine bleeding during hormonal failure, as well as inflammation of the vaginal mucosa. Therefore, medicinal plants, such as Chamomila recutita, Calendula officinalis and Potentilla erecta, have long been used in folk and scientific medicine and are widely used in a number of diseases.

Aim. To conduct a search for plants, mainly floras of Ukraine, which are used for the prevention and treatment of dysmenorrhea, create a collection, study its morphological and anatomical features.

Materials and methods. The objects of our research were the raw materials of representatives of the families Asteraceae, Rosaceae, Caprifoliaceae.

Results and discussion. We have developed a composition of the collection consisting of Chamomile recutita flowers, Calendula officinalis, and Potentilla erecta.

Conclusions. The obtained data testify to the prospects of further in-depth study of the collection, consisting of flowers of Chamomile, flowers of Calendula officinalis and rhizomes of Potentilla erecta, which favorably affects the symptomatology of dysmenorrhea.

PHARMACOGNOSTICAL STUDY OF LEAVES RHODODENDRON LUTEUM (L.) SWEET AND RHODODENDRON SICHOTENCE POJARK

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Introduction. The trend towards expanding the range of herbal medicines is growing in connection with the performance of their therapeutic effects on the human body and the lack of collateral. Particular attention is attracted to plants that are composed of different groups contain biologically active substances, the combination of which extends and enhances the pharmacotherapeutic effect of plant material. It is to such plants include heather family members of the genus Rhododendron (Rhododendron L.).

In Ukraine grows naturally only two species of this genus – Rhododendron luteum and East-Rhododendron (Rhododendron myrtifolium), the latter listed in the Red Book of Ukraine.

As for cultivation, in Ukraine collection of rhododendrons are in the botanical gardens of Kharkiv, Kyiv, Chernivtsi, Uzhgorod, Zhytomyr, and in the arboretum "Sofiyivka" (Uman). The largest collection of species of Rhododendron collected in Botanical Garden called acad. A.V. Fomin, represented by 162 species, varieties, hybrids and varieties. Collection in Botanical Garden LNU called Franko has 96 species.

Plants of the genus Rhododendron has long been used in folk medicine for the treatment of cardiovascular, gastrointestinal diseases such as antifungal, anti-inflammatory, tonic, anti-hypertensive, diuretic and germicide.

But insufficient and unstructured knowledge of the chemical structure and pharmacological activity of species of rhododendron that grow and are cultivated in Ukraine determines the necessity of pharmacognostical research. This will resolve the question of whether some types in treatment of diseases of the skin.

Aim. Pharmacognostic study on the Rhododendron luteum and *Rhododendron sichotense.*

Materials and methods. As raw materials used leaves collected in the botanical gardens of Kharkiv in 2015, 2016 respectively. For anatomical study used the fresh leaves and fixed. Temporary preparations prepared by generally accepted method. To study investigated the quality of the raw material was dried to air-dry state. For extraction using water-alcohol mixtures of varying value that evaporated for water balance and gradually extracted with solvents of different polarity.

Chemical studies performed by preparative paper chromatography and thin layer of sorbent using the system: n-butanol-acetic acid-water (4: 1: 2), 5% -acetic acid; chloroform / formamide (25%), toluene, ethyl acetate, acetic acid (12: 4: 0.5); chloroform-ethanol (9: 1).

The results of research. Microscopic study of leaf lamina Rhododendron luteum found trichomes, that are represented by large clavate-capitate of emergence and 1-2 opaque simple cellular trichomes. Spiky trichomes opaque, thin, long, slightly wavy, with 8-10-cell rosette at the base. On the surface of the leaf sculpture on the sichotense multicellular glands present-scales. Their formation involved not only epidermal cells, but also cells subepidermalnyh tissues. Cells scales narrow, thin, contain secret. Simple hairs - pointed, conical, unicellular.

The study of the chemical composition of rhododendrons in chloroform fractions in both types found 6 compounds. Two substances classified as triterpenoids, which are ursolova and oleanolova acids. Also identified β-sitosterol. Ethyl acetate and butanol fractions containing 7 flavonoid compounds, 3 of which are identified as hyperoside, rutin and kvertsytryn.

The intensity of color spots in the chromatogram can be said that in a letter rhododendron sichotense hyperoside contained in more than rhododendron luteum. Routine in both forms contained fewer, while in kvertsytryn rhododendron luteum dominated by the number of content Rhododendron sichotense. In the water balance of both species identified chlorogenic acid and gallic guestrooms prevailed in Rhododendron sichotense.

Conclusions. It is known that flavonoid compounds have antispasmodic, choleretic, hepatoprotective, diuretic, hypoazotemic, membrane-stabilizing properties; for coumarins and hydroxycinnamic acids known anti-inflammatory, antimicrobial and antispasmodic action.

Factors such as the popularity of use in folk medicine, the possibility of cultivation in Ukraine rhododendron luteum and rhododendron sichotense, the presence of such biologically active substances as hyperoside, rutin, kvertsytryn, chlorogenic acid and gallic create objective conditions for further detailed study of biologically active compounds species, determining their prospects for use in scientific medicine to create new medications broad spectrum of pharmacological action.

Microscopic study of leaf lamina sheet of yellow and rhododendron luteum and rhododendron sichotense will provide general and specific diagnostic features that will be used in the standardization of raw materials.

REVIEW OF PLANTS AND DIRECTIONS OF THEIR INFLUENCE ON THE HUMAN PSYCHO-EMOTIONAL CONDITION

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Introduction. All living organisms interact with each other. Plants, which surround us, have a great impact on our physical and psycho-emotional condition.

Aim. To search plants, which most effectively influence on the human psycho-emotional condition.

Materials and methods. A review of the scientific literature, using the descriptional, searching and logical methods.

Results and discussion. The influence of plants on human psycho-emotional condition may be determine by the aesthetic enjoyment, which we get from their appearance. The scientists have proved their ability to emit the energy in different ultraviolet spectrum ranges. For example, green colour has soothing and tonic effect at the same time, promote the improvement of working capacity

The indoor plants do not only decorate the room, but also create a favorable energy, improve memory, help to deal with stress. Flowers of the *Violaceae* family could prevent the occurrence of nervous breakdowns, *Begoniaceae* could help to reduce the aggression and prevent conflict situations. The representatives of the *Dracaena* genus could prevent the development of the depression.

It is also possible to influence by a odour of plants, because some neurological processes connect with the sense of smell. These plants have well-developed external secretion structures - glunds, which produce essential oils and balms into the environment. Inhaling the smell of essential oils of *Mentha piperita, Rosmarinum officinalis, Eucalyptus globulus, Artemisia balchanorum, Salvia officinalis* stimulates the cerebration, improves memory. Essential oils of *Citrus limon, Pterocarpus santalinus, Lavandula angustifolia* are used to control the stress.

Some plants, which have a sedative effect on the central nervous system, are widely used in medicine and pharmacy. They are able to normalize sleeping, reduce stress, fear and anxiety. Sedative drugs of plant origin are considered to be the most suitable and optimal because of their good tolerance and absence of side effects and addiction. For example, there are drugs of *Valeriana officinalis, Leonurus quinquelobatus, Adonis vernalis, Crataegus sanguinea, Papaver somniferum.*

Conclusions. Consequently, plants influence on the human psycho-emotional condition in three directions together: by their appearance, smell and special medicinal properties as the sedative drugs.

RESEARCH OF THE MOTHERWORT HERB COMPONENTS AND THEIR TINCTURES

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Introduction. Motherwort is a perennial herbaceous plant of the family *Lamiaceae,* which has been used in medicine from ancient times. It is one of the most widely used medicinal plants with sedative effect. Most often used in the form of alcohol tincture. Motherwort preparations have the ability to reduce mental stress, can be used for sleep disorders and hypertension. In addition, there is evidence that motherwort has cardiotonic, anti-inflammatory, antispasmodic and choleretic effect.

Motherwort tincture is prepared from the herbs of this plant. The herb consists of the leaves, inflorescences and stems. Very interesting contribution of each component of the raw materials in the total chemical composition and pharmacological effect.

Aim. To determine the percentage maintenance of the herb motherwort components and research the phenolic composition of tincture obtained from the leaves, inflorescences and stems of motherwort.

Materials and methods. Objects of research – herb, leaves, inflorescences and stems of motherwort, alcohol tinctures on their basis, obtained by the classical method in the ratio 1:5. The dry residue was determined by gravimetric method according to the State Pharmacopoeia (SP) of Ukraine. Quantitative determination of flavonoids was carried out in accordance with the monograph SP of Ukraine "Motherwort tincture".

Results and discussion. The herb of the motherwort contains of 40.1 % leaves, 24.5% flowers and 35.4% of stems.

The dry residue in the tinctures from the leaves was 1.09%, from flowers – 1.12% and from stems – 0.69%.

Tincture of motherwort by thin-layer chromatography was identified iridoids and flavonoids (rutin and hyperoside).

The content of flavonoids in tinctures of leaves, inflorescences and stems of 0.06, 0.09 and 0.02 %, respectively. Thus, the content of flavonoids is the smallest in stems and the highest in inflorescences.

Conclusions. In the manufacturing of tincture of motherwort, it is advisable to normalize the content of large stems in the motherwort herb, since their contribution of phenolic compounds to the overall chemical composition of the tincture is the smallest.

ANTIMICROBICAL ACTIVITY OF LIPOPHILIC EXTRACT OF *FRAGARIA MOSCHATA L.* LEAVES

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Introduction. *Fragaria moschata* L. - perennial herbaceous plant, species of the genus Strawberry (*Fragaria* L.) belong Rosaceae family. It is known that the fruits of this plant contain a wide range of biologically active substances (BAS) and are used as a vitamin and dietary product in many countries of the world.

Since *Fragaria moschata* L. successfully cultivated, its leaves are available raw materials and promising source of BAS. It was found that in the lipophilic fraction of *Fragaria moschata* L. leaves there are fatty acids, chlorophylls, terpenoids, higher alcohols. It is known that these BAS can exhibit antimicrobial activity. So, scientific interest is the study of antimicrobial activity of lipophilic fraction of leaves of *Fragaria moschata* L.

The **aim of our study** was to investigate the antimicrobial activity of lipophilic complex of *Fragaria moschata* L. leaves against the most important in the epidemiological significance bacterial cultures.

Materials and methods. The object of the study was the lipophilic extract of leaves of *Fragaria moschata* L. collected in June 2016. We are used air dry raw material. Extract was obtained by used the method of circulating extraction. Extractant – chloroform.

For determining the activity of the lipophilic complex we used the standard bacterial cultures*: Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Proteus vulgaris* ATCC 4636, *Bacillus subtilis* ATCC 6633, *Candida albicans* 885-663. To determine the antimicrobial activity, the bacterial cultures were cultivated on meat pepton agar at 37°C for 24 hours. Antimicrobial activity was measured as a radius in mm to give a zone of inhibition.

Determination of sensitivity of microorganisms was performed by successive twofold serial dilutions in liquid nutrient medium. The method is based on titration in liquid nutrient medium investigational antibacterial preparation by successive dilutions certain volume of liquid in the first test tube using these controls - nutrient medium, which does not receive the drug. In all the test tubes were added daily allowance agar suspension of bacterial cultures.

The results were determined after 48 - 72 hours to assess growth delay of micro-organisms in the test tubes containing the appropriate dilution of the drug. The last tube with growth retardation (clear broth) corresponded to minimum inhibitory

concentration of antibiotic tested against the strain. For evaluation the bactericidal properties the drug from 2 - 3 tubes the last lack of growth been doing application to dense nutrient media.

After 24 - 48 hours incubation in thermostat that determined the lowest concentration of antibiotic drug in vitro, crop, of which has not given of growth and taking the minimum bactericidal concentration. For most microorganisms as nutrient media used peptonnyy meat broth, for mushrooms - nutrient media Saburo.

Determination of the sensitivity of bacteria was performed by diffusion in agar. In the Petri dish poured 10 ml of molten nutrient uncontaminated environment. After solidification of this layer placed on it sterile stainless steel cylinders (height - 10 mm inner diameter – 6 mm) and filled them "infected" agar of 15 ml.

For this purpose, melted and cooled agar agar added daily washings cultures of microorganisms. For the second layer of agar solidification cylinders were removed in the the wells formed, made investigational antimicrobial agents in volume (0,3 ± 0,05) ml.

Crops were incubated at 37^{o} C for 24 - 48 hours, then take into account the results of measuring the area of growth delay test microbe. In an experiment used a 2% solution extracts.

Results and discussion. As a result of the study it was found that the lipophilic extract of *Fragaria moschata* L. leaves shows a high activity against *S.aureus* and *B.subtilis*, moderate against *E. coli*, *P.vulgaris* and *C.albicans*. The results are shown in Table 1.

Table 1

Indicators of delayed growth of microorganisms under the action of lipophilic complex of *Fragaria moschata* L. leaves

S.aureus 25923	*E. coli* 25922	*P.aeruginosa* 27853	*B.subtilis* 6633	*P.vulgaris* 4636	*C.albicans* 885-663
25,5±0,6	14,7±0,7	x	22,5±0,8	15,0±0,8	15,7±0,7

Conclusions. Established the antimicrobial activity of lipophilic complex of *Fragaria moschata* L. leaves. The results of the study found that the resulting lipophilic complex has a pronounced antibacterial activity against *S.aureus* and *B.subtilis.* Taking into account the obtained results, it can be assumed that this substance can be used to create medicinal forms for external use for the treatment of skin diseases caused by *S.aureus* (eczema, dermatitis, dermatosis).

RESEARCH OF TANNINS SMALLANTHUS SONCHIFOLIUS

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Introduction. Plants are an inexhaustible source of medicines. The rapid increase in the incidence of diabetes worldwide has prompted an expansion in the search for natural sources of biologically active substances that improve the quality of life and enrich the diet of this category of patients. The World Association of Scientists named the four most useful plants for humans, dubbed them plants of the 21st century. These plants are Stevia rebaudiana, Amaranthus, Helianthus tuberosus and Smallanthus sonchifolius (yakon). One of the most promising is the yakon. Yakon (Smallanthus sonchifolius) is a species of perennial herbaceous plants of the genus Smallanthus of the Asteraceae family. It grows wildly in South America, Colombia, Ecuador.

Yakon is introduced into the culture in many countries of the world. It renders hypoglycemic, restorative, anti-inflammatory, immunomodulating, antioxidant effects.

Aim. Continuing the study of the biologically active substances of the yakon, a determination of the qualitative and quantitative content of tannins in the root crops and the herb of the plant under investigation was made.

Materials and methods. The objects of study were the root crops and the yakon herb which were harvested in 2015 in the Kharkiv region.

To carry out qualitative reactions, the water extract of the root crops and the yakon herb were used. Well-known qualitative methods (with 1% gelatin solution, with iron (III) chloride, with vanillin in acid medium, with lead acetate in acetic medium) were used. The quantitative content of tannins in root crops and herb was determined by the method of permanganatometric titration given in State pharmacopoeia XI.

Results and discussion. It is established that in the root crops and herb of the studied plant contain condensed tannins.

This method determines not only the content of tannins, but also all oxidative compounds: simple phenols, phenolcarboxylic acids and other polyphenols.

The amount of polyphenolic compounds in the root crops is 2.25%±0.01, in the herb 6.79%±0.04. We used the «Statistica» software package according to the State Pharmacopoeia of Ukraine.

Conclusions. Yakon is a promising raw material for the treatment and prevention of diabetes, therefore it is advisable to study it more deeply.

COMPARATIVE STUDY OF FRACTIONED POLYSACCHARID COMPLEXES AND MICROELEMENT COMPOUND *PRUNUS DOMESTICA* FRUITS

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Introduction. At present, the preparation complexes of biologically active substances and the development of drugs on their basis are an urgent task. A promising medicinal raw material for this is prunes. The first evidence of using of prunes dates back to the period of the Roman Empire. Prunes perfectly help in the early stages of any cardiovascular disease and are included in the diet of hypertensives. Prunes contain potassium one and a half times more than bananas. It improves the appearance and condition of the skin. Prunes are also a wonderful antibacterial. Prunes are also rich of B group vitamins, normalizes carbohydrate metabolism, increases body resistance to stressful situations.

Aim. The purpose of our work is isolation of polysaccharide complexes determination of the content of neutral sugars in them by spectrophotometry and study of elements of *Prunus domestica* fruits.

Materials and methods. The plant raw material was *Prunus domestica L.* fruits (family *Rosaceae*), harvested in Uzbekistan and dried.

Fractions of polysaccharides as water-soluble polysaccharides (WSPS), pectins and hemiceululoses (HC), types A and B were separated sequentially from the dried raw material with known method.

All polysaccharide complexes were dried in a drying oven to constant weight.

0.5 g of each obtained complex was hydrolysed with an acid hydrochloric acid concentrated for 2.5 hours. The solutions were cooled and quantitatively transferred with water purified to volumetric flasks with a capacity of 25.0 ml, adjusted to the mark with the same solvent and mixed. Then were taken 5 ml from each obtained solution and neutralized by the universal indicator paper first with a solution of 30% sodium hydroxide.

The neutralized solution was filtered through a paper filter, transferred quantitatively to a 25.0 ml volumetric flask, diluted to volume with water, and stirred.

Then 2-5 ml of the solution were taken from the each volumetric flasks into other 25.0 ml capacity volumetric flasks, 1.0 ml of 1% picric acid, 3.0 ml of 20% sodium carbonate were added in each flasks and heated at 100 ° C for 20 minutes. After cooling, the volume was adjusted to water and stirred. In parallel, under the same conditions, 2.0 ml of a standard sample (SS) of glucose was prepared. The

optical density of the test solution and glucose SS solution was measured on a Hewlett Packerd 8453 spectrophotometer at a wavelength of 463 nm in a cuvette with a layer thickness of 10 mm. A mixture consisting of 1.0 ml of 1% picric acid, 3 ml of 20% sodium carbonate and 1.0 ml of water was used as the reference solution.

The elemental composition was determined by atomic emission spectrophotometer at State Scientific Institution “Institute for Single Crystals” of NAS of Ukraine. To obtain spectra and their registration plate spectrograph DFS-8 with a diffraction grating 600 line / mm was used. Measuring intensities of lines in the spectra of analyzed samples and calibration samples was carried out by micro photometer MF-1.

Results and discussion. As a result of fractionation, we obtained WSPS - 8.04%, pectins-1 - 2.8%, pectins-2 - 2.96%, HC B - 2.5%, HC A - 1.75%.

By the results of the analysis, neutral sugars were the most in the WSPS - 61.5%. Their content in other complexes was: in pectins-1 - 19.21%, pectins-2 - 5.75%, HC B - 4.42%, HC A -1.29%. The most of the neutral sugars were determined for WSPS and pectins-1.

The second extraction of pectin showed that the pectic substances can be extracted completely by extracting consecutively at least two times. The fractions obtained differ in composition. The content of neutral sugars in the second extraction is 4 times less.

The study of the content of macro- and microelements is important for assessing the useful properties of raw materials, its further standardization and the development of quality control procedures. According to the analysis of the trace element composition, the most potassium content in fruits was found - 3100 μg / 100 g. The content of other trace elements was (μg / 100 g): calcium - 52, magnesium - 52, sodium - 31, phosphorus - 21, silicon - mg / 100 g, aluminum - 1.0, iron - 0.8, zinc - 0.6, Strontium-0.52, copper-0.41, manganese-0.26, molybdenum-0.05, lead-less than 0.03, nickel <0.03, Co <0.03, Cd <0.01, As <0.01, Hg <0.01. Potassium is a systemic electrolyte and is essential in coregulating ATP with sodium. Prune is an important source of this element. The presence and content other elements also play role for health. For example, copper maintains the normal blood composition, is contained in enzymes, participates in the delivery of oxygen to the cells. Zinc strengthens immunity, is important for growth, supports the hormonal background. Magnesium has an antispasmodic and antiplatelet effect. Also, our research has determined that the content of heavy metals in the raw materials in question does not exceed the norms established by the State Pharmacopoeia of Ukraine.

Conclusions. The data obtained shows that this raw material is valuable and can be used to create new medicines on its basis.

CLIMATE CHANGES AND CARBOHYDRATE EXCHANGE IN LEAVES OF A WORMWOOD WHITISH

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Introduction and objectives of the study: Given the important role of terpenoids in the wormwood tissues whitish, we set out to study the carbohydrate metabolism in its aerial part.

Methods of investigation: the experiments were carried out on the territory of forestry, which is located in the Farish district of the Djizak region. The content of carbohydrates was determined by the formula of I.L.Zakharyants(1971).

Research results: the results of numerous studies and our studies show that complex carbohydrates are widely represented in carbohydrate metabolism of wormwood whitish. Wormwood whitish contains a lot of starch (up to 15%), which gives grounds for attributing the plants of wormwood to the starchy type of carbohydrate metabolism studied by us, and the dextrins are found in the amount available to the definition.

The amount of hemicelluloses in the tissues of the aerial part of wormwood whitish reaches up to 16.5%, which largely depends on the degree of drought resistance of this plant. The amount of cellulose in the tissues of the aerial part of this plant varies depending on the phase of the plant; the highest fiber content reaches 17.3% of the dry matter of the tissue of the aerial part of this plant. In leaves and roots of wormwood whitish there are glucose, fructose, sucrose, as well as up to 5 types of oligosaccharides, which differ from each other in the degree of polymerization. As noted by I.L. Zaharyants. (1971), the presence of this group of carbohydrates is specific for carbohydrate metabolism in the plant, wormwood whitish. Monosaccharides in the phase of wormwood regeneration whitish are more synthesized than, sucrose (2.4-0.8%). By the beginning of the arid and hot period, sugars are appreciably consumed. Starch is rapidly consumed in the period of discarding the peduncle.

Conclusion: Therefore, in the early period of development, that is, during the period when the wormwood grows whitish, low temperatures promote the accumulation of monosaccharides, and vice versa, the increased temperature and drought to an increase in the amount of sucrose and hemicelluloses in the tissues of the plant we are studying.

INSECURES MEDICINAL POTTED PLANTS OF THE BOTANY DEPARTMENT OF NUPH

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Introduction. Indoor plants accomplish not only aesthetic, but also sanitary and hygienic purposes. Among these plants, there are a lot of well-known medicinal species, but there are dangerous ones. Potted plants are teaching aids, which are indispensable for high-quality lectures, seminars and workshops.

Aim. To analyze the types of indoor plants, to identify unsafe ones for human health, to study their usage in the educational process and to specify security measures when working with them.

Materials and methods. Comparative, descriptive method of systematization and definition of plants.

Results and discussions. At the Department of Botany NUPh are grown about 50 kinds of indoor plants, the selection of which is dictated primarily by the needs of the educational process. The largest number of species refers to the families of Araceae, Euphorbiaceae, Moraceae and Geraniaceae, that are widespread in gardening of interiors and office spaces. The Araceae family includes

Dieffenbachia bausei Regel., *Monstera deliciosa* Lieb., *Scindpsus pictus* Hassk., *Syngonium podophyllum* Schott., *Philodendron sodiroi* Hort. *Zamioculcas zamiifolia* Lood. The most widespread and dangerous of them is *Dieffenbachia bausei*. Poisonous sap of its shoots contains oxalic acid and calcium oxalate. After contact with the skin it causes severe irritation. *Dieffenbachia bausei* has phytoncidic activity – greatly reduces the content of pathogenic microorganisms in the air. In the educational process are used while studing the types of stomatal apparatuses and crystals of calcium oxalate.

Euphorbiaceae are represented by *Codiaeum variegatum* L., *Euphorbia leuconeura* Boiss., *E. mill* L., *E. tirucalli* L. and others. In all organs of these plants there is poisonous milky sap, that contains euforin poison. During skin contact it causes strong inflammation, and is dangerous at eye contact. In modern medicine preparations from representatives of this family are used in the form of extracts for the treatment of the stomach disease, kidney, dysentery, cystitis, hemorrhoids, externally are used to remove warts, freckles, trophic ulcers. In the educational process at the Department of Botany Euphorbiaceae is used to study

metamorphosis of stipules, stomatal apparatus types, endogenous secretory tissues.

From Moraceae are cultivated *Ficus alii* L., *F. benjamina* L., *F. elastica* Roxb at the Department. These plants can cause a variety of allergic reactions at people with an increased sensitivity, such as asthma, mucosal edema, vomiting. *Ficus* have a poisonous milky sap, which, when in contact with skin causes an acute inflammation, eczema, dermatitis. Members of the genus *Ficus* in the educational process are used in the study of plant morphology: life forms, branch types, leaf arrangement, leaves venation; fitogistologii: periderm, endogenous secretory tissues.

To the family of Geraniaceae are belonged *Pelargonium grandiflorum* Wild., *P. roseum* Wild., *P. zonale* L. The most popular representative is *Pelargonium roseum*. Leaves and stems are covered with glandular trichomes that secrete essential oil. Often allergy is due to this essential oil. In the perfume and pharmaceutical industries it replaces more expensive rose oil. It is used at the treatment of cardiovascular system, hypertension, asthma, kidney stones. In the educational process the species of *Pelargonium* are a classical object of studying of the structure of the escape, the morphology of the leaf epidermis and trichomes.

When using these species at the learning process and when looking after them it's necessary to keep simple safety rules. Working with plants one needs to wear gloves, after the work one should obviously wash his hands with soap, to cut parts of the plant – use a separate tool. If the sap nevertheless has got on the skin or mucous membrane, it should be carefully washed off with water, if necessary - to take anti-allergic agent. With the deterioration of general condition is necessary to seek medical help. After studying the properties of unsafe indoor plants, we can correctly use them in the studying process and bravely grow them in the classrooms.

Conclusions. Having studied the properties of unsafe indoor plants and the rules of working with them, we can safely grow in classrooms and use these plants competently in the learning process.

IN VIVO STUDY OF ANTI-INFLAMMATORY ACTIVITY OF SOME SALVIA OFFICINALIS EXTRACTS DERIVATIVES

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Introduction: Different forms of Salvia Officinalis are known to be used in stomatology and non-traditional medicine as an antimicrobial and anti-inflammatory agent. Nowadays inflammation of various etiology is being treated mostly using non-steroidal anti-inflammatory drugs (NSAIDs) which have many side effects such as nausea, ulcerations, hepatic toxicity, etc. Search of safe and effective component among different Salvia Officinalis extracts with anti-inflammatory activity has been given priority in our study.

Aim: The aim of the present work was to investigate anti-inflammatory activity of decoction of Salvia, lysine complex, phenolic complex, flavonoid complex of Salvia.

Materials and methods: Anti-inflammatory activity was evaluated on Carrageenin induced rat paw edema test. Animals were divided into 4 groups of 12 in each, group of control (water) and comparison group (diclofenac). Dosages in study groups were 10, 20, 50, 70 mg/kg. One hour after extract/water/diclofenac were induced intragastric, animals were injected 0.1 ml of 1% Carrageenin water solution under the plantar aponeurosis of right hindpaw, intradermally. The thickness of paw was measured using oncometer just before the experiment and every hour later after Carrageenin injections during 4 hours.

Results and discussion: Decoction of Salvia in dosage 10mg/kg showed 98% anti-inflammatory activity, in dosage 20mg/kg - 83%, 50mg/kg – 85%, 70mg/kg – 100% respectively. Lysine complex of Salvia in dosage 10mg/kg showed 92% anti-inflammatory activity, in dosage 20mg/kg - 81%, 50mg/kg – 98%, 70mg/kg – 98% respectively. Phenolic complex in dosage 10mg/kg showed 13% anti-inflammatory activity, in dosage 20mg/kg – 19%, 50mg/kg – 13%, 70mg/kg – -6% respectively. Flavonoid complex of Salvia in dosage 10mg/kg showed 6% anti-inflammatory activity, in dosage 20mg/kg – -2%, in dosage 50mg/kg – 6%, 70mg/kg – -8% respectively. Diclofenac showed 93% anti-inflammatory activity in dosage 8 mg/kg whereas control group had 0% anti-inflammatory activity. The present study showed that the decoction of Salvia and lysine complex possessed significant anti-inflammatory effect, flavonoid and phenolic complex did not show anti-inflammatory activity in comparison to diclofenac.

Conclusions: In search of effective anti-inflammatory agent four kinds of Salvia extracts' anti-inflammatory activity has been studied. The results of studies have shown decoction of Salvia officinalis and lysine complex obtained high level anti-inflammatory profile and appeared to be promising substance for making anti-inflammatory drugs in comparison to the phenolic complex and flavonoid complex which did not to show anti-inflammatory effect.

THE DEFINITION OF MORPHOLOGICAL AND ANATOMICAL CHARACTERISTICS OF PERSEAE AMERICANAE

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Introduction. The main tasks of modern medicine and pharmacy are the search and investigation of poorly studied plant materials. Our attention was attracted by a plant of the Lauraceae family, Persea genus – Persea Americana, which in Ukraine started being cultivated relatively recently. The Lauraceae family consists of more than 2000 types taking a significant part in the structure of forests in tropical and subtropical regions. Lauraceae are woody plants (except a parasite Cassytha) with leathery, simple, entire or dissected leaves without stipules. The plant material of most members of this family contain fatty oil, vitamins (PP, A, C, B_6, B_2, B_1, B_9), essential oils, formic, butyric, lauric acids, minerals, tannins, resins, bitters.

Some species of the Lauraceae family are cultivated in Ukraine. Bay Laurel, for example, Camphor tree, as wellas Cinnamomum verum, Persea Americana can be seen in the greenhouses.

Aim. The study of morphological and anatomical structure of Persea Americana fruits with the establishment of diagnostic features.

Materials and methods. The raw material was collected in spring of 2017. The micro specimens were prepared from freshly collected and fixed in a mixture of alcohol-glycerin-water (1:1:1) fruits. The study was performed using a microscope MBR-1, MBI-6 LOMO (100-600). The received micropreparations were photographed on camera “Kodak-400”. Pictures were processed using the computer program "Photoshop CS5".

Results and discussion. The morphological and anatomical study of the Persea Americana fruit was carried outof the Persia American. Fruit is a pear-shaped seeded berry. It was determined that the diagnostic fuatures of to the fruit are: size and shape, dark green color and thickness of the pericarp, its density, the presence of tubercles on it. The fruit pulp is buttery and soft, yellow-green color on the cross section. There is an ovoid large seed in the center of the fruit. The diagnostic features which are of a great importance for the identification of the fruit as a type of plant material weredetermined. These include the specific epidermal structure, character and thickness of the pericarp, presence of brown pigmented spots, large amount of fatty oil spots in the pulp which are coloured orange by Sudan III in orange.

Conclusions. Thus, the obtained data will be used for further study Persea Americana, which is a promising plant for producing new types of medicinal plant material with relevant directions of action.

RESEARCH OF THE DRY ALCOHOLIC EXTRACT FROM BEARBERRY LEAVES

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Introduction. Bearberry is one of the plants, which is actively used not only in traditional, but also in officinal medicine. It is a small evergreen shrub. In the medical purposes are used the collected during blossoming leaves bearberry. The medicinal based on bearberry, have antibacterial, antiseptic, anti-inflammatory, disinfectant, diuretic and astringent properties. Using decoctions prepared from this plant eliminates inflammatory processes of the bladder, urinary tract and kidneys. The leaves of bearberry are included to the diuretic compositions № 1 and № 2, "Detoxifit", "Nefrofit". But the decoction as a medical form has disadvantages such as: short expiration date, irregularity of the water extracts because of the numerous factors with influence on their quality of preparation; duration of the preparation. Therefore the craetion of the national galenics and newgalenics medicines on the basement of biologically active substances of bearberry leaves is an important task of modern pharmacy.

Aim. Make a phytochemical research of the dry extract from bearberry leaves, received with using of 96 % ethanol.

Materials and methods. The research object is the dry extract of bearberry leaves received with 96 % ethanol. The identification of substances was carried out by the thin-layer chromatography with using pharmacopoeia methods. Pharmacopoeia spectrophotometry methods were used for determination of the assay of arbutin, hydroxycinnamic acids, flavonoids and sum of phenolic compounds.

Results and discussion. Arbutin, hydroxycinnamic acids, flavonoids and tannis were defined in the extract. The content of these groups of substances in the dry extract in comparison with the decoction is given in the table below.

Table

The results of assay of biologically active substances in the extracts

Group BAR	Assay, %	
	The decoction	The dry extract
Derivatives of hydroquinone	8,59 ± 0,05	5,78
Hydroxycinnamic acids	1,58 ± 0,01	1,65
Flavonoids	1,59 ± 0,04	1,43
Phenolic compound	8,80 ± 0,05	13,33

These results will be used in the standardization of the dry extract from the bearberry leaves.

Conclusions. The further chemical and pharmacological researches of the dry alcoholic extract of bearberry leaves will be a basement for the creation of a new medicine from this raw material.

A STUDY OF FLAVONOIDS OF THE UNDERGROUND ORGANS OF SYRINGA VULGARIS BERRYER VARIETY

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Introduction. Flavonoids are widespread in the plant world. They are mainly found in the epidermal cells of plant fruits, flowers, seeds, shoots and roots. This group of biologically active substances are found in fungi, lichens, algae.

More than 4000 different substances of flavonoid nature, isolated from plant material, are known now. Flavonoids have a wide range of biological effects antioxidant, antitumor, antianginal, antiallergic, anti-inflammatory, radioprotective are among them. They also have P vitamin activity.

Aim. Previous studies have shown the presence of flavonoids in the flowers, leaves and bark of *Syringa vulgaris* Berryer variety (lilac species). The aim of our study was to investigate qualitative and quantitative content of flavonoids in the underground organs of *Syringa vulgaris* Berryer variety.

Materials and methods. Raw materials were harvested in autumn of 2014 and 2015 in the botanical garden of the V. N. Karazin Kharkiv National University.

Thin-layer, paper chromatograpy and well-known qualitative reactions were applied to determine the qualitative composition of flavonoids in the underground organs of *Syringa vulgaris* Berryer variety. N-butanol-acetic acid-water (4:1:2), 5%, 15%, 30% acetic acid were used as mobile phases. Chromatograms were analyzed in daylight and UV-light before and after treatment with chromogenic reagents.

Quantitative determination of flavonoids was carried out spectrophotometrically on the Mecasys Optizen POP (Korea) device after reaction with 2% alcohol solution of aluminum chloride.

Extraction of the sum of biologically active substances (BAS) from the raw material was carried out with 70% ethanol. The shredded raw material (50.0 g) was placed into a ground glass flask and treated with 150 ml of purified water. The extraction was performed for 5 times at 100°C for 30 minutes. The obtained extracts were combined, concentrated to a volume of 200-250 ml, refrigerated, filtered through a paper filter into the 250 ml volumetric flask. Then solution was adjusted to the mark with purified water for getting the right volume (solution A).

Solution A (2.0 ml) was placed into a volumetric flask with a capacity of 25 ml, then 2.0 ml of a 3% solution of aluminum chloride in 96% ethanol was added and mixed. The optical density of the resulting solution was measured after 30 minutes. Solution containing 2.0 ml of solution A was added to a volumetric flask with a

capacity of 25 ml and adjusted to the mark with 96% ethanol used as a compensation solution. The optical density of Pharmacopoeial standard solution of rutin was measured in parallel under the same conditions: 0.01 g of rutin was placed into a volumetric flask with a capacity of 25 ml, dissolved in 96% ethanol, the volume of the solution was adjusted with 96% ethanol to the mark and mixed. 2.0 ml of a 3% solution of aluminum chloride in 96% ethanol was added to 1 ml of the resulting solution and the volume of the solution was adjusted with 96% ethanol to the mark. The optical density of the resulting solution was measured after 10 minutes. The optical density was measured on the spectrophotometer at a wavelength of 420 nm using a cuvette with a layer thickness of 10 mm. The content of sum of flavonoids was determined in recalculation for rutin.

The content of sum of flavonoids (X,%) in the recalculation for rutin was calculated by the formula:

$$X = \frac{A \cdot m_0 \cdot 100 \cdot 100 \cdot 100}{A_0 \cdot m \cdot 100 \cdot (100 - W)};$$

where A – optical density of test solution;
A_0 – optical density of Pharmacopoeial standard solution of rutin;
m_0 –weight of rutin, g;
m – mass of raw materials, g;
W – mass loss during drying of raw materials, %.

Results and discussion. The chromatographic analysis showed that the underground organs of *Syringa vulgaris* Berryer variety contain rutin and luteolin. As a result of the studies, it was found that the content of flavonoids in the underground organs of lilac of the studied variety was 0.14±0.08%.

Conclusions. Qualitative and quantitative analysis of the flavonoids of the underground organs of *Syringa vulgaris* Berryer variety was carried out. The conducted studies have shown the presence of flavonoids in the raw material. The results of the studies showed the perspective for further study of the underground organs of the *Syringa vulgaris* Berryer variety. Results will be used for new phytomedication development.

ALTERNATIVE SOURCES OF SECONDARY METABOLITES SYRINGA VULGARIS L.

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Introduction. Syringa vulgaris L. is in demand as an ornamental plant. Syringa is also used in official medicine as medicinal raw material. Thus, bark which quality assessment is made according to VFS 42-2106-92 "Bark of Syringa Vulgaris" is used in Russian Federation. But bark stocking leads to the damage of the plant, that's why raw material base enlargement is an urgent problem. Leaves as raw material have big raw mass and devoid this disadvantage. During systematization of literature data it has been stated that leaves of Syringa vulgaris L. also contain substances of flavonoid nature, which syayes availability of studying this object. The tendency of modern biotechnological manufacture is getting culture of plant tissues, that's why investigation of tissue culture Syringa vulgaris L. of leaf origin is one of prospective objects while studying alternative sources of secondary metabolites.

Aim. To carry out analysis of chemical composition of leaves of native plant Syringa vulgaris L. cv. "M. Sholokhov" with callus tissue of leaf origin according to the known BAV groups. To compare content of the sum of phenolic compounds (PhC) in the given objects.

Materials and methods. Callus tissue Syringa vulgaris L. cv. "M. Sholokhov" of leaf origin is grown on medium Murashige and Skoog with contents of nitrogen and phosphorus salts KNO_3 (1900 mg/l), NH_4NO_3 (825 mg/l); KH_2PO_4 (170 mg/l) with 1.0 mg/l α-naphthyl acetic acid and 1.0 mg/l benzyladenine. Lighting variant: 16 hours light, 8 hours dark. Identification of PhC was made by methods of gas, paper, thin-layer high efficiency liquid chromatography. Determination of PhC sum was made by spectrophotometric method by the reaction products of nitrogen combination and by the reaction products with the reagent Folin-Ciocalteu.

Results and discussion. In the leaf of the intact plant the presence of isoquercitrin, rutin, syringin, cempherol-3-ramnoglycosid, acids: para-coumaric, para-hydroxybenzoic, para-hydroxyphenylacetic, caffeic, o-hydroxycinnamic, benzoic; thyrozol, rutin has been stated. In the callus of leaf origin astragalin; acids: para-hydroxyphenylacetic, caffeic, syringing, acteozid has been found. The sum of PhC in the leaves of the native plant Syringa vulgaris L. cv. "M. Sholokhov" is 17% higher than in callus tissue of leaf origin that shows high efficiency of callus.

Conclusions. On the example of the leaves of the native plant and callus culture Syringa vulgaris L. cv. "M. Sholokhov" availability of their use as alternative raw material to decrease the damage made to plant during harvesting time has been studied.

RESEARCH ELEMENTAL COMPOSITION OF DOMESTIC RAW ACORUS CALAMUS RHIZOMES

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Introduction. Minerals are essential for the human body. Work of virtually all regulatory systems somehow depends on the balance of inorganic elements that are part of cells and tissues. They come with food, water and air, and then absorbed by the body and distributed in the tissues and are included in the metabolic processes. Micro- and macro elements are an important catalyst for various biochemical reactions are part of many enzymes, hormones, to specialized proteins.

Aim. Explore the accumulation of macro and micronutrients in acorus calamus rhizomes, harvested in Ukraine.

Materials and methods. The samples acorus calamus rhizomes collected in Kharkiv (Series №1 and 6), Sumy (Series №2), Poltava (Series №3), Kyiv (Series №4), Chernihiv (Series №5) and Zhytomyr (Series №7) regions to study. Definition of quality and quantitative content macro and micronutrients conducted by atomic emission spectral analysis.

Results and discussion. The content of heavy metals in the studied raw materials does not exceed the maximum permissible limits with the exception of lead (see. Table.). In the raw materials of Kyiv, Chernihiv and Kharkiv regions this substance accumulated in large amounts (0.76, 0.84 and 0.80 mg/100g, respectively). Raw harvested near Pechenehskoho reservoir and Sumy region of lead contained at 0.08 mg/100g and 0.49 mg/100g respectively. Among the elements iron and manganese accumulate in large quantities then other. Since the raw material collected in Kyiv, Zhytomyr, Kharkiv (m. Kupiansk) and Chernihiv regions contained iron in large amounts (45 mg/100g, 35 mg/100g, 22 mg/100g and 17 mg/100g, respectively). Magnesium in the first six series of raw materials (see. Tab.) Accumulated at the level of 1.5 - 5 mg/100g. The content of copper was virtually identical in samples of Sumy and Kharkiv regions (2.0 mg/100g and 1.9 mg/100g, respectively). Zinc accumulates in large quantities in the samples of the Kharkiv region (2.5 mg/100g), and (2.8 mg/100g). Among macro accounted for the largest number of potassium, calcium, phosphorus. Potassium contained in the sample number in the number 410mh/100g, sample №5 - 1960 mg/100g. Calcium ranged from - 125-335 mg/100g, phosphorus - 87-270 mg/100g.

Table

Accumulation of elemental in samples of acorus calamus rhizomes

	mg/100g						
	№1	№2	№3	№4	№5	№6	№7
Na	16	40	13	75	110	110	140
Mg	10	60	22	95	110	67	210
Al	1	12	0.45	19	5.6	14	70
Si	12	40	9	150	28	56	280
P	175	140	270	195	190	95	87
K	410	1230	450	1330	1960	1680	1050
Ca	125	245	135	230	335	280	260
Mn	1.4	1.6	2	4.7	2.8	4.2	17.5
Fe	0.3	6,1	0.2	45	17	22	35
Ni	<0.03	0.04	<0.03	0.04	<0.03	<0.03	<0.03
Cu	0.2	2.0	0.1	0.9	0.4	1.9	0.35
Zn	2.5	2.0	0.45	0.9	1.7	2.8	1.7
Pb	0.08	0.49	<0.03	0.76	0.84	0.8	<0.03
Mo	<0.03	<0.03	<0.03	<0.03	<0.03	<0.03	<0.03

Remarks. Co < 0.03 mg/100g; Cd < 0.01 mg/100g; As < 0.01 mg/100g; Hg < 0.01 mg/100g.

Conclusions.

1. For the first time a comparative analysis of the accumulation of macro- and microelements in the rhizomes acorus calamus harvested in Ukraine depending on growth.

2. The data will be included in the standardization of raw materials, development of quality control methods and recommendations on the procurement of raw materials.

STUDY OF MORPHOLOGY AND ANATOMY OF CARDUUS PSEUDOCOLLINUS

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Introduction. The Carduus generation numbers more then hundred species in the world and thirteen species in Ukraine. The most widespread species in Ukraine are Carduus nutans, Carduus acantoides and Carduus pseudocollinus. Analysis of literature sources shows that herb of Carduus nutans and Carduus acantoides are used in medicine and have anti-inflammatory, choleretic, diuretic and bactericide activity. It helps to normalize metabolic processes in organism. The plants of these three species are very similar by morphological features and Carduus nutans and Carduus acantoides are used in medicine that is why the studying of morphology and anatomy of Carduus pseudocollinus was actual as it can be admixture of Carduus nutans and Carduus acantoides.

Aim. The aim of the work is studying morphology and anatomy of Carduus pseudocollinus herb.

Research techniques. The Carduus herb was prepared in the area of Vinnytsia and Khmelnitskiy regions in 2015-2016 in phase of mass flowering. The fresh, dried and fixed raw material was used for preparing microslides. The anatomical structure was studied on the surface and cross section view.

Results and discussion. It was determined macroscopical features of Carduus pseudocollinus herb. It is a branchy and upright stem with dentate wings on the length. The leaves of root rosette and basal stem leaves are short petiolar, pinnatisected and elliptical oblong. The middle and upper stem leaves are pinnatipartite, pinnatilobate and oblong. All leaves have crisp venation and small thorns on the margin. Flowers are formed inflorescence of anthodium. The involucres of anthodium are calyciform. The leaves of involucre are narrow spear-shaped with short thorns on the top.

The form of epidermal cells, character of indumentums and structure of trichomes, the multilayer angular collenchyma in edges of vein, the parenchymatous encasing of vein’s and stem’s conductive bundles is microscopical features.

Conclusions. As the result of studying morphology and anatomy of Carduus pseudocollinus herb the macro- and microscopical features were determined. The obtained data will be used in further researches and for identification of raw material.

INVESTIGATION OF THE PERSPECTIVE TYPE OF MEDICINAL RAW MATERIAL WITH HYPOTENSIVE ACTIVITY

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Introduction. Cardiovascular diseases are the leaders among the diseases and causes of mortality of economically developed countries. One of the most common cardiovascular diseases is hypertension. The World Health Organization (WHO) and the International society for the suppression of arterial hypertension give the following definition of this disease - it is a disease diagnosed in the case of a patient with a persistent increase of arterial pressure to levels 140/90 and higher. Hypertension is a frequent cause of life threatening acute heart disease (myocardial infarction) and brain (stroke). For the treatment are usually used synthetic drugs. However, in the early stages of the disease will also be effective herbal medicine. The use of medicinal plants including anti-hypertensive plant collection helps to stabilize blood pressure and reduce the number and doses used synthetic drugs. In the literature available to us, there is an information about the hypotensive activity of 86 plants of the world's flora. Of these, 39 are found in the temperate climate. We analyzed the composition of more than 55 plant collections comprising more than 90 plants of the families Apocynaceae, Araceae, Asteraceae, Betulaceae, Ericaceae, Fabaceae, Lamiaceae, Loranthaceae, Polygonaceae, Rosaceae and others.

Aim. Conduct a search for plants that have hypotensive effects on people, mainly in the flora of Ukraine.

Materials and methods. We created 2-5 component collections of plant raw materials from the families Rosaceae, Lamiaceae, Asteraceae, Fabaceae.

Results and discussion. The most common are these medicinal plants: Leonurus quinquelobatus has a pronounced sedative and hypotensive action and weak diuretic; Crataegus sanguinea has cardiotonic, hypotensive, sedative effect; Gnaphalium uliginosum has hypotensive and sedative effect; Mentha piperita has a pronounced sedative and hypotensive action; Valeriana officinalis has a pronounced sedative and hypotensive action; Equisetum arvense has a pronounced diuretic and hypotensive effect; Viscum album has a pronounced hypotensive, sedative and diuretic effect.

We have studied the morphological and anatomical features of 7 plant collections and allocated diagnostic features.

Conclusions. Certain features of the external and internal structure of the 7 collections were the first step in the creation and standardization of a new original plant collection.

Section 3.

THE STANDARDIZATION OF MEDICINES. PHARMACEUTICAL AND CHEMICAL-TOXICOLOGICAL ANALYSIS

"VARIKOZNET" HELIUM DETERMINE THE AMOUNT OF SULFUR ORGANIC COMPOUNDS

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Introduction. The legs, chronic venous insufficiency (OSVE) the following group of drugs used to prevent and treat: coumarins; flavonoids, saponins (chestnut extract and other plant extract). These compounds have veinactivity properties, common in European countries. The fermentation process Allium cepa L. extract antiplatelet action. Based on the above-mentioned plants for the treatment and prevention of OSVE "Varikoznet" helium production. The development of methods to control the quality of pressing challenges.

Aim. Local youth "Varikoznet" based on the crude helium to determine the amount of sulfur organic content compounds (SOCC) that keep the.

Material and methods. Spectrophotometric method of extraction "Varikoznet experience" helium (2.0 g), and extracted two times with 10 ml of ethyl alcohol and 25 ml flask, tube delivered with a mark of alcohol. 5 ml, 2 ml of the extract which zincates alkaline solution of sodium added. The resulting mixture is dried on the refrigerator at a temperature drying racks 200ºS. That the residue of the original cooling, and then 60 ml of acetic acid is dissolved in a solution of 2% held a flask of 100 ml and 5 ml of 0.5 mol/l ironammoniumrancid, 5 ml of 0.1% n-amino N, N-dimethyl aniline was established. After 15 minutes, the measuring tube delivered with the volume of purified water mark. The layer thickness of 1 cm cuvette optical density measured at a wavelength of 665 nm. The resulting solution was compared with a control solution without spectrophotometer (Shimadzu UV-2700, Japan) were analyzed.

Results and discussion. On the based of results from the spectrum you can see absorptions points. They are minimum of 457 and 568 nm wavelength, the maximum 497 and 665 nm wave length. Quantitative analysis of the absorption appears in a wave length of 665 nm was carried out. Standard samples as 3,3`-ditiodipropan acid solution (Sigma Aldrich, USA) was used. "Varikoznet" keep the helium SOCC in the structure of is carried out once the amount of experience (5) 14,3 mg/gel relative error, the experience will not exceed 3.81% of the tests.

Conclusion. For the first time antitrombogen on the basis of local raw materials and capillarprotector "impressive" Varikoznet gel developed the drug."Varikoznet" helium substances which affect the structure of the main body SOCC spectrophotometric analysis methods and standardization of medicines.

DEVELOPMENT OF SIMULTANEOUS DETERMINATION METHOD FOR CAPTOPRIL AND FUROSEMIDE IN COMPOUNDED SYRUPS

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Introduction. Captopril is a potent, competitive inhibitor of angiotensin-converting enzyme (ACE), the enzyme responsible for the conversion of angiotensin I to angiotensin II. It is indicated for hypertension, heart failure and proteinuria in nephritis. Syrups consisting of ACE inhibitors and diuretics combinations are also compounded as convenient dosage forms for both paediatric and geriatric patients for management of hypertension. As a physicochemical method, thin layer chromatography (TLC) is effective but not limited to separation and identification of substances in multicomponent formulations. It may also be used for stability study if compounded preparations.

Aim: The purpose of our work is to simultaneously identify captopril and furosemide in multicomponent compounded syrups using TLC method and observe the influence of excipients and dispersion media on obtained results.

Materials and Method: For this purpose, a compounded syrup containing syrup USP, commercial tablets of captopril (Arterium batch 149682, Ukraine) and furosemide (Sanofi batch 114402, Ukraine) was prepared. Pharmaceutical substances: 15mg furosemide (Ipca Laboratories Ltd. India, certificate of analysis batch 5074HRII) 15mg (Changzhou Pharmaceutical Factory, certificate of analysis batch EC160811) were dissolved in 30ml methanol and sonicated for 5 minutes. The solutions were filled to 50 ml with the same solvent to form 0.3 mg/ml analytical solutions. For test solution, a quantity of syrup containing the same amount of substances as above was dissolved in 50ml methanol and filtered. 5 μL each of these samples were applied to the start line of a silicagel 254 nm chromatographic plate and allowed to migrate over a distance of 8cm in a chloroform-ethylacetate-glacial acetic acid (7:3:0.5 v/v ml) mobile phase. The plates were then dried in air and observed under a 254nm ultraviolet (UV) light. The plates were later sprayed with iodine fumes and observed under the UV light.

Results and Discussion: In day light, no spot is seen on the chromatographs. Under UV light, purplish spots corresponding to furosemide (R_f- 53) are seen. After spraying the plate with iodine fumes, yellow spots representing are seen. Dark brown and purplish spots corresponding to captopril (R_f- 28) and furosemide respectively are seen for both reference and test solutions when placed under the UV light. Sucrose and excipients remained on the start line and had no effect on the analytes.

Conclusion: This method could be used for simultaneous identification of captopril and furosemide in compounded syrups after optimisation and validation. Excipients and dispersion had no significant effect on results of analysis.

INVESTIGATION OF DUOVIR BY THIN LAYER CHROMATOGRAPHY

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Introduction. As it is well known the epidemy of AIDS has started in the first part of 1980^{s} and since then it has a great importance. HIV/AIDS is treated with medicines that stop the virus from multiplying. This treatment is called antiretroviral therapy (ART). In the past, people with HIV infection would start antiretroviral treatment after their CD4 count dropped or they developed HIV complications. Today, HIV treatment is recommended for all people with HIV infection, even if their CD4 count is still normal.

Taking into account specifity of epidemic situation in the world, necessity of constant supervision about this problem and features of medical support, are very interesting and important researches targeted on improvement and creation of new analysis techniques for the known substances, which are applied for treatment HIV, and AIDS. Some preliminary stages of elaboration of technique applied in the researches and investigation of the specific features of behavior and skills in various conditions of some substance used in the AIDS therapy were carried out at the pharmaceutical chemistry department of the National University of Pharmacy.

Aim. To investigate chromatographic behavior of compositional parts of Duovir on various thin layers of sorbent and in various systems of solvents of various nature. On the basis of the data obtained to choose the most appropriate system for identification on Duovir in thin layers of sorbent and systems of solvents of various nature.

Materials and methods. For our researches two type of chromatographic plates: Sorbfil and Merck have been chosen. As a detectors have been chosen such reagents as: Dragendorff reagent, Iodine vapors, UV light, mercuric sulphate with 0,05% diphenylcarbazone solution in chloroform. As a movable phases have been chosen systems of solvents of acidic character; systems of solvents of alkaline nature and systems of solvents of neutral character.

Results. As it has been stated according to the data of the conducted investigations, the most suitable systems for the identification of duovir and its compositional parts identification by TLC method on plates Sorbfil and Merck are systems of alkaline character using Dragendorff reagent, UV light, iodine vapours as detectors on plates.

Conclusions. The systems of solvents and detectors mentioned above can be taken for identification of duovir and its compositional parts by thin layer chromatography method on the plates Sorbfil and Merck.

DEVELOPMENT OF THE METHODS OF ANALYSIS OF 5-METHYLPYRIDINE-2-AMIDE 1- PENTYL-2-OXO-4-HYDROXYQUINOLINE-3-CARBOXILIC ACID

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Introduction: Quinoline nucleus occurs in several natural compounds (Cinchona Alkaloids) and pharmacologically active substances displaying a broad range of biological activity. Among the quinoline derivatives quinoline-3-carboxilic acid are the most interesting in creation of new substances and studying of their biological activity. The quninoline-3-carboxylic acid derivatives have various kinds of biological properties: antimicrobial, anti-tubercular, antifungal activity. They can be used also for treatment against human *African trypanosomiasi*s, HIV-1 integrase inhibitors and others.

During researching of anti-TB activity of newly synthesized derivatives of pyridyl-2-amides of the 1-R-2-oxo-4-hydroxy-quinoline-3-carboxylic acid substances with high level of anti-TB activity has been found.

Aim: Development of the methods of analysis of 5-methypyridine-2-amide-1-pentyl-2-oxo-4-hydroxyquinoline-3-carboxilic acid and the procedures required.

Method and materials: For identification of 5-methypyridine-2-amide-1-pentyl-2-oxo-4-hydroxyquinoline-3-carboxilic acid are:

- UV- Spectrometry
- reactions for enol hydroxyl group with heavy metals - in alkaline medium

For the quantification of 5-methypyridine-2-amide-1-pentyl-2-oxo-4-hydroxy-quinoline-3-carboxilic acid is proposed method of UV-spectrometry.

The results: The identification of 5-methypyridine-2-amide-1-pentyl-2-oxo-4-hydroxy-quinoline-3-carboxilic acid was successfully proven the results of quantitative determination were subjected to static processing as the procedure was repeated can therefore makes it possible to conclude that they are reliable, making it possible to assay the substance by the method of UV-spectrometry..

Conclusion: the analyzed substance can be quantified by the method of UV-spectrometry and can be identified by the formation of coloured products with heavy metals in alkaline medium.

DEVELOPMENT OF THE ANALYTICAL METHODS FOR SULFANILAMIDE AS PART OF EXTEMPORANEOUS OINTMENT

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Introduction. Extemporal formulation has a number of advantages over preparations made at the factory, for example: individual selection of ingredients taking into account the patient's allergy, the ability to combine substances in one dosage form and others. However, from the point of view of quality control, combined extemporal dosage forms are much more difficult to analyze, especially in pharmacies.

The **purpose** of our work is developing the methods for identification and assay of sulfanilamide in extemporaneous ointment:

Rp.: Streptocidi 1,0
Novocaini 0,5
Sulfuris 0,5
Ung. Tetracyclini 3% - 15,0
M. D. S.

Materials and methods. For operation measuring glassware of class A and excipients met the requirements of the State Pharmacopoeia of Ukraine were used.

Results and discussion. Since studied ointment is a multicomponent, we propose to carry out separation of the components during the sample preparation for their identification.

A weighed sample of the ointment was dissolved in hexane R and then were extracted the water soluble components. A suspension of sulfur and sulfanilamide in hexane is treated with hydrochloric acid and the sulfanilamide is determined by reaction of a primary aromatic amino group.

Sulfanilamide in the composition of this ointment is proposed to be determined by titration in sum with procaine hydrochloride using nitritometry, with further recalculation after determining the quantitative content of procaine hydrochloride photometrically. This is due to the complex composition of the ointment analyzed, in which each component has an effect on the other in the analysis.

Conclusions. The developed methods for identification and quantitative determination of compounds in combine extemporaneous ointment will be used in the further development of technological instructions for this dosage form and in the stability studies.

VALIDATION OF CEFUROXIME IODOMETRIC ASSAY USING POTASSIUM CAROATE

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Introduction. Cephalosporins are a large group of antibiotics derived from the mold Acremonium, which are widely used in the pharmacotherapy of many diseases. Cefuroxime (Cefuroxim), is a derivate of 7-ADCC and belongs to semisynthetic cephalosporin *β*-lactam antibiotics of the II generation. EPh and BPh recommend to determine cefuroxime using the method of HPLC.

Aim. The aim of the proposed research is to validate the procedure of the quantitative Cefuroxime determination in pure substance and powder for injection preparation by oxidimetric method using potassium caroate as analytical reagent ($KHSO_5$).

Materials and methods. The preparation Cefuroxime, powder for injection preparation 0.75 №1, «Lekchim-Kharkov» production, serial number 10712230412 was used. As analytical reagent the triple potassium salt of Caro's acid, $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ (Acros Organics) was used. Its active substance is potassium hydrogen salt of peroxomonosulfuric acid, $KHSO_5$. The method was validated according to the State Pharmacopoeia of Ukraine and the guidelines of the International Conference on Harmonization. The statistic calculation were performed using Microsoft Excel 2016. The Precision and Accuracy on these procedures were investigated with respect to repeatability and determined by performing five repeated analysis of the samples on the same day, under the same experimental conditions. The Linearity was determined for a wide range of concentration. The calibration curve was obtained, each research comprises 7 experimental points. LOD and LOQ were calculated from regression equation as $3.3\ S_0/b$ and $10\ S_0/b$ respectively, where S_0 and b are standard deviation slope of the calibration curve.

Results and discussion. The proposed method is based on the S-oxidation reaction of Cefuroxime by potassium caroate in acidic medium to the formation of corresponding S-oxide. The recovery percent ranged from 0.57 ÷ 0.97 %, δ= 0.3 ÷ 0.91 %). The Limit of Quantification (LOQ) is 0.05 mg mL^{-1}.

Conclusions. The proposed reaction of Cefuroxime S-oxidation using potassium caroate can be applied into analytical analysis. The obtained results have good agreement with those in SPhU. The obtained data shows that the proposed method can be applied for the determination of Cefuroxime in pure substance and medical preparation and can be used as alternative to current pharmacopoeia methods with confidence.

QUANTITATIVE DETERMINATION OF ANISE OIL IN AMMONIA-ANISE DROPS BY THE METHOD OF PEROXY ACIDOMETRY

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Introduction. Ammonia spirit-anise spirit drops (*lat.* Spiritus ammoniacatus anisatus, ATC code R05C A10) - combined medication with expectorant and anti-inflammatory action. 100 ml of drops contain anise oil 2.81 g, ammonia solution 15 ml the rest – auxiliary substances ethyl alcohol 90%. Anise oil stimulates the secretion of bronchial glands, ammonia contributes to the release of sputum and its easy release. In addition, anise oil helps digestion and has a laxative and antiseptic effect. Narrow-anise drops are used in the complex treatment of respiratory diseases: pharyngitis, tracheitis, bronchitis (acute and chronic), bronchopneumonia, bronchiectasis, pertussis in children. As a result of treatment, the digestion improves in the patients, the secretory and motor functions of the stomach and intestine are normalized, and flatulence disappears.

Epoxidation as alkenes using peroxy acids is one of the most fundamental reactions in chemistry, yet there are very few examples illustrate this important reaction in quantitative analysis. For the quantitative determination of the prevailing components of the essential oil, we used an epoxidation reaction with the use as oxidizing agent of the higher aliphatic peroxy acid – peroxycapric acid (C_{10}) in a medium of methylene chloride at the room temperature.

Aim. To develope of a simple method for quantitative determination of anise oil in ammonium anise drop by means of peroxy acid oxidation.

Materials and methods. Peroxydecanoic acid (peroxycapric acid) was obtained by D. Swern method. Method of iodometric titration. The standard solution is 0.0200 M sodium thiosulfate. Microburette for 10 ml. Aqueous solution of acetic acid (1:1). An aqueous solution of 5% KI. Methylene chloride, grade p.a. The object of the study was "Ammonia-anise drops" oral drops, solution in 25 ml bottles produced by "Ternopharm" (Ukraine, Ternopil). In 100 ml drops - anise oil 2.81 g, 10% ammonia solution 15 ml. 90% ethanol - 100 ml as excipient.

Results and discussion. It was found that using only a slight excess of peroxycaprinic acid maximized conversion of anethole to epoxide anethole. One mole peroxide is consumed per mole of anethole, that is, the reaction is quantitative (Fig.).

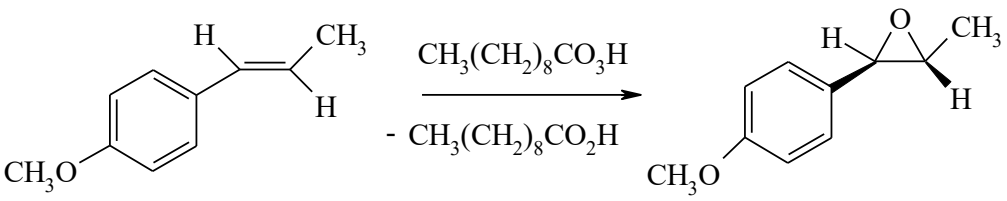

Fig. A scheme for the epoxidation reaction of *p*-Methoxy-*trans*-β-methylstyrene (*trans*-Anethole) by peroxydecanoic acid (peroxycapric acid)

Procedure of analysis. A mixture a preparation (5,0 mL) and sulfate acid diluted (10 mL) and saturated solution NaCl (10 mL) was stirred well (5 min) and leave to stand to layer separation. To the mixture was added 20 mL CH_2Cl_2 (2×10 mL) and resulting mixture was stirred for an additional 5 min and left to separation of layers. The organic layer was separated and washed with 10% aqueous Na_2CO_3 (1×25 mL) and dried (10 mg Na_2SO_4). A solution of peroxy capric acid (1.0 g/25) in CH_2Cl_2 (5.0 mL) was added drop wise. After the addition was complete, CH_2Cl_2 is added until the total volume of solution is 25.0 mL. The mixture is allowed to stand for 40-45 minutes until the reaction is complete at room temperature. An aliquot solution volume (1.00 mL) is titrated after preliminary addition of 1 ml of 5% KI and 2 mL of CH_3CO_2H (1:1) with a standard 0.0200 mol/L solution of $Na_2S_2O_3$ using microburette (*V*). The control experience is similarly carried out: To 20.0 ml of CH_2Cl_2 is added 5.0 ml of a solution of peroxycapric acid, thoroughly mixed and an aliquot of the resulting solution (1.00 mL) is titrated as before (V_0). The content of anise oil is determined from the difference in the volume of the titrant consumed in the control and working experiments, respectively (V_0 -*V*), using a titer found in a separate special experiment with an exact sample of the anise oil (0.1405 g / 5.00 mL). For n=7; P=0.95 RSD < 1.2 % (δ<RSD).

The verification of the correctness was carried out by comparing the results obtained with those of an independent (reference) GLC method using standard samples of individual basic components of anise oil and pharmacopoeial standard volumetry method of oil. The content of the main components relative to each other was established by the normalization method.

Conclusions. A simple method of analysis anise oil has been developed. The proposed method may be extended for the analysis of medicinal forms with anise oil.

A NEW METHOD FOR DETERMINATION OF THE CHOLINESTERASE ACTIVITIES

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Introduction. The cholinesterase (ChE) activity is an individual, stable characteristic and changes little throughout life. Row In the case of human diseases, changes in ChE in his blood. ChE activity decreases with stagnation in the liver (due to hemodynamic disturbances), obstructive jaundice, gallstone, disease, cholecystitis, cholangitis, liver cirrhosis, inflammatory processes in the liver , myocardial infarction, rheumatism, inflammatory Lesions of the skin and muscles (dermatomyositis), muscular dystrophy, chronic kidney disease, poisoning with some insecticides and pesticides, applied in agriculture and others. ChE activity increases with bronchial asthma, severe kidney disease (nephritis), uterine myoma, hypertensive disease nor, inflammatory diseases of the small intestine (exudative enteritis), exudative enteropathy, stomach ulcer, obesity, hyperlipidemia Teinemii, type II diabetes mellitus (in obese patients), alcoholism. It should be noted that a single analysis of ChE has limited diagnostic significance. More important is the laboratory monitoring ChE - data on changes in its activity - the results obtained during the systematic measurement of activity enzyme over a period of time. It causes requires a simple and inexpensive method of analysis ChE. Of the many methods developed so far for determining the activity of ChE, colorimetric methods are most popular, for which ease of analysis, high speed and sensitivity are characteristic. However they have some significant drawbacks. A new colorimetric enzymatic method for ChE determination has been proposed.

Aim. To develop a simple and express colorimetric method for determination of cholinesterase activities.

Materials and methods. All chemicals and reagents used were of analytical grade: Pharmacopoeial acetylcholine chloride (Ach) medication – 0.2 g per amp/5 ml; dry protein drug of ChE from horse serum–4 mg/ L (IV class) 28 AO/mg (SMU "Biomed", Russia), 3,3',5,5' -tetramethylbenzidine dihydrochloride monohydrate (TMB), 98,5% (Sigma). All the absorbence spectral measurements were made using photoelectric concentration colorimeter KPK-3-01 (Russia); filter №3, l = 3 cm). The rate of reactions described value of optical density of the solution for 10 minutes (by fixed time). Hydrogen Peroxide 30-40%" (LLC "Inter - Synthes", Boryslav, Ukraine).

Preparation solution of ChE: Standart stock solution was prepared in double distilled water by taking 0.0800g of dry *ChE* drug in a 20 ml volumetric flask and it

was diluted up to the mark. After that it was at thermostat 10 min at +38±0.5 ºC. The solutions of the test model samples are prepared similarly. The new photometric technique has been developed for determination ChE, based on the rate of enzymatic hydrolysis of acetylcholine ester by the enzyme sample (Fig 1.)

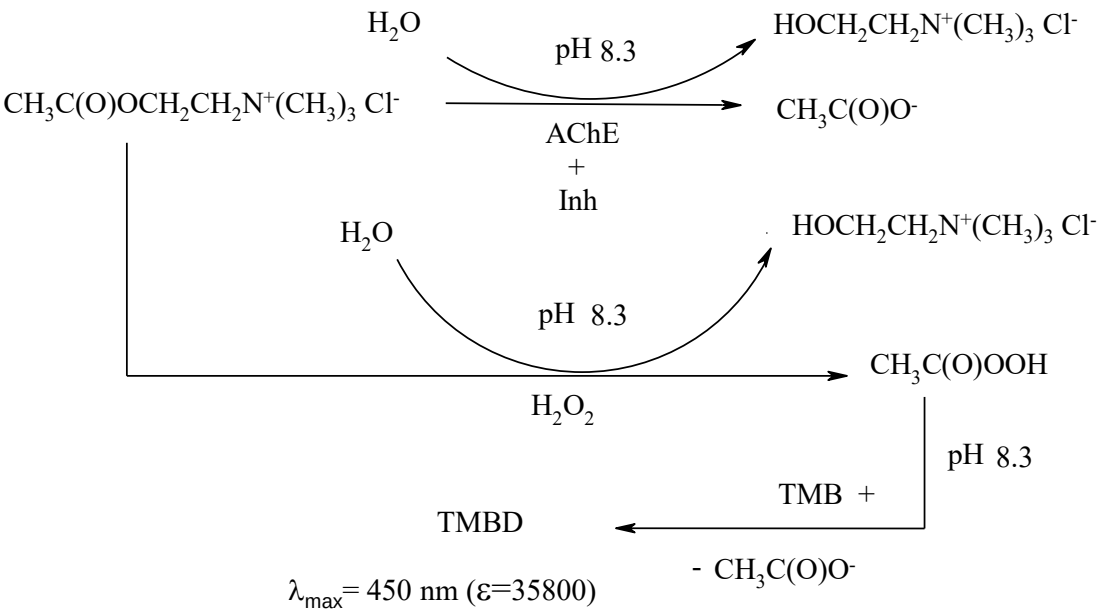

Fig 1. Scheme for determination ChE activity based on the use of conjugated perhydrolysis reactions and peroxy oxidation.

The activity of the enzyme is estimated from the concentration of acetylcholine, which is unreacted during the incubation with the enzyme, which is determined by the preliminarily constructed grading dependence of the absorption of the oxidation product of the indicator reaction (TMBD) on the concentration of the acetylcholine, taken after incubation in the absence of enzyme. For five averaged values of optical density using equation calibration curve found specific activity of the test sample enzyme (*U*), in international units (AO) - kmol/min to 1 mg of substance.

Results. The calibration graph the linear dependence of the activity of the enzyme (*U*, AO/mg) upon A was observed $U=(31.6\pm0.35)-(33.0\pm0.6)\cdot A$, (r=0,999). The results confirmed that the method is linear at concentrations ranging from 3.5 AO/mg to 28 AO/mg. Metrological characteristics of the proposed method is RSD= 1.8%. Accuracy is -0.5%.

Conclusion. A simple and inexpensive method of analysis ChE has been proposed.

IDENTIFICATION OF FLUOROQUINOLONES WITH COLOR REAGENTS

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Introduction. Rapid development of the pharmaceutical industry and large consumption of pharmaceutical products leading to the fact that drugs and their metabolites accumulate in the environment.

Particular threat among this class of contaminants are antibiotics that are widely used not only in medicine but also in agriculture. Getting to environmental this type of pollutants become a source of resistance to many strains of microorganisms. In many countries, confirmed the presence of trace concentrations of of antibacterial drugs in wastewater, surface water and in soil.

For Ukraine, where the proportion of production and consumption of antibiotics is quite large, this issue is very important and requires detailed study and develop methods to identify and remove this type of pollutants from the objects of biosphere.

Aim of the work was the development of methods of identification fluoroquinolones (ciprofloxacin, norfloxacin and ofloxacin) by colored reagents in a thin layer of sorbent for the purposes of ecotoxicological monitoring.

Materials and methods. Objects of research: eye/ear drops, containing ciprofloxacin («Ciprofarm», «Farmak», Ukraine), norfloxacin («Norfloxacin», Ukraine), ofloxacin («Unifloks», «Unimed Pharma», Slovak Republic).

Preparation of samples for research: to 1 ml of antibiotic solution (concentration is 3000 μg/ml) was added 10 ml of distilled water (Solution 1, concentration is 300 μg/ml). To 1 ml of Solution 1 was added 10 ml of methanol (Solution 2, concentration is 30 μg/ml).

The appropriate solution of fluoroquinolones in concentrations 0.3 μg, 0.6 μg, 0.9 μg in the sample was applied with capillary to the center of chromatographic plate Sorbfil (size 2x2 cm). After evaporation of the solution a glass stick was applied the appropriate reagent. After some time observed the appearance of characteristic color. Parallel control experiments were carried out. The results are presented in the table (Table 1).

Results and discussion. Was determined the color of the fluoroquinolonesand spots and their sensitivity during TLC determination. For this purpose, we used:

1) irradiation of UV-light (λ=254 nm);

2) iodine vapors;

3) Dragendorff's reagent (modificated by Munje);

4) ninhydrin;

5) bromothymol blue.

Reagents were prepared by known methods immediately before use.

Table 1

The identification of ciprofloxacin, norfloxacin and ofloxacin with color (chromogenic) reagents

Reagent	**Results**					
	ciprofloxacin		**norfloxacin**		**ofloxacin**	
Irradiation of UV-light (fluorescence)	white	0.6	white	0.6	green	0.6
Iodine vapors	light brown	0.6	light brown	0.6	light brown	0.6
Dragendorff's reagent (modificated by Munje)	brick red	0.3	brick red	0.3	brick red	0.3
Ninhydrin	pink	0.3	pink	0.3	pink	0.3
Bromothymol blue	orange	0.6	orange	0.6	orange	0.6

The results showed, that the most sensitive reagents for fluoroquinolones identification are Dragendorff's reagent (modificated by Munje) and ninhydrin. It formed the color with the solution of fluoroquinolone at a concentration 0.3 μg in the sample.

Reactions with bromothymol blue, iodine vapors and irradiation of UV-light were less sensetive – limit of detection was 0.6 μg in the sample.

Conclusions. Were investigated the conditions of the antibacterial drugs detection – fluoroquinolones derivatives with chromogenic reagents. Most sensitive reagents for fluoroquinolones identification are Dragendorff's reagent (modificated by Munje) and ninhydrin.

ELEMENTAL IMPURITIES IN THE LIGHT OF ICH Q3D REQUIREMENTS

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One of the most important parameters of the quality of drug product is their purity, namely the absence of substances which are not expected to be a part of the drug. In recent years the great attention was focused on the organic impurities which represent residues of starting materials of active pharmaceutical ingredients (APIs), or side products of API synthesis, or degradation as a result of storage of the medical product.

Control of potentially hazardous elemental impurities such as Cd, Pb, As, Hg was carried out by determination of the parameter "Heavy metals."
This parameter is set for APIs and excipients in Ukrainian and European pharmacopoeias but is excluded from the United State Pharmacopoeia (USP) with official entry into force will happen on 1 January 2018.

The disadvantage of the approach of the evaluation of elemental impurities by test "Heavy metals" is that the method does not take into account the presence of other elemental impurities such as iron, chromium, nickel.
In addition, the old method is not accurate enough, it is difficult to judge about accuracy of determination of volatile metals (such as mercury) by using the sample ignition for its preparation.

The risk assessment related to systemic exposure of elemental impurities on the human body can be done by their quantitative determination depending on the way of administration of the medicinal products (oral, parenteral, inhalation, etc.). This approach is described in ICH Q3D recommendations. The tougher requirements are introduced for inhalation and parenteral administration in comparison to oral administration.

ICH recommends certain established limits for elemental impurities based on the toxicological data and daily permissible dose (Permitted Daily Exposure, - PDE). Elemental impurities are divided into three classes.

Class 1 of the elements (As, Cd, Hg, and Pb) are human toxicants that have limited or no use in the manufacture of pharmaceuticals. Class 2 includes elemental impurities which toxicity depends on the method of administration (class 2a: Co, Ni, V, can be used as catalysts for chemical reactions in the synthesis of APIs and excipients; and subclass 2b: Ag, Au, Ir, Os, Pd, Pt, Rh, Ru, Se, Tl – elements which

are not used as catalysts, but can contaminate pharmaceutical product otherwise). Although Class 3 impurities (Ba, Cr, Cu, Li, Mo, Sb, Sn) is characterized by relatively low toxicity after oral administration, in the case of inhalation or parenteral administration the toxicity of this class may increase. Therefore, the above items are subject for adequate control.

Other elements are selected (Al, B, Ca, Fe, K, Mg, Mn, Na, W, Zn), for which is not established PDE due to the low inherent toxicity and due to national differences in regulation.

It should be noted, that the requirements of ICH Q3D applied for finished dosage form (FDF), but risk assessment takes into account potential sources of elemental impurities in the FDF, APIs, excipients and special aspects of the manufacturing process, packaging and so on.

For the quality control of content elemental impurities it is necessary to use appropriate sensitive instruments like ICP-OES (optical emission spectrometer with inductively coupled plasma) and ICP-MS (mass spectrometer with inductively coupled plasma).

The mentioned above methods are recommended by USP for the quantitative analysis of elemental impurities, which are breakthrough in comparison to the boundary determination of metals.

ICH Q3D requirements has already entered into the force in June 2016 for new drugs, and would be provided to commercialized drugs since December 2017. The new sections in the USP: "232" - element impurities limits and "233" - procedures, has already introduced and take the effect from 1st January 2018.

Therefore, to support the suitable quality in accordance with the guidelines of ICH Q3D, it is necessary to assess the health risks of the patient by determining the content of elemental impurities in APIs, excipients and FDF, and establish a routine control if it is necessary.

Thanks to the implementation of ICH Q3D principles, conditions for producing qualitative and safe medicines will be provided.

Therefore, Farmak JSC has already implemented approaches of ICH Q3D for new drugs. It was found that the content of elemental impurities in them does not exceed the set of limits. Moreover, we established the risk management system in sense of the evaluation of the elemental impurities in the approved medicines, taking into account the information of API and excipient manufacturers, as well as data regarding the content of elemental impurities in the FDF during their storage.

DEVELOPMENT OF EXPRESS IDENTIFICATION OF FUROSEMIDE SYRUP

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Introduction: The usage of test systems for the quality control of active ingredients is the very important part of express analysis of medicinal forms. Furosemide (4-chloro-2-[(furan-2-ylmethyl)amino]-5-sulphamoylbenzoic acid) is a widely used diuretic medication prescribed both for adults and children. The pediatric dosage form of furosemide is its suspension in the simple syrup of sucrose prepared ex tempore.

Purpose of the study: The purpose of our study was to elaborate a convenient method for the identification of furosemide in the dosage form of syrup based on its composition and properties.

Materials and methods: We used the analytical balance Axis ANG-200 and the methods of chemical identification.

The object of our investigation was furosemide syrup prepared from furosemide tablets and simple syrup of sucrose. The object was checked for the possibility of express identification for the functional groups.

The substance of furosemide forms the coloured precipitates with such salts of heavy metals as copper sulphate, ferric chloride and cobalt (II) chloride (nitrate). But in the presence of sucrose the salts of cobalt (II) cannot be used as in alkaline medium as they form a violet colouration with sucrose. To elaborate the usage of salt-formation reaction for the express analysis of furosemide we checked the possibility of it taking place on the paper strips treated with copper sulphate and ferric chloride. Our studies showed that furosemide suspension in the simple syrup gives green spots with copper sulphate, and orange-red spots with ferric chloride on the corresponding paper strips. We determined the minimum concentration of furosemide in simple syrup (5mg/ml) for which identification reaction with salts of heavy metals gives a positive result, and the optimum syrup-sodium hydroxide dissolution ratio for which the identification takes place on the test strips. Furosemide suspension in simple syrup after the extraction of the active ingradient in the reaction for a primary aromatic amino group (diazotization by sodium nitrite in the presence of hydrochloric acid and next azo coupling) gives a characteristic red colour of azo dye.

Results and conclusion: The obtained results suggest the ways of furosemide express identification in the pediatric dosage form of syrup and give the possibility to identify furosemide reliably.

SPECTROPHOTOMETRIC DETERMINATION OF BIOLOGICALLY ACTIVE SUBSTANCES AMONG THE DERIVATIVES O-HALOGEN NITROBENZOIC ACIDS

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Introduction. Among the aromatic acids important are replaced nitrobenzoic acids and their derivatives, interest that is due to high chemical activity that allows them to synthesize a number of structures. Based nitro-, bromo-, chloro-, 3-oxamoyil (suktsynoyil) - and 3- or 5-sulfamoyil substituted o-halogen benzoic acids synthesized and studied the biological activity of the following compounds: D - (+) - glucosylammonium salt; D - (+) - glucosamine; methyl esters; alkyl, aryl and heterylamides; hydrazides and their derivatives - R-edenhydrazides, arensulfohydrazides, β-N-atsylhydrazides, β-N- (o-tolylsuktsynamido) hydrazides; hydrazides, R-idenhydrazides 3-carboxy-2-chloroksanile and 3-carboxy-2-chlorsuktsynanile acids and their campaign, they, benzoyl peroxide and perbenzoic acid with chloro-, bromo-, sulfamoyil- and nitrosubstitutes at benzene ring.

Aim. The results of our research was discovered the possibility of using azo dyes derived imidazole for simultaneous extraction separation and spectrophotometric determination of o-halogen derivatives nitrobenzoic acids.

Materials and methods. The method of formation of derivatives assigned o-nitrobenzoic acids with halogen compounds such as azo dyes ionic associates that are able to be removed with chloroform. Important factors that affect the conditions of formation of associates, the difference in chemical properties of o-halogen nitrobenzoic acids and azo dyes.

Results and discussion. The dominant factor in the formation of ion associates in the aqueous phase is to create conditions for dominance anion nitrobenzoic acid derivative (A-) and azo dye cations (K +). Since azo dyes can exhibit properties amfolites and halogen derivatives of o-nitrobenzoic acids are weak organic acids is an important factor that affects the mechanism of extraction separation and spectrophotometric determination is to create an appropriate pH environment. An equally important factor is the selection of reagent concentrations of reagents and kinetic factors reaction.

Conclusions. Was studying the dependence extraction capacity of the location of substituents in the benzene ring, which allows extraction separation and spectrophotometric determination of orthohalogen derivatives nitrobenzoic acid in mixtures.

VERIFICATION OF DISSOLUTION TEST FOR DOXYCYCLINE HYCLATE IN CAPSULES

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Introduction. "Dissolution" test is recommended by the State Pharmacopoeia of Ukraine to determine the capsules kinetics of dissolution and their compliance with the requirements. According to the State Pharmacopoeia of Ukraine and the international pharmacopoeias recommendations, before being used in the laboratory, pharmacopeia method or test should be verified. This is necessary to confirm, that this laboratory is able to reproduce chosen method.

The **aim** of study was to verify the "Dissolution" test analytical method for doxycycline hyclate capsules, recommended by the US Pharmacopoeia.

Materials and methods. Getting the experimental data was performed simultaneously by a standardized procedure. Total uncertainty, linearity, accuracy, precision and specificity of model mixtures of a series samples with the known amounts of active substances were defining. For those 9 points within the investigated range of method 55-135% with 10% increment was studied. This was carried out in parallel on three measurements for each concentration. The results were treated statistically accordance with SPU.

Results and discussion. Carried out forecast showed that the total uncertainty of the methodic results is 1.04% and doesn’t exceed a critical value (3.0%). To determine the specificity investigated the effects of placebo. Our calculation showed that the overall effect of placebo on the total drug absorption is insignificant. The method is linear for all range of concentrations. Results systematic error satisfies the recommended criteria. Analysis of doxycycline hyclate model mixtures study showed that the investigated procedure is correct.

Conclusions. During the experiment the verification of the test "Dissolution" analytical method of doxycycline hyclate capsules was held. Characteristics of validation were determining using eligibility criteria. Researched validation characteristics confirm linearity, precision (convergence), the accuracy and specificity of the chosen method. Forecast total uncertainty of the proposed methodic meets the eligibility criteria. This method can be used in the future to study the solubility profile of doxycycline hyclate capsules.

THE REACTIVITY OF SUBSTITUTED 9-AMINOACRIDINES

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Introduction. Derivatives of 9-aminoacridine have a wide range of the pharmacological activity, which depends on their reactivity.

Aim. Therefore, to create drugs with the expected high therapeutic effect the reactivity of this series has been investigated for the first time in reversible conditions by studying the process of ionization of acids conjugated with substituted 9-aminoacridines.

Materials and methods. The study of acid-base equilibria was conducted on an EV-74 ionomer using a glass electrode (ESP-43-074) and a silver-silver chloride electrode (EVL-1M) at the temperature of 25^0C. The titrant was 0.01 M aqueous solution of HCl. The concentration of the solutions to be titrated was 0.001 M. Titration of each substance was performed in triplicates. Assessment of the accuracy of the results obtained was carried out by methods of mathematical microstatistics (the confidence interval was 0.95). To prepare the binary solvent a bidistillate, which was free of CO_2, and ethanol were used.

Conclusions.

1. The reactivity of substituted 9-aminoacridines has been studied in reversible conditions.
2. The ionization constants of the corresponding conjugate acids ($pK_{BH}+$) have been determined for 19 compounds by the method of potentiometric titration in the binary ethanol-water solvent at 298 K.
3. The influence of the electronic nature and position of substituents in the molecule of 9-aminoacridine on the basicity of these compounds has been analyzed. The electron donating substituents have been shown to increase their basicity, and the acceptor ones weaken it.
4. Within the principle of linearity of free energies the unified correlation equation for all members of homologous series (except 4-OCH_3) describing the relationship of $pK_{BH}+$ with the Hammett σ-constants with convincing statistical characteristics has been determined.
5. This equation allows to predict the acid-base properties of various substituted 9-aminoacridines; it is of great importance for the molecular design of active pharmacophores in this homological series.

DETERMINATION THE QUANTITATIVE "STRUCTURE – ANTIBACTERIAL ACTIVITY" RELATIONSHIPS IN A SERIES OF N-SUBSTITUTED AMINO ACIDS

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Introduction. The presence of the antibacterial and antifungal activity in derivatives of amino acids is determined by different mechanisms; therefore, a promising field of research is to obtain new N-substituted amino acids and study their antibacterial action.

Aim. To determine the quantitative "structure – antibacterial action" relationships in a series of N-substituted amino acids.

Material and Methods. The quantitative dependencies of the antibacterial action of the compounds studied on AlogPs values were calculated using the STATISTIKA 8 program.

Results. The satisfactory values of the levels of correlation of AlogPs parameters calculated with the experimental data of the antibacterial activity of N-substituted amino acids against *S. aureus*, *E. coli*, *P. vulgaris*, *P. aeruginosa*, *B. subtilis*, and *Cl. perfringens* are statistically significant. The absence of the relationship between the antibacterial effect against *C. albicans* and the structure of threonine derivatives may indicate a possible role of the latter in the metabolism of these fungi.

Conclusions.

1. To determine the quantitative "structure – antibacterial action" relationships the correlation and regression analysis of the AlogPs values calculated for N-substituted amino acids taking into account the results of the experimental study of the antibacterial action of the compounds under research has been conducted.
2. The statistically significant correlation values of AlogPs with the values of the antibacterial action of N-substituted amino acids against *S. aureus*, *E. Coli*, *Pr. Vulgaris*, *P. Aeruginosa*, *B. Subtilis*, *C. Albicans* and *Cl. perfringens* have been determined, and it quantitatively confirms the earlier assumptions of the existence of the "structure–action" relationship in this series of compounds and the degree of its manifestation.

RESEARCH OF THE KINETICS OF DISSOLUTION FOR MEDICINE SONDOX IN COMPARISON WITH ORIGINAL MEDICINE DONORMIL

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Introduction. Most drugs produced in the Republic of Belarus are reproduced medicines, the bioequivalence of which can be confirmed by studying bioavailability and pharmacokinetics in humans (volunteers) and animals. There is often a different rate of release of the drug substance from the drug in the therapeutic non-equivalence of drugs. Therefore, before carrying out expensive bioequivalent tests, it makes sense to conduct the "dissolution" test. In addition, in some cases, the dissolution test allows one to judge the bioequivalence of drugs (for example, in the study of tablets and capsules containing instant drugs). The "dissolution" test is also carried out during inter-series quality control at the production, which allows to prove the constancy of the composition and quality of the produced medicine.

Aim. Research of the kinetics of dissolution for generic drug Sondox (tablets 15 mg) in comparison with the original drug Donormil (tablets 15 mg).

Materials and methods. A working standard sample of doxylamine (series 030615, W = 100.09%) was used in the work. Reagents: purified water, potassium hydroxide, potassium phosphate disubstituted. For the preparation of placebo solutions, magnesium stearate, lactose monohydrate, potato starch, microcrystalline cellulose were used. The study was carried out using the spectrophotometer Specord 250 and the drug dissolution determinant “NevaPharm”.

Results and discussion. The kinetics of dissolution was studied in the "Rotating basket" instrument with a rotation speed of 100 rpm. The volume of dissolution media (0.1 M hydrochloric acid solution, 0.05 M phosphate buffer solutions with pH 4.5 and 6.8) was 500 ml. Sampling was carried out after 15 minutes.

The degree of release of doxylamine succinate from the original and generic drug after 15 minutes was statistically significantly ($t_{exp} > t_{crit,\ n = 12,\ P = 0.95}$) exceeded 85% in all three dissolution media. This allows us to conclude about the pharmaceutical equivalence of the Sondox and Donormil tablets without calculating the similarity coefficient.

Determination of the concentration of doxylamine in dissolution media was carried out by the method of derivative spectrophotometry. The absorption spectrum of doxylamine succinate has one absorption maximum of about 262 nm. The specific absorption coefficient of doxylamine succinate at 262 nm is small and amounts to only 232. A study of the dissolution kinetics of the doxylamine succinate tablets was performed using a minimum volume of a 500 ml dissolution medium.

Measurements should be carried out at a fixed pH value to minimize errors.

This is achieved by adding 2.5 ml of the test solution and 100 µl of a 4 M hydrochloric acid solution to the cuvette.

The absorption spectrum of doxylamine succinate has one maximum at 262 nm. Placebo has a significant effect on the measurement results at the indicated wavelength (Figure 1). The use of the first derivative at 259 nm makes it possible to eliminate the interfering effect of the background (Figure 2).

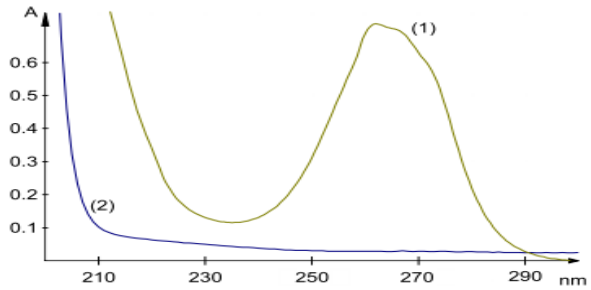

Figure 1. The absorption spectrum of a solution of doxylamine succinate 30 µg / ml (1) and a placebo solution (2)

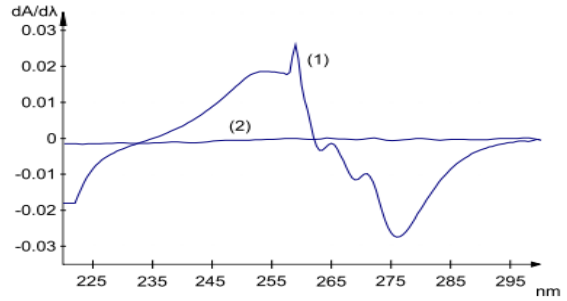

Figure 2. The first derivative of the absorption spectrum of the solution of doxylamine succinate 30 µg / ml (1) and placebo solution (2).

The developed procedure is validated to a range of concentrations of doxylamine succinate of 18.0-36.0 µg / ml, which corresponds to the degree of release of 60-120%. This is sufficient to research of the kinetics dissolution of tablets containing doxylamine succinate. Table 1 presents the results of the validation of the method for the parameters "precision" and "accuracy" for model solutions obtained with the use of placebo.

Table 1.

The results obtained when the procedure is performed accuracy (n = 3, P = 0.95)

Degree of release of the active substance (AS)	Introduced AS, µg / ml	Found AS, µg / ml	R, %	RSD, %
0,1 M HCl				
60	18,0	18,1±0,2	100,6	1,03
100	30,0	30,4±0,4	101,2	1,08
120	36,0	35,5±0,1	98,6	0,33
0.05M phosphate buffer solution (pH 6.8)				
60	18,0	18,1±0.3	100,8	1,57
100	30,0	29,8±0,1	99,3	0,35
120	36,0	35,6±0,2	99,0	0,43

The method is linear in the range of concentrations of doxylamine succinate from 6.0 to 36.0 µg / ml, the correlation coefficient is more than 0.99, and the free member of the calibration curve is 0.72% of the value of the analytical signal corresponding to 100% drug release.

Conclusions. A comparative research of the kinetics of dissolution was carried out for generic drug Sondox tablets 15 mg in comparison with the original drug Donormil tablets 15 mg. Determination of the concentration of doxylamine succinate in model solutions was carried out by the method of derivative spectrophotometry. The procedure was validated on parameters of specificity, accuracy, precision. The range of drug concentrations is 18,0-36,0 µg/ml. It is sufficient for the test.

RESEARCH OF RHEOLOGICAL AND QUALITY VALUES OF GEL "LAGODEN"

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Introduction. Structural-mechanical and rheological properties of semisolid medicinal forms are important parameters and qualities characterize the «permanence» of their properties on the stages: development, production and promotion to the consumer, including the application. The study of quality indicators of any drug is the main criteria for their production. pH environment, mechanical stability and identity is serve as objective characteristics of quality.

The aim of work is research of rheological parameters and quality indicators of gel "Lagoden."

Materials and methods. Composition of gel "Lagoden", which was used in experiments: Lagoden - active substance, carbopol – gelling agent, solution of sodium hydroxide, glycerin, nipagin, nipasol and treated water. Active substance – Lagoden is sodium salt of labdan acid. In the experiments used physical, physical-chemical and chemical methods qualitative analysis of drugs. Measurement of the rheological parameters of gels of samples was performed on a rotary viscometer «Reotest 2». Stability identified in centrifuge SUM-1. pH environment identified in potentiometer EV-74.

Results and discussions. To determine the authenticity made two reactions. The presence of diterpenes skeleton proved the reaction of the drug mass 0.2 g with 1ml concentrated sulfuric acid on the water bath at a temperature of 333 K to 2-3 minute. At the same time there was a yellow color, to your queue passed in red, then in the dark red. In another experiment 1.2 g gel was stirred with 2ml water and added 2ml 20% solution of sulfuric acid. As a result of the reaction was formed white precipitate was that proves the presence of lacton ring.

Stability gels to centrifugation defined as follows: 5.00 g hitch gel was centrifuged a machine SUM-1 at 1500 rpm / minutes for 5 min. It was no bundle gel or allocation of the liquid part of the gel. For the study of the impact of temperature on the gel 10.00 g gel was placed in a closed, dried porcelain cup diameter 4-5 cm and left in the thermostat at a temperature of 333 K 2-3 minutes. As a result of heating no change in the structure and appearance drug not observed. To study the effect of temperature on rheological properties and to determine thixotropic effect experiments were performed with gel system containing 0.50% lagoden and 0.80% carbopol. On the base results were plotted graphic [Fig. 1].

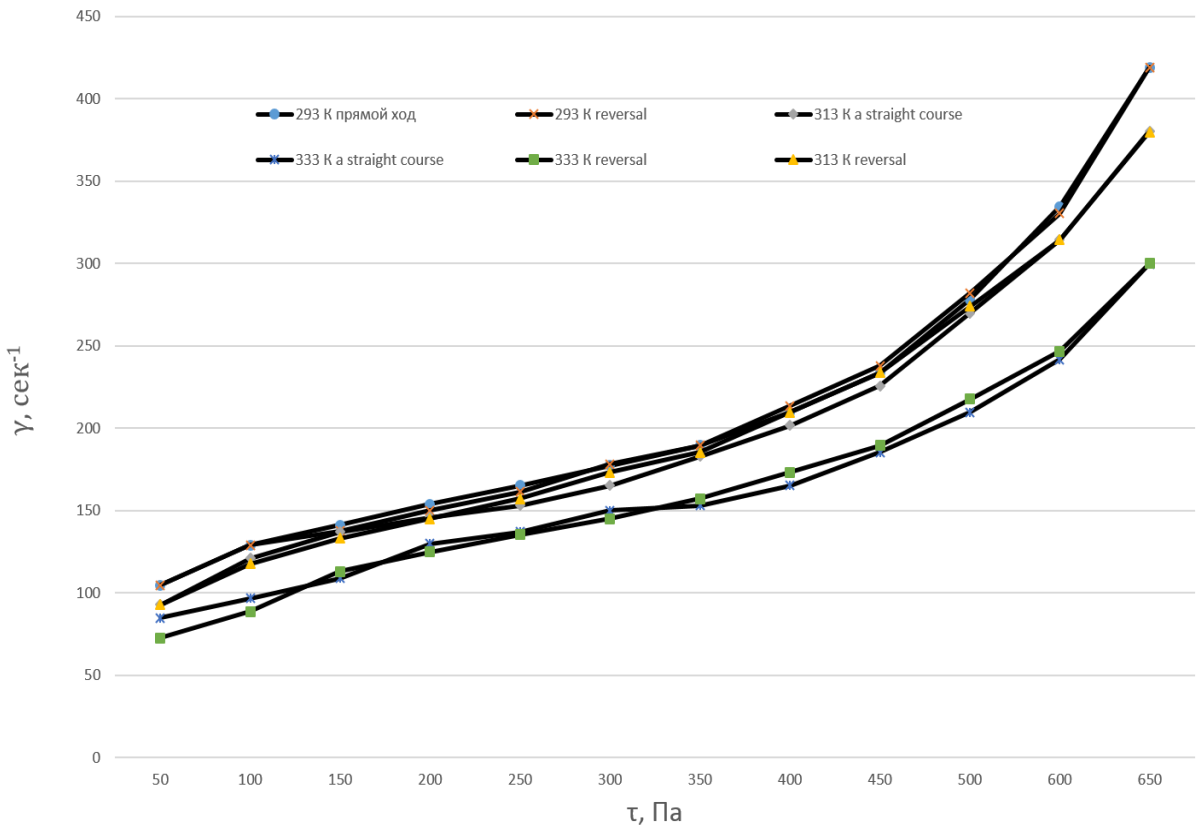

Fig. 1. The temperature decreases with increasing shear stress, the viscosity of the gel “Lagoden”.

From Fig. 1. shows that the temperature decreases with increasing shear stress, the viscosity of the system. The observed phenomenon leads to the conclusion that this is broken due to the very low energy and subsequently occurs destruction gel. On the chart you can see the thin hysteresis loop. If present pronounced hysteresis loop, then we could talk about the thixotropic gel. In this case, too, there is thixotropic, but it is impossible to measure. In the literature, this type of thixotropic called "instant thixotropic" namely, a system with this type of thixotropic quickly restore their structure after removal of the external influence.

pH gel identified potentiometric by: 5.00 g gel was heated to 323-333 K with 50 ml water, and then intermixed in the magnetic mixing machine. Filtered the contents of the flask through the "ash-free filter" and identified pH environment filtrate potentiometer (calomel reference electrode). Set the value of pH gel is 7.82.

Conclusions. 1. For the first time was studied rheological properties of gel “Lagoden” on the base carbopol and was determined that gel has certain structure in formation system.

2. According to the results carried out analyzes (determination of pH environment, mechanical and the temperature stability) found that gel "Lagoden" has a satisfactory quality values.

THE USE OF THIN-LAYER CHROMATOGRAPHY IN IDENTIFICATION OF GLAUCINE HYDROCHLORIDE

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Intoduction. The group of cough medicines includes drugs, which enhance the sputum elimination and help to ease the exhausting cough in patients. Drugs, that inhibit the cough center may be applied in specific cough therapy, but their use is restricted because of the possibility of drug addiction development. Nowadays the drugs, use of which doesn`t lead to this complication are most commonly involved in therapy and the glaucine hydrochloride is one of them. Glaucine hydrochloride (Glauvent) posesses an antitussive and mild hypertensive properties and also doesn`t inhibit the inspiratory center when compared to codeine. The drug is perscribed in those patients with lungs and upper respiratory tract disorders, who also experience severe cough. Glauvent also promotes interest in sence of chemical toxicology.

Aim. Development of conditions for detection of glaucine hydrochloride in presence of other substances via thin-layer chromatography (TLC) is the goal of our work.

Materials and methods. In our research we used the Sorbfil plates (silicagel TLC-IA, fraction of 5:17 μm), glass plates for high performance thin-layer chromatography (HPTLC, silicagel CGGS, fraction of 5:20 μm, layer thickness of 130±25 μm), glass plates by Merck (Germany) (silicagel GF-254), systems of mobile solvents with acid, alkaline and neutral properties and developing reactants.

Results and discussion. The most optimal mobile solvents systems for identification of gluacine hydrochloride are: methanol─ammoniac (100:1,5), (Rf=0,56), plates Sorbfil, butanol-1-acetic acid─water (66:17:17) (Rf=0,47), plates Merck, ethylacetate─methanol─diethylamine (30:20:1,5) (Rf=0,55), plates Sorbfil. The possibility of dividing the glaucine hydrochloride from other drugs with similar activity was also investigated. Division was reached in following systems: methanol─ammoniac (100:1,5), ethylacetate─toluole─diethylamine (30:20:1,5). For development of glaucine hydrochloride on chromatogram we used the following reactants: bromphenol blue, iodine vapour, Dragendorf`s reactant in different modifications. The Dragendorf`s reactant appeared to be the most sensitive: we have identified 0,5 μg of the drug in a sample.

Conclusions. The results of our research may be used during the toxicological analysis for glaucine hydrochloride.

DEVELOPMENT OF THE EXTRACTION METHOD OF PREDNISOLONE FROM AN OINTMENT WITH A HYDROPHILIC BASE FOR QUANTITATIVE SPECTROPHOTOMETRIC DETERMINATION

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Introduction. The composition of an ointment with a hydrophilic base includes 0.5g of prednisolone, 10.0g of urea, 1.0g of sodium edetate, propylene glycol, liquid paraffin, cetyl alcohol, stearyl alcohol, macrogol cetostearyl ether, purified water. Components, that constitute the base, and emulsifiers do not dissolve in ethyl alcohol. The urea, which is extracted from the ointment together with prednisolone, absorbs only in the region of 200-220 nm and does not affect the analysis results.

Aim. The aim of our work is to select a filter and determination of the necessary conditions for extracting prednisolone from an ointment with a hydrophilic base.

Materials and methods. The pharmacopoeial standard sample of prednisolone PSS State Pharmacopoeia of Ukraine (SPhU) No.11/1-2143 (the content of prednisolone is 99.8%) and hydrophilic ointment with active substance prednisolone ointment were used. The following analytical equipment was used: a “SPECORD 200” spectrophotometer, cuvettes with the thickness of 10 mm, AV 204 S / A METTLER TOLEDO analytical balance, a “Sartorius AG” pH meter. Reagents, measuring glassware of class A meeting the requirements of the SPhU were used for the work.

Results and discussion. It is established that during a single filtration approximately 70-80% of prednisolone from the nominal amount is extracted, therefore it is recommended to carry out the procedure three times. To select the optimal filter, filtration was carried out with a paper filter of the "Blue Ribbon" type and a glass filter of Schott. When using a glass filter of Schott, excluding prednisolone, auxiliary substances are extracted, the alcohol solution has fatty inclusions, and the investigated spectrum has an overestimated optical absorption. It is therefore advisable to use ashless filter paper such as "Blue Ribbon". The operations of heating, cooling, and filtration were first carried out for the standard solution, in order to determine the error introduced by the losses during filtration. It was found that the losses are insignificant $(A_{st}=0,781;\ A_{st(filter)}=0,775;\ \Delta_{Handle}=0,78\% \leq 1,024\% = max\delta)$ and fit within the framework of statistical uncertainty.

Conclusions. The extraction method of prednisolone from an ointment with a hydrophilic base was developed: a filter ("Blue Ribbon ") was selected and the necessary extraction conditions were determined. It was found that the procedure for extracting prednisolone from the base must be repeated three times – then the concentration is 99.62% of the nominal concentration.

LIQUID CHROMATOGRAPHY FOR QUALITY CONTROL OF CALCIUM CHANNEL BLOCKERS

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Introduction. Owning to its high resolution and sensitivity, high performance liquid chromatography (HPLC) is the most commonly used analytical technique for the quality control of pharmaceuticals. It allows fast separation and quantification of compounds in pharmaceutical dosage forms and biological fluids. Therefore, it is widely employed in academic and pharmaceutical industrial settings. HPLC methods with reversed-phase analytical columns give best results, but require centain amounts of time and organic solvents. The unique properties of acetonitrile or methanol make them the solvents of choice to develop validated HPLC methods for the separation and the quantification of many pharmaceuticals. These advantages made the developed chromatographic methods an attractive protocol for the routine quality control and dosage form analysis of pharmaceuticals.

Aim. The objective of this research was to develop more simple, sensitive, accurate and less expensive analytical methods for the determination of calcium channel blockers (amlodipine, nifedipine, verapamil hydrochloride) in medicines by HPLC.

Results and discussion. We have used columns which provide high speed and high efficiency at a lower pressure system. This reduces the number of used mobile phase and reduce the cost analysis. The proposed methods have the advantage over American pharmacopoeial methods due to speed and ease of preparation of the mobile phase and reduced chromatography time. Under these conditions the peaks of API elution are not more than 4 minutes.

According to the requirements of the SPhU and ICH guidelines, methods of quantitative determination of medicines must be validated. We have studied the following validation characteristics: linearity, accuracy, precision, robustness and range of application.

Conclusion. A powerful, simple, sensitive, accurate and attractive HPLC methods have been developed for quality control and dosage form analysis of calcium channel blockers. The proposed methods were validated as per ICH guidelines and can be applied for routine analysis in quality control laboratories.

REACTIVITY OF N-[(2-OXOINDOLIN-3-YLIDENE)-2-OXIACETYL]AMINOACIDS PROPYL ESTERS

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Introduction. In the study of the pharmacological activity of N-[(2-oxoindolin-3-ylidene)-2-oxiacetyl]aminoacids and their esters, synthesized at the Department of Analytical Chemistry, National University of Pharmacy it was found that a wide spectrum of biological effects is characteristic for them.

Aim. The aim of this work was to study the reactivity of propyl esters of N-[(2-oxoindolin-3-ylidene)-2-oxiacetyl]aminoacids to optimize the conditions of their synthesis and develop mathematical models of interrelation "structure-biological activity" enabling targeted searches of compounds with desired high level of biological effects.

Materials and methods. Acid - base balance was studied by potentiometric titration. The titrant used was a standard 0.05 M aqueous solution of potassium hydroxide, free from carbon dioxide. Concentration of solutions titrated – 0.005 M at the point of half neutralization. Potentiometric titration was performed on ionomer EV - 74 using a glass (ЭСП 43-074) indicator electrode. The reference electrode was a silver chloride electrode (ЭПВ-1). The experiment was carried out at 25ºC with a threefold repetition. The accuracy of the results was assessed by means of mathematical statistics of small samples (confidential probability 0.95). Mixed solvent was received from bidistillate free from carbon dioxide and 1,4 - dioxane.

Conclusions.

1. By studying acid-base balance the reactivity of propyl esters of N-[(2-oxoindolin-3-ylidene)-2-oxiacetyl]aminoacids was investigated. It was found that they have the function of weak monobasic acids. An equation of ionization by enol hydroxyl was worked out.

2. Measuring of 9 propyl esters N-[(2-oxoindolin-3-ylidene)-2-oxiacetyl] aminoacids ionization constant has shown that the extend of polymethylene chain weakens ionization.

3. By Hammett equation a quantitative assessment of the impact of methylene units on the aminoacid fragment of molecule was carried out and a low sensitivity of the reaction center to extend of polymethylene chain was identified.

THIOTRIAZOLIN ANALYSIS BY ELECTROCHEMICAL METHODS IN PHARMACEUTICAL PRODUCTS

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Introduction. 1,2,4-triazole derivatives are known as effective cardioprotective, anti-ischemic, antiarrhythmic, hepatoprotective, cerebroprotective, anti-inflammatory, immunomodulatory, antioxidant medicines. One of these compounds is thiotriazolin – morpholine salt of 3-methyl-1,2,4-triazol-5-thioacetic acid.

In the literature sources it was described the procedures of determining the content of the main ingredient in the biologically active substance of thiotriazolin by the method of acidimetric non-aqueous potentiometric titration, and also the procedures of simultaneous quantitative determination of thiotriazolin and piracetam, thiotriazolin and carbamazepine or isoniazid in combined medicines when their joint presence by the method of high-performance liquid chromatography (HPLC). Therefore, the actual analytical problem is to develop new alternative procedures of thiotriazolin quantitative determination; they should be of required analytical and metrological parameters, high sensitivity and rapidity, and may be used to determine thiotriazolin both in substance and dosage forms.

Materials and methods. ***Amperometric titration.*** *Reagents.* 12-phosphomolybdic acid (PMA) $H_3PMo_{12}O_{40}\cdot 26H_2O$ and 12-phosphotungstic acid (PTA) $H_3PW_{12}O_{40}\cdot 29H_2O$ were of analytical grade.

Place 2.2940 g of PMA into the measuring flask with the capacity of 100.0 mL, dissolve in distilled water when heating on a water bath and dilute the solution to the volume with the same solvent (the concentration is $1.0\cdot 10^{-2}$ mol/L).

Thiotriazolin ($C_9H_{16}N_4SO_3$) was of pharmacopoeial purity and purchased from the State Enterprise «The Plant of Chemical reagents» of Scientific and Technological Corporation of «Institute for Single Crystals», Kharkiv, Ukraine.

Equipment. The device «АУ-4М» consisted of such units as the microammeter M-95, the power supply and the system of two electrodes; the indicator electrode is the butt graphite electrode with the working surface diameter of 5 mm (rotation speed is 660 rps); the reference electrode is saturated calomel half-cell.

Results and discussion. Keggin structure heteropolyacids (HPAc) are widely used analytical reagents for determination of a number of biologically active substances, which contain a basic atom of nitrogen. However, in the literature sources there is not enough data about application of such Keggin structure

heteropolyacids as 12-phosphomolybdic heteropolyacid and 12-phosphotungstic heteropolyacid for analysis of nitrogen-containing biologically active compounds. Keggin structure heteropolyacids are used owing to the ion-exchange properties, and the ability to reduce easy, to precipitate large organic cations with formation of slightly soluble compounds with associative nature of chemical bond, and these compounds are able to dissolve in organic solvents and are poorly soluble in water. Experimental data analysis has shown that the optimal electrode characteristics has the ISE with the following parameters:

– electrode-active substance has the composition of $(TTZH_2)_3(PMo_{12}O_{40})_2$;
– the quantitative content of the EAS in the ISE membrane is equal to 0.01 g;
– application of dibutyl phthalate as a solvent-plasticizer.

The response time of the electrodes is 40 – 50 s, the linearity range of the dependence of $E = f(pC)$ is from 10^{-5} to 10^{-2} mol/L with the slope S of 29 – 30 mV, which is close to Nernst value for the divalent cations. It has been investigated the possibility of application of the developed ion-selective electrode with EAS based on the associate of thiotriazolin OC and heteropolyanion of 12-phosphomolybdic acid in the analysis (Table 6) of pharmaceutical dosage forms (the tablets and solution for injections of the JSC «Kyivmedpreparat» and also the combined tablets of thiotriazoline and famotidine). The study of dependence of ISE electrochemical properties on the solution pH has shown that the slope of the calibration curves has the constant value within the pH range from 4.0 to 6.0. It is observed narrowing of the linearity range and decreasing the slope of the electrode function when shifting the solution pH in the acid or alkaline medium (Fig.). Therefore, we used the batch of thiotriazolin standard solutions with pH = 4.0 for further studies.

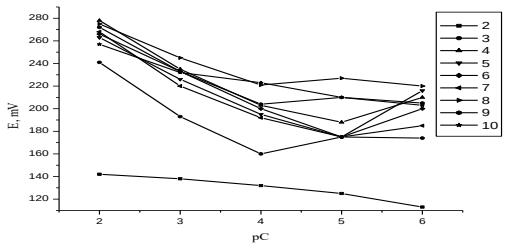

Fig. Influence of pH on the electrode function of ISE, which is reversible to thiotriazolin OC

The conducted investigations of the reaction between heteropolyanion of $PMo_{12}O_{40}^{3-}$ with organic cation of thiotriazolin nave been used for the development of the procedures of thiotriazolin quantitative determination by the methods of amperometric titration and direct potentiometry (using the developed ISE), which allow to carry out the analysis without complicated steps of sample preparation and preliminary separation of interfering components.

QUANTITATIVE DETERMINATION METHODS OF PARACETAMOL IN COUMPOUNDING PREPARATION

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Introduction. There are many treatments for catarrhal diseases, most of which are based on the administration of anti-inflammatory and antipyretic drugs. Paracetamol (or acetaminophen) is a part of the class of drugs known as "aniline analgesics"; it is the only drug which is still in use today. For decades, this substance is part of many drugs taken for colds and viral diseases. Paracetamol is used as an analgesic and antipyretic, in the treatment of a wide variety of arthritic and rheumatic conditions involving musculoskeletal pain and in other painful disorders such as headache, dysmenorrhoea, myalgia and neuralgia.

Extemporal compounding in their arsenal contains a large number of formulations, which include acetaminophen, which can be made in appropriate dosage forms, suspensions, powders, capsules.

Many methods are available in literature for assay of paracetamol in diverse types of samples including pharmaceutical preparations. These methods are as diverse as a simple titrimetric method to HPLC and spectrophotometric methods. Owing to wide spread use of paracetamol in different kinds of pharmaceutical preparations, rapid and sensitive methods for the determination of paracetamol are being investigated.

Aim. The aim of our research is to develop in accordance with the requirements of SPU quality control methods paracetamol, which is part of extemporal LF in the form of capsules. A simple, sensitive, accurate UV absorption spectrophotometric method for routine assay of paracetamol dosage forms for determination of chemical and biological stability.

Materials and methods. Based on the studies, quantification of paracetamol capsules is recommended by absorption spectrophotometry in the UV region. As the solvent used 0.1 M sodium hydroxide test solution optical density measured at 257 nm wavelength. Calculation of the quantitative content was performed by standard and specific absorption rate, which are set independently.

Results and discussion. In the study of subordination solution Beer–Lambert–Bouguer law found that the direct relationship observed in solution concentration of the active ingredient of $1.5 \cdot 10^{-4}$ to $1.3 \cdot 10^{-3}$ g/ml at length wave 257 nm, specific absorption rate is from 838 to 717.Check the stability of the solution was carried out for 60 minutes. It was established that the analytical solution is stable for hours.

Conclusions. Thus, the results can be possible to use techniques developed by us to quantify paracetamol in dosage forms.

DEVELOPMENT OF HPTLC METHODS FOR QUALITY CONTROL OF COMPOUNDING ORAL SOLUTION WITH HERBALS

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Introduction. There are list of often prescribed compounding preparations in pharmacies of Ukraine, which have license for preparation of compounding formulations. The necessary requirements for all drugs are its safety, efficacy and quality. To ensure the quality of preparations during their storage period they should be controlled with the usage of appropriate quality control methods developed and validated with modern techniques and stability study should be carried out.

The aim of this paper was development of quality control methods for compounding oral drops with herbals.

Material and Methods. The object of our work was compounding oral solution with herbals for internal usage. As active ingredients oral drops contained mixture of Leonurus and Valeriana tinctures and 2 % solution of Sodium Bromide. This preparation is often used as sedative drug in pediatrics. As quality control technique high performance thin layer chromatography (HPTLC) was used. Instrumentation used was: CAMAG ATS 4; ADC 2; Plate Heater; Immersion Device III; TLC Visualizer; vision CATS software; Analytical Balance MS 205 DU, Mettler-Toledo.

Results and Conclusions. For identification of oral solution the marker substances such as valerenic and acetoxivalerenic acids specific for Valeriana and flavonoids specific for Leonurus were used. In addition the HPTLC fingerprints of oral drops were compared with fingerprints of Valeriana and Leonurus tinctures and its mixtures. To determine the presence of Valeriana root in composition of oral drops such chromatographic conditions were selected: solvent for sample preparation – butanol; the mobile phase – cyclohexane, ethylacetate, glacial acetic acid (60:38:2); derivatization – anisaldehyde reagent, use (dipping time – 0, speed – 5), heat at 100°C for 3 min; examination under white light and under UV 366 nm. To determine the presence of Leonurus herba in composition of oral drops such chromatographic conditions were selected: solvent for sample preparation – butanol, the mobile phase – ethyl acetate, methylethylketone, formic acid, water (5:3:1:1); derivatization – NP/PEG, use (dipping time – 0, speed – 5), heat at 100°C for 3 min; examination under UV 366 nm. Thus, the optimal chromatographic conditions that ensure specific, robust and precision results of identifications were determined. Developed methods will be used for stability study of compounding preparation.

EXTRACTION OF METRONIDAZOLE FROM AQUEOUS SOLUTIONS

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Introduction. The choice of sample preparation procedure for biological liquids exerts key influence on parameters of bioanalytical method. The main stage of sample preparation of biological objects for subsequent determination of the target substances is the analyte extraction from the aqueous medium by organic solvents.

Aim. To study the process of metronidazole extraction from aqueous solutions by organic solvents for further development of the sample preparation procedure for blood and urine.

Materials and methods. Metronidazole was of pharmacopoeial purity. The metronidazole solutions with concentrations of 20, 40, 80 and 140 μg/mL in water, $1 \cdot 10^{-2}$ mole/L and $1 \cdot 10^{-5}$ mole/L hydrochloric acid solutions, $1 \cdot 10^{-2}$ mole/L and $1 \cdot 10^{-5}$ mole/L sodium hydroxide solutions were prepared.

The extraction procedure: 10.00 mL of metronidazole solution was placed into the separating funnel and extracted with 10.00 mL of chloroform or mixture of chloroform and isopropanol (8:2). The obtained organic extracts were separated, filtered through the paper filter with 1 g of sodium sulphate anhydrous (wetted with the respective solvent) into the measuring flask with the capacity of 25.0 mL, and diluted to the volume with the same solvent. Two aliquots of the obtained solution (in 10.00 mL each) were used for quantitative determination of metronidazole by the method of UV-spectrophotometry. The extract was evaporated and the dry residue was dissolved in 10.00 mL of 0.1 mole/L hydrochloric acid solution or 10.00 mL of 96% ethanol. The absorbance of the obtained solutions was measured at 277 nm or 310 nm respectively using the respective solvent as compensation solution.

All spectrophotometric measurements were carried out using a single beam UV/VIS spectrophotometer SPEKOL®1500 (Analytik Jena AG, Germany).

Results and discussion. Metronidazole extraction from aqueous solutions was carried out with organic solvents immiscible with water; the medium pH was equal to ≈ 2, 5, 7, 9 and 12 that corresponded to the values commonly used to isolate analytes from body liquids in forensic toxicology. To create pH acid and alkali were used instead of buffer solutions to model the real conditions of sample preparation.

Conclusions. Metronidazole is extracted from aqueous solution in all types of medium (acid, weak acid, neutral, alkalescent and alkaline) with effectiveness not less than 30%. The most effective extragent for metronidazole is the mixture of chloroform and isopropanol (8:2) at pH ≈ 12 (97%) and pH ≈ 9 (90%).

DEVELOPMENT AND VALIDATION OF NEW METHOD FOR ASCORBIC ACID IN COMPOUNDING PREPARATIONS

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Introduction. Vitamin C, also known as ascorbic acid and L-ascorbic acid, is available in various dosage forms, it is an ingredient of a number of vitamin preparations, some cough and cold remedies and also extemporal forms. It is found in supplements alone or in combination with other ingredients, including herbal formulations. It is usually found in multivitamins, including ones made for children, adults, and prenatal care.

Aim. The aim of our study is to develop methods for quality control of ascorbic acid in pharmacy-prepared capsules.

Materials and methods. We used chemical methods of quantitative determination of ascorbic acid in the pharmacy-prepared capsules which prepared in pharmacy "Leda" (series DU0261511546). Reagents, volumetric solutions and indicators that meet SPU. Analytical scales «AXIS» ANG 200 (Poland) and measuring vessel class A.

Results and discussion. For identify the active pharmaceutical ingredient in the composition of pharmacy-prepared capsules was selected chemical reactions - gray sludge formation under the influence of silver nitrate, blue solution of 2,4-dyhlorfenolindofenole discoloration and reaction of ascorbinase of iron (II) blue-violet color.

To quantity determine of ascorbic acid, which has restorative properties, was used chemical rapid method of determining, in particular redox method. The titration is carried out in a mixture of water and sulfuric acid or in an aqueous medium of 0.05 M iodine solution as without indicators way to slightly yellow color, and with the use of indicator - starch solution (to steady blue color). To quantitative determination of ascorbic acid was chosen as an alternative method of acid-base titration. Titrated 0,1 M sodium hydroxide solution, using phenolphthalein as an indicator. The content of the active ingredient in the capsules was calculated in grams, based on the average weight of the contents of the capsule. The most accurate method proved iodometric quantitative determination, based on titration of active ingredient capsules in water with sulfuric acid.

Conclusions. We are working to develop methods to identify and the quantitative determination of ascorbic acid in pharmacy-prepared capsules.

COMPARATIVE ANALYSIS OF STANDARDIZATION OF DIETARY SUPPLEMENTS AND MEDICINES CONTAINING VITAMINS BY CHEMICAL COMPOSITION

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Introduction. One of the group of the products possessed the leadership position in the actual pharmaceutical and parapharmaceutical market is the vitamin medicines and dietary supplements.

Aim. To systematize information about assortment of monocomponent and combined dietary supplements and medicines containing fat-soluble vitamins and vitamins of B-group, their qualitative and quantitative composition, and control parameters of the presence and content of active ingredients.

Results and discussion. Monitoring of the data of the State list of drugs of Ukraine shows that more than 100 medicines containing fat-soluble vitamins (D, E, F, K) and vitamins of B-group (B_1, B_2, B_5, B_6, B_9, B_{12}) are registered in Ukraine. The medicines are represented mainly by combined products. Dragee, tablets and capsules are dominated among dosage forms for *per os* application. Content of the analysed vitamins is approximately at the same level for all selected combined medicines – it is varied within ±20% from the median.

Information from the State list of food products of special dietary application, functional food products and dietary supplements, and also Internet-sources shows that the number of vitamin dietary supplements exceeds the number of respective medicines in 2 – 3 times. Selected products are represented mainly by combined supplements. Dosage forms for *per os* application (dragee, tablets and capsules) are also the main group. The single doses of vitamins in such products are very different; they are varied within 10% – 300% from the median, and in all cases are less than for respective real drugs – in 1.5 times and more (till 20 times).

Conclusions. Vitamins are the natural compounds and usually should be ingested with food in common amounts. In a number of cases vitamins may be taken as medicines, but their chemical state in the medicine composition differs from their natural state; therefore, they should be standardized by chemical parameters – identification should be carried out, impurity content and also content of active ingredient should be checked.

The requirements to the parameters of chemical standardization of real drugs and dietary supplements containing vitamins should be normalized and harmonized within the general approaches.

QUANTITATIVE DETERMINATION OF CALCIUM CARBONATE AND MAGNESIUM HYDROXIDE IN THE SIMULTANEOUS PRESENCE IN SUSPENSION WITH FAMOTIDINE

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Introduction. Tendency to the increasing of part of extemporaneously prepared drugs on pharmaceutical market is observed at last time. One of the basic conditions of making drugs in pharmacies is the presence of precise, easily reproducible and economically accessible assay methods for each prescribed component. Famotidine suspension with $CaCO_3$ and $Mg(OH)_2$ is one of the spread extemporaneous produced medications. Simultaneous assay of Mg^{2+} and Ca^{2+} in sample is inconvenienced because of similar chemical properties of those cations.

Aim. Development of the method for simultaneous quantitive determination of Ca^{2+} and Mg^{2+} cations in sample in the ex tempore prepared suspension with famotidine was the aim of our study.

Materials and methods. The famotidine suspension with $CaCO_3$ and $Mg(OH)_2$ was chosen as the study object. The "AB 204 S/A Mettler Toledo" analytical balances, class A measuring glassware, and reagents and substances meeting the requirements of the State Pharmacopoeia of Ukraine (SPhU) were used in the investigation.

Results and discussion. The SPhU (as other leading world's pharmacopoeias) recommends a complexonometric titration for drugs containing salts of alkaline earth and heavy metals. Simultaneous determination of $CaCO_3$ and $Mg(OH)_2$ in sample was based on some differences in their acid-base properties. The total amount of cations was determinated by titration with 0.1M EDTA using eriochrome black T as an indicator. Titration was carried out with adding ammonia buffer solution pH 10.0 to pH 9-10. Individual titration of Ca^{2+} was carried out with using murexide as an indicator in more basic medium sfter adding diluted NaOH to pH 12-13. In these conditions Mg^{2+} precipitates as $Mg(OH)_2$. The volume of 0.1M EDTA used for determination of Mg^{2+} is calculated as the difference between volumes for determination of total amount of cations and for determination of Ca^{2+}. The study was carried out on the model mixtures and on the suspension sample. Uncertainty of average results of assay was 0.94% for $CaCO_3$, and 1.42% for $Mg(OH)_2$.

Conclusions. Simultaneous complexonometric titration method for $CaCO_3$ and $Mg(OH)_2$ in sample in the suspension was developed for the first time. The proposed assay method was used on the model mixture and on drug sample.

COMPARATIVE ANALYSIS OF STANDARDIZATION OF DIETARY SUPPLEMENTS AND MEDICINES CONTAINING *Ginkgo biloba L., Crataegus L., Vaccinium myrtillus L., Hippophae rhamnoides L., Vaccinium vitis idaeae L.* BY CHEMICAL COMPOSITION

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Introduction. The actual market of phytomedicines is presented not only by real drugs, but it is oversaturated with so-called dietary supplements. Often the composition of supplements and drugs is the same.

Aim. To systematize information about assortment of monocomponent and combined dietary supplements and medicines containing the target plants, their qualitative and quantitative composition, and control parameters of the presence and content of active compounds.

Results and discussion. Information from the State list of food products of special dietary application, functional food products and dietary supplements, and also Internet-sources was studied, and it was selected the dietary supplements containing *Ginkgo biloba L., Crataegus L., Vaccinium myrtillus L., Hippophae rhamnoides L., Vaccinium vitis idaeae L.* Selected products are represented mainly by combined supplements (44 of 49), monocomponent products are present only for last three plants (2, 2 and 1 respectively). Dosage forms for *per os* application (tablets and capsules) are dominated. The medicinal plants are introduced into the supplements composition in the form of raw material or extracts; their content is unavailable in 90% cases.

Monitoring of the data of the State list of drugs of Ukraine showed that 94 medicine containing the target plants were registered in Ukraine. Combined and monocomponent drugs are represented in approximately equal amounts, excluding medicines from sea-buckthorn presented only as individual products. The products are mainly the mixtures of dry plant raw materials or different kinds of extracts; their content may differ in 1,5 – 3 times.

Conclusions. The specified plants are included into the State Pharmacopoeia of Ukraine or described in another Pharmacopoeias, their quality is checked by chemical composition (presence and content of the groups of biologically active compounds or individual components), and medicines containing them should be analysed by these parameters, but dietary supplements are entered into the market without such control.

Therefore, it is necessary to harmonize the requirements to the parameters of chemical standardization of real drugs and dietary supplements containing the same active plant ingredients.

QUANTIFICATION OF METHYLURACIL BY THE METHOD OF SPECTROPHOTOMETRY

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Introduction: the search of easy and not-time consuming methods of analysis of active pharmaceutical ingredients is being carried out at the Pharmaceutical Chemistry Department of National University of Pharmacy. Methyluracil (6-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione) belongs to non-steroidal anabolic medications for the systemic use and the external application. It accelerates the processes of cellular regeneration and healing of wounds. It also has an anti-inflammatory effect. A characteristic feature of the medication is the stimulation of erythropoiesis and especially leucopoiesis, hence it is also referred to the group of leucopoiesis stimulants. Methyluracil is not included neither in the European Pharmacopoeia no in the State Pharmacopoeia of Ukraine but is present in the Russian Pharmacopoeia. The assay of methyluracil by the Russian Pharmacopoeia is carried out by the method of non-aqueous acid-base titration that needs the special appliance and such hazardous organic solvents as methanol and benzene.

Purpose of the study: The aim of our work was to check the possibility of usage of ultraviolet spectrophotometry method for the quantification of methyluracil and the development of a procedure for its assay.

Materials and methods: We used the analytical balance Axis ANG-200 and the measuring glass wear of class A. For the spectrophotometric investigations we used the spectrophotometer Evolution 60S. The statistical studies were carried out by the common procedure.

The electron absorption spectra of methyluracil in water and ethanol were studied. It was found that its spectra in water and ethanol have the absorption maximum at 265 nm and 267 nm.

The specific absorbance of methyluracil in water solution in the maximum at 265 nm was calculated. Its metrological characteristics were determined.

As the spectrophotometric quantification of methyluracil can be carried out by the methods of specific absorbance and the method of standard the corresponding procedures were developed. The validation characteristics that prove the possibility of the suggested methods for the assay of methyluracil were obtained.

Results and conclusion: The simple UV spectrophotometric procedure for the assay of methyluracil that provides good accuracy of the results has been developed.

QUALITY CONTROL OF PHARMACEUTICAL INGREDIENTS IN MULTICOMPONENT MEDICAL FORM

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Introduction. Dehydration is a deficiency of body fluids that results when the amount of fluid lost from the body exceeds the amount of fluid taken in. The symptoms of mild to moderate dehydration include thirst, fatigue, restlessness, irritability, headaches, and decreased urine output, while severe dehydration is a life-threatening emergency characterized by confusion, lethargy, apathy, dizziness, unconsciousness, and rapid heartbeat and breathing.

Therapy violation of water-salt metabolism is usually carried out by drugs, outpatient and chemical methods and balanced diet.

Mild dehydration can be effectively treated by drinking regular water or beverages that contain electrolytes, which you can buy in chemists in packets, which containing combination of different salts. Oral rehydration mixture (ORM) formulation to treat clinical dehydration irrespective of the cause or age group affected. The ORM consists of a balanced combination of sugar (glucose), sodium and potassium chloride, and tri-sodium citrate.

Aim. Development of methods of quality control of active pharmaceutical ingredients mixture (sodium chloride, potassium chloride, sodium citrate and glucose) to restore water-salt balance away from the use of them and establish chemical and microbiological stability of the dosage form.

Materials and methods. Dosage form "Mixture for the restoration of water-salt balance" drug production "Leda" (Series 011216), which composition as active ingredients include sodium chloride, potassium chloride, sodium citrate, glucose relevant quality certificates. Reagents, volumetric solutions and indicators that meet SPU. Analytical scales «AXIS» ANG 200 (Poland) and measuring vessel class A.

Results and discussion. For identify the components of the mixture recommended response to sodium cation, chloride and citrate ions and determine the influence of glucose copper-tartaric solution. Quantitative of mixture content was determined by several methods. The amount of sodium chloride, potassium chloride and sodium citrate determined by argentometric titration, sodium citrate titration by cuprumetry method. To quantify the glucose used redox method – iodometry in an alkaline environment, the reverse titration, using starch solution as an indicator.

Conclusions. We are working to develop methods to identify all of the API and the quantitative determination in the test dosage form.

IDENTIFICATION OF RAW CRUDE DRUGS BY MEANS OF RAMAN SPECTROSCOPY

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Introduction. The development of pharmaceutical enterprises follows the path of active introduction of innovative and science-intensive technologies that ensure the conformity of production to GMP standards. At the present stage, the increased technical equipment of enterprises allows solving complex tasks of ensuring and controlling the quality of medicines. High-tech analytical equipment is equipped with computer systems that allow processing and statistical analysis of a large amount of data.

One of the promising methods used in pharmaceutical enterprises is Raman spectroscopy. Raman spectroscopy is a method for studying the vibrational and rotational states of molecules of an investigated substance in the interval from about 2 to 4000 cm-1, based on the phenomenon of inelastic (Raman) Raman scattering of monochromatic light in the visible, near UV or near IR ranges. The spectra are very sensitive to the nature of chemical bonds – both in organic molecules and polymeric materials, and in inorganic crystal lattices and clusters.

Purpose of the study. To consider the possibilities and advantages of Raman spectroscopy in problems of control and identification of input medicinal raw materials using statistical methods.

Results. Raman spectroscopy is used in:

- Biological and medical diagnostics: allows to detect changes in molecules, analyze cell interactions, investigate microorganisms in cells, detect cancer;
- Pharmaceutical: allows to analyze the composition of tablets, solutions and gels; To control the drying processes of mixing and coating the preparations; Control the purity and quality of medicines; To check raw materials, allowing to identify with high accuracy input materials.

The high resolution and sensitivity of the Raman spectroscopy method allow rapid identification and analysis of the composition of drugs. The Raman effect is highly sensitive to small differences in chemical composition and crystallographic structure, allows the use of non-contact and non-destructive technology, which practically does not require sample preparation.

The method of Raman spectroscopy makes it possible to obtain an individual spectral imprint, unique with respect to the molecule in question or an entire molecular structure. This makes it possible to successfully apply statistical methods of analysis in the identification and quality control of drugs.

The report considers the application of statistical analysis methods when distinguishing closely-spaced spectra of medicinal raw materials.

Conclusions. The Raman spectroscopy method has significant advantages: it can be used for the analysis of aqueous solutions; The intensity of the spectral lines in the solution is directly proportional to the concentration of specific compounds; The Raman spectrum does not depend on changes in the temperature of the solution; The method of Raman spectroscopy practically does not require sample preparation, application of reagents, and is not influenced by the material of the cell, for example, glass.

The advantages associated with the specific nature of the method make the Raman spectrometry a powerful tool for analyzing the quality of the input medicinal raw materials. The main limitation of Raman spectrometry is the fluorescence of impurities. However, fluorescence can be avoided by choosing a source of exciting laser radiation with large wavelengths, for example, the near infrared region of the spectrum.

The use of statistical methods of data analysis in applied problems of quality assurance of medicines makes it possible to:

- to classify and quantify the properties of substances in the test sample;
- to identify and quantify the use of standard samples by statistical approximation of the spectra obtained;
- identify and perform a comparative analysis of data with libraries of spectral characteristics of different samples.

DEVELOPMENT OF QUANTIFICATION METHODS FOR PROCAINE HYDROCHLORIDE IN COMBINE EXTEMPORANEOUS OINTMENT

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Introduction. Currently compounding pharmacy drug production is wide enough. At the same time, the quality requirements for medicines are also significantly higher. However, the quality control of factory medicines and pharmaceutical manufacturing is still different. This is due to the fact that in pharmacies, often, there is no expensive equipment and production volumes are much less.

To expand the pharmacological action of drugs in pharmacy conditions, individual selection of components is possible. Therefore, the development of rapid, accurate and reproducible methods of drug quality control in pharmacy conditions is very relevant in our time.

The **aim** of our work was the development of methods for the identification and quantification of procaine hydrochloride in the following ointment:

Rp.: Streptocidi 1,0
Novocaini 0,5
Sulfuris 0,5
Ung. Tetracyclini 3% - 15,0
M. D. S.

Materials and methods. Analytical studies were performed at spectrophotometer Evolution 60S. For operation were used measuring glassware of class A and excipients met the requirements of the State Pharmacopoeia of Ukraine.

Results and discussion. Since studied ointment is a multicomponent, we propose to carry out separation of the components during the sample preparation for their identification.

A weighed sample of the ointment was dissolved in hexane R and then were extracted the water soluble components. The aqueous layer was separated and carried out the identification of procaine hydrochloride by the reactions: bleaching of potassium permanganate (1 g/l) solution, the formation of Schiff's bases and formation of azo dye. The reactions of identification the chlorides are also made.

This multicomponent ointment is very difficult from the point of view of the analyst. Using the most appropriate titration methods for the pharmacy is impossible because each of the components will interfere with the definition of the other. Thus, when titrating the procaine hydrochloride, the sulfanilamide, which also contains the

primary aromatic amino group, will be titrate by nitritometry. If we titrate procaine hydrochloride by related hydrochloric acid alkalimetrically or argentometrically, along with it will be titrated tetracycline hydrochloride.

Therefore, we decided to develop a physico-chemical method for the quantitative determination of procaine hydrochloride in our ointment.

At the first stage of development, we studied the literature data, from which we found out that procaine hydrochloride is able to form ion associates. To confirm this, we tested the ability of procaine hydrochloride to form associates with various indicators. Proceeding from the experimental data obtained, it is proposed to use methyl orange as the reagent for the development of the quantitative determination method.

In the second stage, our task was to develop an optimal method of sample preparation. For this purpose, a model solution of procaine hydrochloride was prepared with a concentration close to that prescribed in the ointment. To create a specific pH medium, use a saturated solution of sodium bicarbonate.

To avoid the influence of tetracycline hydrochloride on the absorption of this associate, it is proposed to convert the indicator into an acid form by changing the pH of the resulting solution.

For the ointment preparation we propose the next method: the exact sample of the ointment is dissolved in chloroform, placed in a separation funnel; saturated sodium bicarbonate solution is added to create the pH of the medium and a solution of methyl orange is added also. Extraction is carried out, the chloroform layer placing into a volumetric flask.

Absorbance is measured at 522 nm wavelength. The quantitative content is calculated according to the standard method, using as a standard SPS of procaine hydrochloride.

One of the main requirements, which allow using spectrophotometric methods for substance assaying, is the subordination to Bouger-Lambert-Beer law. To check the submission of substance solution light absorption to the Bouger-Lambert-Beer law, we need to draw graph dependence of the absorbance on the solution concentration. Solutions light absorption obeys Bouger-Lambert-Beer law within concentration, in which the constructed calibration graph appears as a straight line.

To study this dependence, solutions of different concentrations were prepared. After series of experimental studies we established that the procaine hydrocloride solution obeys this law within concentrations from 0,02 to 0,5 mg/ml.

Conclusions. The developed methods for identification and quantitative determination of procaine hydrochloride in combine extemporaneous ointment will be used in the further development of technological instructions for this dosage form and in the stability studies.

PROJECT OF THE EXPERIMENT ''THE DEVELOPMENT OF DISSOLUTION TEST FOR MEDICATED CHEWING GUMS''

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Introduction. Medicated chewing gum is solid, single-dose preparation that has to be chewed and not swallowed. Chewing gums contain one or more active ingredients that are released by chewing. A medicated chewing gum is intended to be chewed for a certain period of time, required to deliver the dose, after which the remaining mass is discarded. During the chewing process the drug contained in the gum product is released from the mass into saliva and could be absorbed through the oral mucosa or swallowed reaching stomach for gastro-intestinal absorption. This dosage form has many advantages: fast onset of action; high bioavailability; easy for administration without water promotes higher patient compliance; ready for use; easy to take by children and patients who find swallowing tablets is difficult; side effects are fewer.

The development of quality control methods helps to expand the range of medicated chewing gum. The current edition of the Russian State Pharmacopeia does not have General monograph on medicated chewing gum and the article on dissolution test for medicinal chewing gum, making it difficult to realize new drugs in this form. Therefore, the introduction of a common monograph on the dissolution test for this pharmaceutical form is an actual task.

There is no manufacturer of the device for carrying out the dissolution test for chewing gum in the Russian Federation. The equipment and service offered by the United States and Europe is expensive.

Aim. The development of the experiment reproducing dissolution test for medicated chewing gum.

Materials and methods. In the first stage of the study it was necessary to review literature about the application and existing quality control methods of chewing gum. Particular attention was given to the study of current regulatory documents. We studied monographs about dissolution test for medicated chewing gum presented in European Pharmacopoeia, The State Pharmacopoeia of Ukraine and The State Pharmacopoeia of the Republic of Kazakhstan.

Results and discussion.

After analyzing monographs about dissolution test for medicated chewing gum, we concluded that the same apparatus basically are used overall. Key elements of equipment for performing the dissolution test medicated chewing gum are: cell for testing; vertical piston with the upper grinding surface; main camera with the lower chewing surface; device to perform chewing movements; device for rotating the vertical rod. We can simulate the process of chewing in the laboratory by kneading movements of a pestle in mortar. As a chamber for placement the testing chewing gum is used a mortar (volume 100 ml), as a simulator of piston is used pestle with diameter of the work surface is about 27 mm.

The dissolution test should reproduce the conditions for releasing of the drug from the gum. It is necessary to study the process of chewing to develop a dissolution test for chewing gum. We decided to simulate the process of chewing through using a buffer with a pH 6.0-7.0 (pH of human saliva) and taking the temperature of the mouth 37ºC after reviewing scientific data.

Only one chewing gum «Nicorette» is registered as a drug in The Russian Federation. So that's what we chose to study as the object. There are chewing gums registered as oral nutritional supplement in the drugstores of Russian Federation. They contain vitamins and substances (extracts) of plant origin. We plan to take these chewing gums as further objects of study.

Conclusions.

We investigated the literature data about existing monographs from different countries, studied the chewing process and selected conditions of simulating chewing in the lab. We proposed a testing method of dissolution test for medicated chewing gum in the laboratory.

Testing method: the 20 ml of the dissolution medium (phosphate buffer solution pH 6.0) heated to a temperature of 37ºC are placed in a mortar. Then pre-weighed piece of chewing gum or whole chewing gum is placed in the mortar. The gum is kneading with a pestle, turning it about 20º. After a certain period of time samples are taking, in which determine the amount of the released substance in the appropriate way. Medium replacement may be made after each sampling procedure.

THE CHOICE OF THE ELECTRODE ACTIVE SUBSTANCE FOR THE ION-SELECTIVE ELECTRODE ON GENTAMICIN

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Introduction. Gentamicin sulfate belongs to aminoglycoside antibiotics and has a wide spectrum of the antibacterial action. However, its long-term use can cause neuritis and the impaired renal function. Gentamicin sulfate has also the ability to suppress respiration up to development of the neuromuscular blockade. Microbiological, spectroscopic and chromatographic methods are used to determine gentamicin sulfate, but ionometry is not practically used. Ion-selective electrodes (ISE) with plasticized membranes based on ion associates of gentamicin with tetraphenylborate and acid black chromium are described in literature. At the same time, the electrodes proposed are characterized by a narrow range of the concentrations determined and a low specificity of the membrane in the presence of organic ions, and it makes analysis of gentamicin in complex dosage forms more difficult. Nevertheless, there are data concerning the use of associates of organic cations with the Keggin structure heteropolyanions ($XMe_{12}On_{40}^{n-}$ where X(P,Si) Me(Mo(V);W(VI);V(V)) as an electrode active substance.

Aim. To study the use of associates of the Keggin structure heteropolyanions with gentamicin as electrode active substances to obtain ISE on gentamicin sulfate.

Materials and methods. The reactions of gentamicin sulfate with different heteropolyacids, such as phosphomolybdic, phosphatotungstic, silicomolybdic, silicotungstic acids, were studied.

Results. As a result of reactions the corresponding ionic associates of gentamicin sulfate with the abovementioned heteropolyacids were obtained. These associates are yellow or white colored compounds, slightly soluble in water. Such parameters of the reaction sensitivity as the limit concentration (C_{lim}) and the limit dilution (V_{lim}) were also calculated. These parameters are within $C_{lim} = 10^{-4}$-10^{-5} g/cm^3, $V_{lim}=10^3$-10^4 cm^3/g. The reaction of gentamicin sulfate with phosphatotungstic acid is the most sensitive: $C_{lim}=(3.2+0.2)\cdot10^{-5}$ g/cm^3, $V_{lim}=(3.1+0.1)\cdot10^4$ cm^3/ g.

Conclusions. Thus, the ionic associate of gentamicin sulfate with phosphatotungstic acid should be used as an electrode active substance for ISE on gentamicin.

DEVELOPMENT OF A SIMPLE RP-HPLC-ELSD METHOD AND EXTRACTION PROCEDURE FOR QUANTIFICATION OF TERPENE LACTONE IN GINKGO PREPARATIONS

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Introduction. *Ginkgo biloba* is one of the most popular medicinal plants. Active compounds in Ginkgo extract possess antioxidant, antiasthmatic and wound-healing properties, improve blood circulation, discourage clot formation, reinforce the walls of capillaries and protect nerve cells from harm when deprived of oxygen. Due to its notable pharmacological effects, *Ginkgo biloba* is widely used for the treatment of Alzheimer‘s disease, concentration difficulties and memory impairment, cerebral insufficiency, intermittent claudication, vertigo and tinnitus.

Terpene lactones are a family of compounds with unique chemical structures, first recognised in an extract of *Ginkgo biloba*. The major problem in Ginkgo terpene trilactone analysis still lies in the sample clean-up of the crude initial leaf extracts or solutions of standardised extracts. Standardised extracts not only contain 6 % terpene trilactones but also 24 % flavonol glycosides which can interfere with the ensuing separation and detection step if not removed.To solve the analytical problems of Ginkgo terpene lactones, the development of a reliable and robust extraction and analytical method is required as alternative to the conventional analyses.

Aim. This paper presents the development of simple extraction and analytical method for the simultaneous identification and quantification of the terpene lactone chemical markers in *Ginkgo biloba* preparations.

Materials and methods. The object- Phytopharmaceutical preparations of *Ginkgo biloba* were provided by the producers or bought in a pharmacy.

Qualitative and quantitative analysis was performed by Waters 2695 Alliance system with photodiode array detector Waters 996 and evaporative light scattering detector Waters 2424 (Waters Corporation, Milford, USA). The chromatographic separation was carried out using a 250 × 4.6 mm, 5 μm LiChrospher 100 RP 8 endcapped column (Merck KGaA, Darmstadt, Germany) that was thermostated at 25 °C. Mobile phase consisted of tetrahydrofuran, methanol, water (10:20:75 V/V/V). Eluent flow rate – 1.0 ml/min, injection volume – 20 μl.

The drift tube temperature for ELSD was set at 55 °C and and nebulizing gas (N_2) flow rate was 1.5 $L \cdot min^{-1}$. The DAD detector was employed at the wavelength range from 210-400 nm for obtaining a sufficient number of detectable peaks. As a result 350 nm was selected by comparing all the chromatograms and UV

characteristic spectra of referenced compounds.

Calibration graph method using logarithmic calibration method was selected for quantitative analysis of terpene lactones. Estimates obtained the parameters of validation confirmed its selectivity, linearity repeatability and the limits of accuracy.

Results and discussions. To avoid flavonoids, the sample is first hydrolyzed with HCl at 100 °C and then using ELSD detection analyzed. A rapid extraction procedure has been developed for quantification of terpene lactone in *Ginkgo biloba* extracts. Suitable extraction conditions were optimized as follows: Ten tablets of each sample were weighed and ground to fine powder using a mortar and pestle. Ten capsules were opened and emptied, and the contents were mixed and weighed. 7.5 ml of methanol –water mixture (1:1 V/V) was added to each vial containing weighted sample. The vial was performed in ultrasonic bath for 5 min and centrifuged. Upper part gently was taken out from the residue and moved to 25.0 volumetric flask. 7.5 ml of methanol – dilute hydrochloric acid mixture (1:1 V/V) was added to each vial containing residue from previuos step. The vial was performed in ultrasonic bath for 5 min and centrifuged. For each sample, the extraction with 7,5 ml of methanol – dilute hydrochloric acid mixture (1:1 V/V) was repeated one more time. All fractions were collected and diluted to 25.0 ml with methanol-water mixture (1:1 V/V). 10 ml of the combined supernatant extracts were placed in a 10 ml brown-glass vial and closed with a rubber seal and aluminium cap and heated on the water-bath for 2.5 hour. Solution was cooled to room temperature. The extracts were filtered through 0.45-μm nylon syringe filters prior to injection into the HPLC system.

It was found that evaporation light scattering detector can be used to analyze *Ginkgo biloba* extract produced from the analysis of medicinal products. This detector is more sensitive than the currently used refractometric detectors, are not sensitive to temperature variations, suitable for use with mobile phase gradient. Therefore, appropriate methods, which previously applied refractometer, to optimize adaptation evaporative light scattering detector. The optimized RP-HPLC-ELSD methodology: selected column – ACE C8, 4.6 × 250 mm, particle size 5 μm, column temperature - 25 °C, injection volume-20 μL, evaporative light cattering detector parameters: nitrogen flow rate – 1.5 L min^{-1}; The drift tube temperature - 55 °C.

Conclusion. The developed and validated analytical procedure presented in this report is profitable for evaluation of the quality of *Ginkgo biloba* phytopharmaceuticals.

DEVELOPMENT OF THE METHODS TO CONTROL THE QUALITY OF BIOLOGICALLY ACTIVE COMPOUNDS IN PHYTOEXTRACTS

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Introduction. At the Department of Pharmaceutical Technology of Drugs of The National University of Pharmacy performed work on the development of technology syrup "Cholophyt" with hepatoprotective and choleretic action, which includes herbs such as artichoke leaves, rose hips, stevia herb, immortelle flowers, and corn silk.

Aim. The aim of our research - development of quality control methods of biologically active compounds in phytoextract, which is part of the syrup. To identify of biologically active substances (BAS) in investigated syrup used physico-chemical and chemical methods.

Materials and methods. Artichoke leaves, rose hips, stevia herb, immortelle flowers, corn silk and reagents that meet SPhU. Chemical crockery class A, weighing «AXIS» ANG 200. The method of TLC plates for TLC Silica gel 60 F25425. The method of absorption spectrophotometry in the ultraviolet and visible spectrophotometer using Evolution 60S. Chemical reactions inherent flavonoids.

Results and discussion. The previous biologically active substances of phytoextract total set by absorption spectrophotometry in the ultraviolet region. Established that all absorption spectra of test solutions are characterized by absorption bands in the region of 290-327 nm, which proves the existence of substances aromatic character.

Have identified BAS of phytoextract by thin layer chromatography in a solvent system as anhydrous formic acid – glacial acetic acid – water – ethyl acetate (11: 11: 27: 100) compared with pharmacopeia standard model, chlorogenic acid and caffeic acid. The data indicate the presence of a total amount phytocomplex hydroxycinnamic acid preferably similar in structure to chlorogenic acid.

Quantitative determination of the amount BAS was performed by absorption spectrophotometry in the UV at 327 nm wavelength. Calculation of the content of hydroxycinnamic acids was performed by standard method.

Conclusions. Established that amount of hydroxycinnamic acids content in terms of chlorogenic acid is 0.10 - 0.15%.

QUANTITATIVE DETERMINATION BY POTENTIOMETRIC TITRATION METHOD OF ACTIVE PHARMACEUTICAL INGREDIENTS IN COMPLEX DOSAGE FORM

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Introduction. The most easily understood and most studied form of drug instability is the loss of drug through a chemical reaction resulting in a reduction of potency. Loss of potency is a well-recognized cause of poor product quality. The factors that determine the chemical stability of drug substances include intrinsic factors such as the molecular structure of the drug itself and environmental factors, such as temperature, pH, buffer species, ionic strength, light, oxygen, moisture, additives, and excipients.

Aim. Working out a method for the quantitative determination of active compounds was one of the important tasks of our study in accordance with existing modern requirements for establishing the stability of drugs.

Materials and Methods. *Instrumentation:* The automatic titrator was used with glass electrode for proposed method. Saturated calomel electrode was used as reference electrode. The potentiometer measurements were carried out using I-135 pH meter, which was more convenient to be used. All measurements were carried out at 25º C. *Chemicals:* A 0.100 g. of complex dosage form was weighted. It was transferred into a clean beaker. Methyl orange was used as an indicator, which is convenient for fixing the point of equivalence of the reaction taking place in the aqueous phase. The titration was carried out with 0.1 M hydrochloric acid in automatic titrator.

Results and discussions. To determine sodium hydrogen carbonate and sodium benzoate in a complex dosage form was used aqueous potentiometric titration. Potentiometric titration system using glass electrode is the simplest electroanalytical technique for determination of stability constants.

X,g recovery of active pharmaceutical ingredients was obtained by using equation.

$$X, g\ assay = \frac{Amount\ of\ titrant \cdot K \cdot T \cdot 7{,}25}{0{,}100}$$

Conclusions. The sensitive and simple potentiometric titration method was carried out for sodium hydrogen carbonate and sodium benzoate in a complex dosage form. The standard 0.1 M hydrochloric acid was used as titrant for quantification. The standard deviation has shown sensitivity. The results of quantitative determination were subjected statistical processing.

QUALITY CONTROL OF THE INDUSTRIAL CONSIGNMENT OF CAPSULES "ALLTROMBOSEPIN"

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Introduction. Inventing technologies of producing medicines based on medicinal plants proven by science and applying them to medical practice is the main responsibility of World Health System. In recent articles, it was published information about obtaining substance "Alltrombosepin" and its technology of capsule drug form. Nowadays, capsules "Alltrombosepin" are being produced in joint venture "Remedy Group". This article gives results of researches on quality control of capsules "Alltrombosepin" received in production.

Aim. Quality control of capsules "Alltrombosepin" manufactured in industry.

Material and methods. In researches it was used UV-spectrophotometry and the State Pharmacopoeia XI edition.

Results and discussion. For the "Alltrombosepin" capsules the following composition was selected: "Alltrombosepin ", aerosil 15 mg, starch 33.5 mg, calcium stearate 1.5 mg, total capsule mass 150 mg.

The evaluation of the quality and standardization of the capsules was carried out according to the requirements of the corresponding regulations. The obtained results are shown in Table 1.

Table 1

The results of the quality assessment of "Alltrombosepin 100 mg" capsules

Parameters	Requirements in Regulations (Manufacturer's Pharmacopoeia Monograph)	Results
Appearance	Hard gelatin capsules №2 filled with a powder of light yellow or yellowish-green colour with strong peculiar smell and taste. In appearance must comply with the State Pharmacopoeia XI edition, vol. 2, p. 143.	Compliant
Average weight and deviation from average weight	The average weight of the capsules should be 150 mg. The deviation from the average weight should be no more than ±10% in accordance with the State Pharmacopoeia XI edition, vol. 2, p. 144.	±6
Residual moisture	5.0 g accurately weighed powder is dried in an oven at 100±5^0 C till constant weight. Weight lost on drying should not exceed 15% (State	8.6

	Pharmacopoeia XI edition, vol. 1, p. 285).	
Solubility	Determination is carried out in accordance with the method given in the State Pharmacopoeia XI edition, vol. 2, p. 144. Disintegration time of capsule shell should not exceed 20 min.	Compliant
Heavy metal content	Accurately weighed 1.0 g of capsule content is tested for the heavy metal content. Lead solution is used as a reference. The heavy metal content should not exceed 0.01% (State Pharmacopoeia XI edition, vol. 1, p. 165; vol. 2, p. 160).	Compliant
Identification	1. Potassium permanganate discoloration reaction. 0.15 g substance is dissolved in 10 mL purified water. To 3 mL of solution 2 drops of 0.1 M potassium permanganate is added. The colour of potassium permanganate disappears in the presence of unsaturated SCOC. 2. The amount of SCOC in the capsules is analyzed by UV-spectrometry at the wavelength of 665 nm.	Compliant
Quantity of SCOC	From the content of 20 capsules 1.5 g is accurately weighed and the amount of SCOC is determined by UV-spectrometry (the method is described in detail in the Dissertation). The total amount of SCOC recalculated to 3,3′-dithiodipropionic acid should be no less than 0.1 mg.	0.34

From the Table 1 it can be clearly seen that "Alltrombosepin 100 mg" capsules fully comply with the requirements of the regulations.

Conclusions.

1. The first time it was established producing "alltrombosepin" drugs with antiplatelet activity based on Allium cepa L. in industry.

2. Quality of "Alltrombosepin" capsules received in production was checked with ФСП 42 Уз-22175941-2909-2016 requirements, the results fully comply with the requirements.

DEVELOPMENT OF UV-SPECTROPHOTOMETRIC PROCEDURES FOR SECNIDAZOLE QUANTITATIVE DETERMINATION

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Introduction. 5-nitroimidazoles are the group of antiprotozoal medicines widely used for treatment of infectious diseases caused by Trichomonas, Lamblia, Leishmania, etc. Secnidazole is one of the medicine from the group of 5-nitroimidazoles, it is characterized by a prolonged serum half-life. Chemically, secnidazole is 1-(2-methyl-5-nitroimidazol-1-yl)propan-2-ol.

Aim. To develop a number of UV-spectrophotometric procedures of secnidazole quantification and carry out step-by-step validation of the developed procedures in the variants of the method of calibration curve and method of standard to choose the optimal variant for further application.

Materials and methods. Secnidazole was of pharmacopoeial purity. All spectrophotometric measurements were carried out using a single beam UV/VIS spectrophotometer SPEKOL®1500 (Analytik Jena AG, Germany).

Results and discussion. The secnidazole chemical structure supposes its existence in different forms when changing medium pH. The presence of such transformations is confirmed by the data of UV-spectrophotometry. UV-spectra of secnidazole in 0.1 M hydrochloric acid solution (A), 96% ethanol (B), 0.1 M potassium hydroxide solution in methanol (C), 0.1 M sodium hydroxide solution (D) have been investigated and it has been set that when increasing the pH value step-by-step shift of substance maximum absorption to the right is observed (277 nm → 310 nm → 314 nm → 319 nm). For each absorption maximum and solvent the values of specific absorbance have been calculated for the concentration range of 5 – 35 μg/mL.

The procedures of secnidazole quantitative determination by the method of UV-spectrophotometry have been developed using the mentioned solvents and wavelengths respectively. Their validation by such parameters as stability, linearity, accuracy and precision in the variants of the method of calibration curve and method of standard has been carried out. The procedures A, B and D of secnidazole quantitative determination are acceptable for application. The best linearity, accuracy and repeatability have been fixed for the procedure D in the variant of the method of calibration curve.

Conclusions. Three new procedures of secnidazole quantitative determination by the method of UV-spectrophotometry have been developed using 0.1 M hydrochloric acid solution, 96% ethanol and 0.1 M sodium hydroxide solution as the solvents. Their validation has been carried out and acceptability for application has been shown.

QUANTITATIVE DETERMINATION OF EFAVIRENZ BY THE METHODS OF UV-SPECTROPHOTOMETRY

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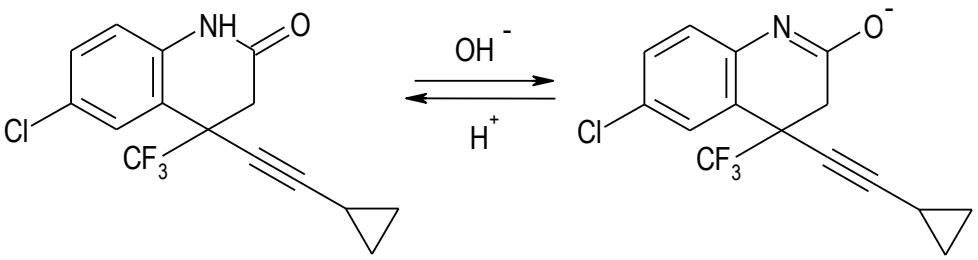
Introduction. To ensure additional reliability of analysis in forensic toxicology it is necessary to determine analyte content in the sample with the help of at least two methods of analysis, which are based on different principles. UV- spectrophotometry may give us such possibilities in the cases, when our analyte exists in the solutions in the form of different tautomers and has the different spectra, for example, in acid and alkaline medium.

Aim. To develop a number of UV-spectrophotometric procedures of efavirenz quantification and carry out step-by-step validation of the developed procedures.

Materials and methods. Efavirenz was of pharmacopoeial purity. All spectrophotometric measurements were carried out using a single beam UV/VIS spectrophotometer SPEKOL®1500 (Analytik Jena AG, Germany).

Results and discussion. The efavirenz chemical structure supposes its existence in two forms when changing medium pH:



The presence of such transformations is confirmed by the data of UV-spectrophotometry. UV-spectra of efavirenz in 0.1 M hydrochloric acid solution, 96% ethanol and 0.1 M sodium hydroxide solution have been investigated and it has been set that when increasing the pH value shift of substance maximum absorption to the right is observed (247 nm → 247 nm → 267 nm).

The procedures of efavirenz quantitative determination by the method of UV-spectrophotometry have been developed using the mentioned solvents and wavelengths respectively. Their validation by such parameters as stability, linearity, accuracy and precision has been carried out.

Conclusions. Three new procedures of efavirenz quantitative determination by the method of UV-spectrophotometry have been developed using 0.1 M hydrochloric acid solution, 96% ethanol and 0.1 M sodium hydroxide solution as the solvents.

IDENTIFICATION AND DETERMINATION OF TESTS OF HERBAL INULIN SUBSTANCES BY THIN-LAYER CHROMATOGRAPHY IN ACCORDANCE WITH THE BRITISH PHARMACOPOEIA

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Introduction. To identify and determine the purity of active pharmaceutical ingredients the method of thin-layer chromatography (TLC) is widely used. It is a quite simple in implementation and economical pharmacopoeia method that has high sensitivity and speed of separation and allows you to separate even close in the connection properties. The TLC method is also applied for assessing the quality of inulin - the fructan that is a mixture of oligomers and polymers of fructose and one molecule of glucose.

On the market today there are a small number of inulin substances of pharmaceutical quality. A significant amount of products contain in their composition the admixture of other carbohydrates; therefore they do not correspond to the declared name “inulin”.

Thus, the implementation of the quality control of inulin substances by the TLC method is a promising research direction.

Aim. To identify the structural components of inulin and to investigate possible admixtures that may be present in the plant substances of given fructan.

Materials and methods. Six herbal inulin substances obtained from such plant sources as Chicory, Agave, and Jerusalem artichoke have been selected for the analysis. The TLC method given in the British Pharmacopoeia 2009, monograph "Inulin" was used as the basis.

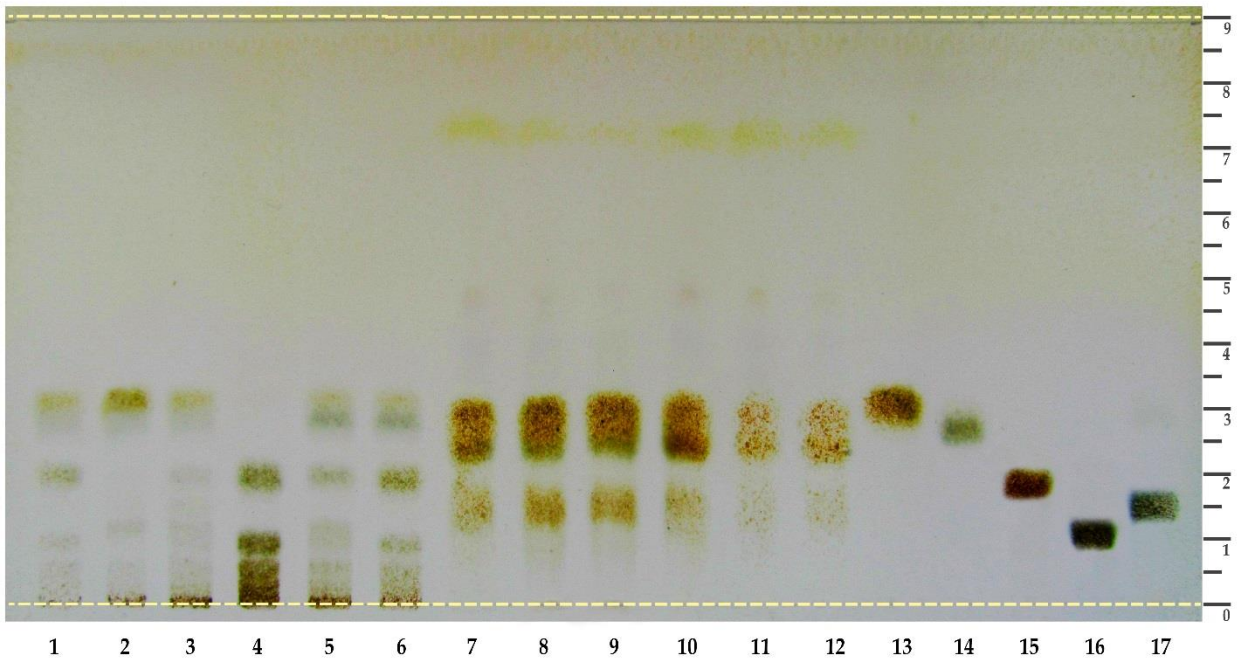
The conditions of chromatography are as follows: stationary phase – plate Silica gel G, Merck; plate activation by immersion in 0.3% solution of sodium acetate; eluent – a mixture of glacial acetic acid – chloroform – water (70:60:10); a mixture of acetone with diphenylamine, aniline and phosphoric acid was used for identification.

3.0 µl of each of the solutions were applied on the plate (Fig. 1). To control the presence of admixtures solutions of sucrose, lactose and mannose standards were additionally applied on the plate.

Results and discussion. According to the results of the study (Fig. 1), the method allows to determine the admixtures present in the analyzed substance before the hydrolysis of inulin (spots 1-6), as well as to identify fructan according to the structural components after the hydrolysis of the base material (spots 7-12).

According to the chromatogram five of six investigated inulin objects have free fructose and glucose before the hydrolysis (samples 1, 2, 3, 5, and 6); however, their small number is valid for herbal fructan substances. In addition, some of them contain free sucrose (samples 1, 4, 5, 6) and lactose (samples 1, 4, 5, and 6).

On the spots 7-12 the analyzed inulin substances were identified with such products of hydrolysis as fructose and glucose. Besides, there are traces of other sugars on the chromatogram of samples 7-12, the determination of which requires further research.



Spots 1-6 – 2.5% solutions of samples of inulin in water;
spots 7-12 – 2.5% solutions of inulin after hydrolysis by 10.0% solution of oxalic acid;
spots 13-17 – 2.5% solutions of standards of fructose (13), glucose (14), sucrose (15), lactose (16) and mannose (17).

Fig. 1. The results of thin layer chromatography of herbal inulin substances

Conclusions. The method given above allows carrying out identification and identifying the admixtures of other sugars in the analyzed samples of the fructan, so it can be used for primary quality control of the pharmaceutically active inulin component.

VALIDATION OF A NOVEL SPECTROPHOTHOMETRIC PROCEDURE FOR CEFUROXIME ASSAY BY MEANS OF POTASSIUM CAROATE

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Introduction. The cephalosporins are the largest and most diverse family of antibiotics of the beta-lactam group. They are structurally and pharmacologically related to the penicillins. Cephalosporins have a beta-lactam ring structure, infused to a 6-membered sulfur-containing dihydrothiazine ring, in place of the 5-membered thiazolidine ring of penicillins. Cefuroxime (Ceftin, Zinacef) belongs to the second-generation cephalosporin it has enhanced activity against gram-negative bacilli while retaining some activity against gram-positive bacteria. They are also more resistant to beta-lactamase. The methods proposed to assay Cefuroxime are variable but have some disadvantages. These include chromatography, spectrophotometry, voltammetry, spectrofluorimetry methods. The State Pharmacopoeia of Ukraine and the British Pharmacopoeia describe HPLC for the cephalosporin determination, which is surely the best method but has a longtime preparation, expensive and complicated in performing. The kinetic-spectrophotometric methods belong to modern and prospective one. The methods obligates a proper oxidation analytical reagent that should require to all the statements of analytical reagents.

The aim of the proposed research is to validate the procedure of the Cefuroxime quantitative determination in pure substance the kinetic-spectrophometric method using potassium caroate as analytical reagent ($KHSO_5$).

Materials and methods. The pure substance of Cefuroxime that meets the requirement of the State Pharmacopeia of Ukraine was used. The triple potassium salt of Caro's acid was used as analytical reagent. The statistic calculation were performed using Microsoft Excel 2016.

Results and discussion. In an acidic medium the Cefurxime S-oxide is formed after the addition of KOH it undergoes the hydrolytic cleavage. The appearance of a new band with absorption λ_{max} = 302 nm demonstrates its formation in the reaction of alkaline hydrolysis of Cefuroxime S-oxide in the presence of potassium caroate (perhydrolysis reaction). The precision was calculated (RSD=1.53 ÷ 2.05 %, δ= 0.55 ÷ 0.71 %) for a wide range of concentrations (1-10 μmol L^{-1})**.** The LOD is 0.33 μg mL^{-1}.

Conclusions. The procedures developed for the Cefuroxime determination in pure substance do not require elaborate treatment and expensive materials. The proposed methods are sensitive enough to enable determination of lower amounts of drug.

ANALYSIS OF PHENCAROL BY HPLC METHOD

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Introduction. Phencarol - Quinuclidyl-3-diphenylcarbinol hydrochloride is the first-generation antihistamine drug, is characterized by moderate antiserotonin action, weak cholinoblocking activity, absence of oppression effect on the central nervous system. Phencarol is used to treat allergy, asthma, allergic rhinitis and dermatitis. When overdosing medication develop symptoms: hallucinations, incoordination, convulsions. In severe intoxication develops a coma with respiratory failure.

Among the modern methods of analysis to create a database of parameter identification and quantification of arrays of analytes in biological objects HPLC method is one of the most suitable methods for sensitivity and selectivity.

The earlier developed methodology of HPLC analysis of Phencarol using a variety of different chromatographic conditions (type of sorbent, composition of the eluent, the elution rate, detection conditions), which are based on the individual properties of the drug. Considering the use mixtures of drugs for the treatment and combined intoxications actual problem of chemical-toxicological analysis is the use of unified HPLC method suitable for solving practical problems of healthcare.

Aim. The identification and quantification of Phencarol, when using unified conditions HPLC, suitable for studies of pharmaceuticals and biological objects.

Materials and method. Investigations of Phencarol by HPLC-method were performed on the basis of scientific-production association "Analytics" (Kharkov). Chromatography of Phencarol was performed on microcolumn liquid chromatograph "Milichrome A-02" ("EcoNova" Novosibirsk, Russia) using standardized HPLC conditions: reversed-phase variant with using of metallic column with non-polar absorbent Prontosil 120-5C 18 AQ, 5 μm; mobile phase in the mode of linear gradient – from eluent A (5 % acetonitrile and 95% buffer solution - 0,2 M solution of lithium perchlorate in 0,005 M solution perchloric acid) to eluent B (100% acetonitrile) as during 40 min. Regeneration of column has been conducted during 2 min with mixture of solvents; the flow rate of the mobile phase has been formed 100 μl/min, injection volume – 4 μl.

The detection of Phencarol has been conducted by UV- detector at 8 wavelengths: 210, 220, 230, 240, 250, 260, 280, 300 nm; the optimal value of column temperature – 40°C and pressure of pump – 4,2 MPa. To select the detection conditions Phencarol were obtained UV-spectrs absorption of drug solutions in solvent mixtures - 5% acetonitrile and 95% buffer solution when using SF-46

spectrophotometer, cuvettes thickness of 10 mm, in the range of 220-350 nm, reference solution - buffer solution.

Results and discussion. The identification of Phencarol conducted with using absolute parameters of retention time (t_R = 20,27 ± 0,10 min) and retention volume (V_R = 2027,1 ± 0,1 μl). To verify the choice chromatography conditions determined coefficients of peak symmetry and coefficients of capacity. Established that the values of coefficients peak symmetry - from 0,63 to 1,01 (less than 2,0 – 2,5) and the coefficients of capacity - from 12,51 to 12,62 (more than 0,5 – 2,0) showed the suitability of HPLC chromatographic analysis system.

To ensure reliable detection of Phencarol used spectral ratio values absorbance at wavelengths - from 220 to 280 nm - the values of absorbance at 210 nm, which are equal: 0,634; 0,255; 0,041; 0,022; 0,028; 0,001; 0,0003. The detection limit of Phencarol HPLC method was 5,0 μg / ml or 20,0 ng of sample.

For quantitative HPLC determination of Phencarol by absolute calibration method using the calibration curve constructed in the coordinates: S, mm^2 (peak area) – C, μg / ml (solution concentration of the substance). In applying the method of least squares regression coefficients were calculated corresponding equation S = вC + a. The proposal the calibration curve meets equation of the line that has the form: S = 0,00849 C + 0,00329, where S - area of peak drug, mm^2; C - concentration of the solution of Phencarol, μg / ml. Established that the linearity of the calibration curve in coordinates (S, mm^2) - (C, μg / ml) was observed in the concentration range 5,0 – 100,0 μg / ml, which corresponds to Phencarol content in the sample (4 μl) of 20, 0 ng to 400,0 ng respectively.

The limit of detection of Phencarol by HPLC method was 5,0 μg / ml, which corresponds to 20,0 ng of sample. In conducting HPLC analysis of Phencarol in sample solutions using the proposed method relative uncertainty of the average results did not exceed ± 1,87%. As a result of the metrological characteristics found no significant systematic errors HPLC analysis.

Conclusions. Identification and quantification of Phencarol by unified HPLC-conditions were conducted. The main parameters of retention, spectral relations and detection limit of the drug (20,0 ng of sample) were established.

As a result of the quantitative determination of Phencarol by HPLC method defined linearity range depending on the peak area and concentration -5,0 - 100,0 μg / ml of the drug and the limit of detection - 5,0 μg / ml. In carrying out HPLC-analysis of Phencarol in model solutions relative uncertainty of the average result equal ± 1,87%.

DEVELOPMENT OF UV-SPECTROPHOTOMETRIC METHOD OF QUANTITATIVE DETERMINATION OF ANTIDEPRESSANT ATOMOXETINE

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Itroduction. Antidepressant poisonings occupy a leading position among the psychotropic drug intoxications all over the world. Atomoxetine (ATX) ((3R)-*N*-methyl-3-(2-methylphenoxy)-3-phenylpropan-1-amine hydrochloride) is a monocyclic antidepressant related to selective norepinephrine reuptake inhibitors. The drug is used for treating attention deficit hyperactivity disorder (ADHD). ATX is associated with the serious complication such as increased risk of suicidal thoughts or actions in children and teenagers with ADHD. Several ATX fatal intoxications have been reported. Postmortem fluid and tissue distribution of ATX were within the range for various cases: aorta blood 0.1–8.3 mg/L, femoral blood 0.1–5.4 mg/L, bile 1–33 mg/L, liver 0.44–29 mg/kg, urine <0.1 mg/L, gastric 16.8 mg (total). According to the literature the main trend of development of bioanalytical methods for ATX determination is the prevalence of HPLC-MS. However, this method of the analysis is not always available for the toxicological laboratory.

The aim of this study was to develop simple and sensitive method for ATX quantitative determination with using UV-spectrophotometry suitable for the chemical and toxicological analysis.

Materials and methods. The UV-spectrum of ATX in 0.1 M hydrochloric acid solution was measured over 215–380 nm wavelength range, 10 mm light pathway cuvette was used. The reference solution was 0.1 M hydrochloric acid. Absorption maxima were detected at 270 nm (E^1_1=45; ε=1300) and 277 nm. UV spectrophotometric determination of ATX was performed at 270 nm. Stock solution (300 μg/mL) and 8 working standard solutions (WSS) (15.0; 30.0; 60; 90; 120; 150; 180 and 210 μg/mL) of the drug were prepared. The absorption values obtained for 8 WSS were processed by linear regression method, its general form is described by the following equation: Y=bX+a.

Results and discussion. The equation of the regression line was the following: $Y=(0.00456\pm8\cdot10^{-5})\cdot X+(0.015\pm9\cdot10^{-3})$;·(r=0.999); LOD and LOQ values were, respectively, 3.2 μg/mL and 9.7 μg/mL. They were calculated from the standard deviation of the intercept of the regression (S_a) accordance with the relevant equations: $LOD=3.3S_a/b$ and $LOQ=10S_a/b$. The linearity of the calibration curve was within the range of ATX concentrations from 15.0 to 210 μg/mL.

Conclusions. Thus, the UV-spectrophotometric method developed satisfies the requirements of the chemical and toxicological analysis by the sensitivity and can be used in toxicological study of the biological samples for presence of ATX.

DEVELOPMENT OF TANDEM PROCEDURE FOR DOXYLAMINE QUANTITATIVE DETERMINATION BY THE METHODS OF UV-SPECTROPHOTOMETRY AND EXTRACTION PHOTOMETRY

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Introduction. Realization procedure of toxicological examinations requires the results of analyte content determination in the sample obtained with the help of at least two methods of analysis, which are based on different principles. Therefore elaboration of so-called tandem procedures allowed to carry out substance determination in the same sample simultaneously by means of two methods of analysis is actual.

Aim. The purpose of our paper is development and validation of tandem UV-spectrophotometric/extraction-photometric procedure of doxylamine quantification.

Materials and methods. Doxylamine succinate was of pharmacopoeial purity. All spectrophotometric measurements were carried out using a single beam UV/VIS spectrophotometer SPEKOL®1500 (Analytik Jena AG, Germany).

Results and discussion. Tandem procedure of doxylamine quantitative determination by the methods of extraction-photometry and UV-spectrophotometry is based on processing the doxylamine succinate solution with 0.02% methyl orange solution in the acid medium (acetic-acetate buffer solution with pH = 4.6) for formation of ionic associates. The ionic associates are extracted by chloroform (under these conditions the chloroform layer becomes yellow; the amount of methyl orange is equivalent to the amount of doxylamine in ionic associates).

The decomposition of such ionic associates is carried out in the way of simultaneous reextraction of their components (methyl orange and doxylamine) in 0.1 mole/l hydrochloric acid solution. The absorbance of methyl orange (λ_{max} = 540 nm) and doxylamine (λ_{max} = 262 nm) in the obtained aqueous solution is measured.

We have carried out validation of the offered tandem procedure in the variant of the method of calibration curve using model solutions.

The obtained data specify that the offered tandem procedure of doxylamine quantitative determination is characterized by satisfactory linearity, accuracy and precision for all variants of range of the methods application and for both variants of the used wavelengths that makes it suitable for further application.

Conclusions. The new tandem procedure for doxylamine determination has been developed; the offered procedure allows to determine simultaneously doxylamine both by its own absorbance in UV-range of spectrum and by absorbance of methyl orange in visible range of spectrum that provides additional reliability of analysis.

DETERMINATION OF SOME DEGREE OF EXTRACTION OF CALCIUM ANTAGONISTS WITH WATER SOLUTIONS DEPENDING ON pH

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Introduction. Calcium antagonists, or calcium channels blockers are heterogeneous group of medicines, which have antihypertensive and antianginal actions. Amlodipine (dihydropyridine derivative), nifedipine (dihydropyridine derivative) and verapamil (phenylalkylamine derivative) use for treatment arterial hypertension, coronary heart desease, Prinzmetal angina and Raynaud`s phenomenon.

Toxic properties, wide using, an evidence of cases of fatal poisoning make calcium antagonists objects of chemical and toxicological researches.

Aim. The objective of our research was to determine degree of extraction of amlodipine, nifedipine and verapamil from aqueous solutions depending on pH.

Materials and methods. There were use organic solvents chloroform, hexane, methylenchlorid and universal buffer mixes (pH of solutions from 2.0 to 12.0) for creating necessary environment.

The number of extracting substances determined by spectrophotometer, measured the optical density of solutions amlodipine and verapamilin in 0.01 M solution of hydrochloride acid and ethanol solution of nifedipine in the ultraviolet spectral region (amlodipine – 366 nm, verapamil – 278 nm, nifedipine – 238 nm).

Results and discussion. The extracting of amlodipine by organic solvents from aqueous solutions is at values pH≥7,0, nifedipine and verapamil - in all senses. However, the greatest degree of extraction of amlodipine from chloroform and methylene chloride observed at pH 7.0-8.0, nifedipine - at pH 5.0-6.0, verapamil - 8.0-9.0. While the hexane extracts the maximum amount of amlodipine and nifedipine at pH 8.0-9.0, and verapamil - at pH 5.0-6.0. Extraction of amlodipine and nifedipine from hexane practically no pH 2.0-3.0 and verapamil - at pH 2.0-4.0.

Conclusions. These indicators can be used for higher quality and full extraction and purification of extracts of these substances. The results can be used in the pharmaceutical and toxicological analysis and for development of new bioanalytical methods of analysis of calcium channel blockers in human plasma.

MODERN ANALITICAL COLUMNS FOR CHROMATOGRAPHY – APPLICATIONS, PROBLEMS AND PROSPECTS

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Introduction. According to leading experts the segment of chromatographic methods in analytical chemistry has approached almost 50% in the last years. Among all chromatographic techniques High-Performance Liquid Chromatography (HPLC) is considered a leader in all areas – development of new theories and methods of separation, development of adsorbents, chromatographic columns, etc.

In 2004 Waters Corporation presented new chromatographic system, which provided 1000 atm pressure, and analytical columns with 1.7μm particles. This system was called UPLC – Ultra Perfomance Liquid Chromatography and was awarded with R&D 100 Award and Pittcon Editors' Gold Award.

Aim. The main purpose of our work was to study normative documents, latest information sources dedicated to development and application of modern analytical columns for chromatography analysis. We tried to assess the prospects of the development of different variants of «fast» liquid chromatography, progress in the implementation of new technologies by leading manufacturers, discussion of difficulties and challenges in development of these methods.

Materials and methods. The «core» of every chromatographic system is a column which provides fast and efficient separation of a complex compound.

Nowadays the leading manufacturers launch more than 1000 different kinds of columns. Experts estimate an annual growth rate of about 50. Labs Column Selection Database was created to make the work with this variety of choices much easier. It is a database where all the columns are classified by "Tanaka" system that includes such important parameters as hydrophoby, selectivity to homologue, structural selectivity, contribution of hydrogen bond, total ion-exchange capacity at a pH of 7,6 and ion-exchange capacity at a pH of 2,7. ACD/ChromGenius program helps to predict the time of separation of substances and kind of chromatograms on the base of the structural formulas of compounds.

A great amount of attention in the leading Pharmacopoeias is paid to global trends of chromatographic methods. We studied materials devoted to methods of chromatography with columns and such variants as Gas Chromatography (GC), Liquid Chromatography (LC), Size-Exclusion Chromatography (SEC), Supercritical Fluid Chromatography (SFC) by The State Pharmacopoeia of Ukraine (SPhU) 2.0 (2014, 2015), The United States Pharmacopoeia (USP) 38 (2015), The European Pharmacopoeia (Ph. Eur.) 8.0 (2013), The British

Pharmacopoeia (BP) (2013), The Pharmacopoeia of Russian Federation 13 (2015).

Results and discussion. For the evaluation of organic related substances Pharmacopoeias usually recommend to use chromatographic methods. Lately experts have marked the trend of changing Thin-Layer Chromatography (TLC) method for HPLC, which is more specific and accurate.

It should be noted that HPLC became the leader in the USP in the area of quantification of medical substances of organic nature at the same time when Ph. Eur. began to recommend using HPLC in about 20% of assay cases.

There is a complete list of packings (L), phases (G) and support (S) used in USP-NF test and assays in USP 38 in the section of Reagents, Indicators and Solutions-Chromatographic Columns.

Among leading manufacturers of packings for chromatographic columns USP recommends Waters Corp., Tosoh Bioscience, Dionex Corp., Agilent Technologies, Chiral Technologies, Metrohm, Sigma-Aldrich (now a part of Merck), ZirCrom Separations, Thermo Fisher and others.

Reversed-phase HPLC is used to assay drugs by LC method. Hydrophobic (modified) silica gels, for example, sorbing agent with C_{18} phase (octadecyl), or C_8 (octyl) and some other polymers with 2-10 μm particles in LC (less than 2 μm in UPLC) are often used as stationary phases. These phases are stable in the pH range of 2-8 in the mobile phase. Columns with porous graphite or some polymers allow working in a wider range of pH. Water-methanol and water-acetonitrile mixtures are often used as a mobile phase in reversed-phase HPLC.

Merck Corporation developed monoliths for chromatography of the first generation in the beginning of 1990s, monoliths of the second generation in 2012. These columns have a high efficiency of separation, they are significantly less resistance to flow of the mobile phase and they compete with columns for UPLC with particle size of 2 μm.

At Pittcon 2016 Merck, which bought Sigma-Aldrich for $17 billions in the end of 2015, presented such new technologies as chromatographic columns Watercol® – new capillary columns with innovative stationary phases for water assay by gas chromatography. They also presented new columns Ascentis® Express Biphenyl for UPLC/HPLC, which separate pharmaceutical drugs and their metabolites, and SLB®IL (i-series) – new capillary columns for gas chromatography which provide selectivity of separation of polar compounds.

Conclusions. Chromatographic methods of analysis are now leading in different fields and in pharmaceutical analysis in particular. The success of every chromatographic assay in GC, LC, HPLC, UPLC, SEC, SFC, CapLC, μLC depends on the right choice of method, chromatographic column, conditions of separation of complex compounds, detector, etc. Future pharmacy specialists, who study at the National University of Pharmacy, successfully master these methods and knowledge.

Section 4.

TECHNOLOGY OF PHARMACEUTICAL, PERFUMERY AND COSMETIC PRODUCTS

JUSTIFICATION OF MEDICINE COMPOSITION FOR CORRECTION OF AGE-RELATED SKIN PROCESSES

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Introduction. Ageing is a very difficult process that takes place in every cell of the body, and ageing of the skin is only a consequence of the manifestations of this process. Skin ageing can be influenced by internal (heredity, stress, endotoxicosis, associated with the pathology of internal organs, dysfunctions of immune and hormonal systems, etc.) and external factors (ultraviolet radiation, adverse ecology, allergens, smoking, alcohol, malaise, mechanical damage, toxic substances of cosmetics, etc.). According to the Danish scientists findings conducted on twins, genetic factors cause skin ageing in only 25 %, while 75 % is the result of unfavourable factors. Depending on the prevalence of certain exogenous and endogenous factors G. E. Pierard identifies 7 types of skin ageing: chronological (time is the determining factor); genetic (anomalies in DNA reparation); actinic (ultraviolet and infrared radiation); domestic (tobacco, alcohol, drugs); catabolic (attendant diseases and chronic infections); endocrine (hormonal dysfunction); mechanical (gravitational stress). Despite the availability of assortment of medicines only few of them show a complex effect.

Aim. The purpose of the study is to justify the composition of the cream to correct age-related skin changes.

Materials and methods. Vegetable oils, emulsifiers, emulsion bases, a complex of biologically active substances were used as the objects of research. Organoleptic, physico-chemical, rheological indicators were investigated during the developing of cream composition.

Results and discussion. Based on the results of the study of organoleptic, physico-chemical, rheological properties and consumer characteristics of model samples of base, a composition, which includes a complex of oils – olive, grape seeds, emulsifiers oleate and stearate PEG 400, MHD and CSA, dipropylene glycol and purified water, is proposed. On the basis of the analysis of literature data and compositions of remedies with similar effects, substances of damping, biogen-stimulating, protective, antioxidant action were chosen. They are hyaluronic acid, placenta extract, vitamins A and E, essential oils of orange and cinnamon bark.

Conclusions. According to the results of experimental work, there was developed an emulsion base and biologically active substances chosen for the composition of the cream to correct age-related changes.

DEVELOPMENT OF EXTEMPORAL OINTMENT WITH AZITHROMYCIN FOR THE TREATMENT OF LOCAL INFLAMMATORY PROCESSES

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Introduction. Achievements in the field of active management of purulent wounds and inflammatory processes of the skin and mucous membranes do not exclude a known method of their treatment under a bandage that is economically advantageous, applicable in any conditions, attracts by its accessibility, simplicity and remains the main one in practical medicine. Ointments are one of the most common medicinal forms for this pathology. Their assortment is very diverse, but the leading place belongs to the ointments containing antibacterial substances and, in particular, antibiotics. The results of numerous experimental and clinical studies indicate the possibility of increasing the effectiveness of local medicinal treatment by creating new ointments on hydrophilic bases that have a multidirectional effect on the main pathogenetic factors of the wound process.

The aim of our work was to develop extemporal ointment with azithromycin for the treatment of local inflammatory processes.

Materials and methods. To achieve the goal of the research - the development of ointment's technology for the prevention and treatment of local inflammatory diseases of the skin and mucous membranes, and having antimicrobial, dehydrating and wound-healing action - the following medicinal and auxiliary substances were used: azithromycin, chamomile extract, cellulose polymers, polyethylene oxides with a molecular weight of 400 and 1500, an emulsion base and petrolatum in combination with anhydrous lanolin.

Results and discussion. The technology of a multicomponent ointment containing azithromycin in combination with a chamomile extract and a polymer base, an alloy of polyethylene oxides, has been experimentally substantiated and developed. The osmotic activity of the ointment has been established.

The study of the antimicrobial activity of the developed multicomponent ointment against the main pathogens of the purulent-inflammatory process was carried out. It is established that it has a pronounced biocidal activity.

The stability of a multicomponent ointment has been established for physical, physical-chemical and microbiological indices in the course of its long-term storage in ointment glass jars at a temperature of (8-15) °C for 6 months (observation period).

Conclusions. On the basis of the conducted research technology of extemporal liniment of methyluracil for the treatment of wounds was developed.

RELEVANCE OF ZINGIBER OFFICINALE-BASED HYPOGLYCEMIC ACTION PHYTOPREPARATION DEVELOPMENT

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Introduction. Disease of diabetes is one of the most serious in modern endocrinology. The increase in the incidence of diabetes mellitus, early disability of patients, high mortality in this pathology require effective prevention and therapy.

In recent decades, the interest of diabetologists around the world to study the pharmacological properties of medicinal plants has increased, since natural biologically active substances are evolutionarily more closely related to the human body than synthetic ones, they are easily included in metabolic processes and have practically no side effects. They render positive effect not only on carbohydrates metabolism, but also on lipids metabolism, regulate water balance, normalize functional activity of kidney and liver, increase adaptation abilities of a body at ecological stress.

It should be noted, that phytotherapy might be used both alone and in combination with synthetic hypoglycemic agents depending on severity and nature of the disease. At this phytopreparations possess the ability to potentiate the action of synthetic medicines, that enables lowering dosage of the latter and, as a consequence, reduce negative side effects of pharmaceutical therapy.

The aim of our work – study of vegetable raw materials of hypoglycemic action, study of modern condition of Ukrainian pharmaceutical market as for phytopreparations based on them in order to evaluate the prospects of new domestic medicines creation.

Materials and methods.

The analysis was carried out on the basis of phytotherapeutic reference books, official publications and electronic sources: the State Register of Medicinal Products of Ukraine, the Compendium Handbook (2016).

Results and discussion. Studies have shown that currently, for the treatment of type II diabetes mellitus, the following vegetable raw materials are mainly used: bilberry shoots, bean pods, rhizomes and roots of elecampane, roots of dandelion, burdock, etc.

According to the literature a promising plant for the treatment of type II diabetes is Zingiber officinale. Ginger contains in its composition essential oil (5-

3%), vitamins C, B1, B2, essential amino acids. Burning taste is due to the presence of a phenolic compound (gingerol).

Due to its composition, ginger restores the absorption of glucose in the body and stimulates β-cells of the pancreas on a par with the above-mentioned common sugar-reducing plants. In addition, it has antioxidant, anti-inflammatory, antimicrobial, spasmolytic activity, lowers cholesterol in the blood. Due to its properties, it is a part of medicinal forms Antifront (Hungary), Bronchomed, Doctor Mom, Doctor cough, Travisil, Cofol (India), Vivabon (Pakistan), Actis, Liponorm, Lipomin, Osteoarthrisin Active (Australia), Maraslavin (Bulgaria) for application in different fields of medicine.

The analysis of the pharmaceutical market in Ukraine conducted had shown the presence of a small amount of hypoglycemic action phytopreparations. On the basis of medicinal plant raw materials, only 2 mono preparations are offered (blueberry shoots and bean pods by the manufacturer - JSC "Lectravy", Zhytomyr, Ukraine), which are presented in the form of crushed vegetable raw materials, as well as combined blends - Arfazetin (JSC "Lectravy" Zhytomyr, Ukraine), Sadifit (PF "Viola" Zaporozhye, JSC "Lectravy" Zhytomyr). It should be noted that preparations of hypoglycemic action on the basis of ginger in the pharmaceutical market of Ukraine are absent.

Conclusions.

Medicinal plant raw materials due to the multicomponent composition can be used as a means of treating diabetes mellitus both independently and in combination with other hypoglycemic agents.

On the pharmaceutical market of Ukraine, a small number of phytopreparations for the treatment of type II diabetes mellitus is presented, which confirms the urgency and expediency of developing new domestic drugs.

A promising medicinal plant for the creation of hypoglycemic phytopreparations on its basis is Zingiber officinale.

STUDY OF RHEOLOGICAL PROPERTIES OF SEMISOLID DOSAGE FORMS

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Introduction. The State Pharmacopoeia of Ukraine defines soft medicines (SM) as semisolid dosage forms (SDF) with specific rheological properties at a fixed temperature: non-Newtonian type of flow, certain structural viscosity, pseudoplastic (or plastic) and thixotropic properties.

Aim. Investigation of the rheological properties of semisolid drugs produced on different carrier bases.

Materials and methods of the study. The research objects were semisolids manufactured by the chemical-pharmaceutical plant Krasnaya Zvezda (Kharkov): Gyoxysone ointment, Prednisolone ointment, Diclofenac 1% gel, Tiotriazolin gel, Levomekol ointment. The rheological properties of the samples have been studied using Rheolab QC rotary viscometer (Anton Paar, Austria). With the help of the Casson's mathematical model, the point of the system flow and "viscosity at an infinite shear rate" were determined.

Results. All the studied samples of SDF, except the "Tiothriazoline" gel, had a plastic flow type, i.e. for the flow of the system, it is necessary to achieve some yield stress, expressed in shear rate. During an increasing shear rate, a shear stress occurs in the system, the shear stress at which the system begins to flow is called the flow point. The calculated point of flow according to the Casson's model for the "Gyoxisone" ointment is 126.35 Pa, for the ointment "Prednisolon" - 109.79 Pa, for the Levomecol ointment - 60.73 Pa, for the gel "Diclofenac 1%" - 93.93 Pa, for the gel "Tiotriazolin" - 1.60 Pa. The higher the value of the point of flow, the greater force must be applied to the tube to squeeze out the ointment, but at the same time, spontaneous leakage from the tube may occur at low values. Gel "Tiotriazolin" - has a pseudoplastic type of flow, the point of flow has a low value. In many models, to describe the rheological curve, it is assumed that the viscosity tends to a constant limit value at high shear rates. Therefore, it is often referred to as "viscosity at an infinite shear rate". The calculated "viscosity at an infinite shear rate" is equal to 0.18 Pa · s for a Gyoxisone ointment, 0.18 Pa · for a Prednisolone ointment, 0.33 Pa · s for Levomecol ointment, for "Diclofenac gel 1%" - 0.52 Pa · s, for the gel "Tiotriazolin" - 2,03 Pa · s.

Conclusions. Thus, the study of the rheological properties of SDF has both theoretical value and practical application of the research results in the development of composition and technology.

THE STUDY OF THE PROPERTIES OF ZEOLITE AS A MEDICAL SORBENT

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Introduction. In medical practice the adsorption treatment is widely used for purification of biological fluids; adsorbents appointed as therapeutic agents for treatment dyspepsia, flatulence, stomach poisoning, poisoning by alkaloids, by heavy metal salts, by barbiturates, by toxins and by other substances. The existing arsenal of medicines do not always meet the requirements of practitioners in dealing with new negative toxic factors influencing on the body. The search for new effective adsorbents encourages scientists to address not only to the plant world, but also to the world of natural minerals, thanks to their unique properties.

Promising substance to create enterosorbent is natural zeolites. Huge reserves of raw materials available to the Ukraine, and low production cost will bring to market a new drug pharmacoeconomic parameters of which will compare favourably with existing analogues.

Aim. The aim of our study was to investigate the properties of natural zeolite from the perspective of its compliance to medical sorbents.

Materials and methods. The studies of the spatial structure and shape of the particles performed were done using a microscope SEM-106. The elemental composition was determined on scanning microscope «Quanta 200 3D». Particle size distribution were analysed on laser analisator «Analysette 22 NanoTec», the specific surface area and porosity on gas analyser «TriStar II 3020". Technological properties were studied by the method described in State Pharmacopoeia of Ukraine.

Results and discussion. It is established that the substance consists of particles of non-uniform shape with a rough surface, of size 0.05-200 microns. The chemical composition represented by elements such as silicon, aluminium, potassium, calcium, iron, magnesium, sodium, copper and titanium. The content of substances soluble in water (0.9%) and in hydrochloric acid (2.7%), the degree of swelling (7.2%), loss in weight on drying (4%), bulk density to shrinkage (0.75 g/cm^3) and after shrinkage (1.09 g/cm^3), the specific surface area - 8.9200 m^2/g (BET), the average pore size (14.86 nm) and pore volume (0.033158 cm^3/g).

Conclusions. Proved natural zeolite compliance to requirements for medical sorbents. The experimental data will be considered further in the development of technologies for drugs based on it.

PHARMACOTECHNOLOGICAL RESEARCH FOR DEVELOPMENT OF INTERMEDIATE PRODUCT IN SYRUP TECHNOLOGY

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Introduction. Creation of phytomedicines largely depends on the rational and grounded choice of the extractant and the optimal technology development. No less important is the development of the proper methods of analysis and specification on their basis.

Aim. The aim of research was to obtain an aqueous extract as an intermediate product for phytosyrup creation and to develop specification on it.

Materials and methods. In the given study comparison of maceration and remaceration methods was conducted with the further research of the rational quantity of extraction stages.

Results and discussion. When research conducting, the aqueous extract was obtained by maceration method with mixing while heating. As remaceration is more effective method it was necessary to determine the number of extraction stages that would ensure the optimal ratio of the biologically active substances concentration and volume of the final aqueous extract. The minimum quantity of extractant that gives a "mirror" equals those in ratio (2.5:1) to the raw material. There were conducted fourfold extraction of phyto composition, extraction time for each stage was 30 minutes. Dry residue, concentration of hydroxycinnamic acids and flavonoids was determined in each portion of the extract. According to the findings, the largest output of extractive compounds and certain groups of biologically active substances takes place on the first and the second stages of extraction. The third and the fourth stages show the significant decrease in the concentration of flavonoids and hydroxycinnamic acids in the extract. Therefore, as the method of extraction, we have chosen remaceration in two stages with an overall ratio of raw material to final extract (1:5).

Conclusions. Thus, based on the conducted studies the aqueous extract was obtained, as an intermediate product for phytosyrup creation and specification development. Extract is reddish-brown liquid with a spicy smell, bitter taste and sweet flavour. The technological process of obtaining aqueous extract and the technological scheme of its production were developed. Identification and quantitative content of flavonoids and hydroxycinnamic acids, dry residue and heavy metals content were assigned as the monitoring parameters.

STUDY OF ANTIFUNGAL ACTIVITY OF GEL FOR CANDIDAL VULVOVAGINITIS

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Introduction. Candidiasis is a common disease of the lower parts of sexual tract, caused in 67-95 % of cases by yeast fungi of genus Candida albicans, Candida krusei less often, Candida glabrata, Candida pseudotropicalis and Candida tropicalis. Candidiasis is characterized by lesions of the mucous membrane of the vagina, which extend to vulva (vulvovaginal candidiasis) and cervix.

Aim. The aim of our work was the development of composition and technology of gel intended for the treatment of vulvovaginal candidiasis and vaginitis with addition of essential oils of lavender, tea tree and lactic acid. To study the antifungal activity have been received three samples of semisolid forms for external use with three different gelling agents in quantity of 3%: sample number 1 – lecigel, sample number 2 – sepimax, sample number 3 - aristoflex.

Materials and methods. Antifungal activity of prototypes has been studied in vitro by agar diffusion method ("wells"). This method is based on the ability of active substances to diffuse in an agar medium which was previously inoculated with cultures of microorganisms. As the test cultures were used pure cultures of fungi with American Type Culture Collection (ATCC): yeast fungus of the genus Candida - Candida albicans ATCC 885-653 and museum cultures of yeast fungi Candida tropicalis, Candida glabrata, Candida krusei.

Results and discussion. The experimental data obtained have shown that the investigated samples of semisolid dosage form have antifungal activity against all fungi cultures used. All samples have an average degree of antifungal activity (diameter of microorganisms growth inhibition zones was 15-25 mm) with respect to the fungi C. glabrata and C. krusei, C. tropicalis culture is sensitive to the sample number 1 and number 3 (growth inhibition zones were 22 2 ± 0,4 and 24,6 ± 0,5 respectively). The most sensitive (diameter of growth inhibition zones exceeded 25 mm) to developed samples of the semisolid dosage form are test strains of C. albicans ATCC 885-653 (sample number 1, 2, 3) (diameters of growth inhibition zones 28,4 ± 0 5, 35,4 ± 0,5, 31,6 ± 0,5 respectively) and C. glabrata (sample number 2) (diameter 25,6 ± 0,5). According to the experiment it has been found that the highest antifungal activity has sample number 2.

Conclusions. Thus samples number 2 and number 3 have the highest antifungal activity against Candida genus yeast fungi and are promising for further work on creating dosage forms with antifungal properties.

DEVELOPMENT OF THE ANTIMICROBIAL ACTIVITY OF CREAM WITH LEVOMITSETIN FOR THE TREATMENT OF ACNE

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Introduction. Acne is one of the most common skin diseases, as more than 85% of adolescents face this problem. Acne develops as the young men and girls. The peak incidence is at the age of 14-16 years, and the disease itself is characterized by a prolonged course with frequent exacerbations and relapses.

The frequency of acne does not have a clear tendency to decrease, but it also increase very much. This can be associated with a violation of the metabolism of fats in the human body, a genetic predisposition, an increase in the formation of sebum, as well as exposure to the skin of substances that have a camedogenic effect that causing an infection.

Therefore, one of the main actions of the drug for the prevention and treatment of acne should be an antiseptic action that will be directed to the destruction of pathogenic microorganisms.

To take account of the mixed composition of microflora that causes acne, it is advisable to use active pharmaceutical ingredients (API) that have anti-inflammatory and antibacterial properties.

Aim. The aim of the work is to study the antimicrobial activity of cream sample, that containing levomycetin, boric and salicylic acid in certain concentrations.

Materials and methods. As API, the composition of the cream includes levomitsetin at 1% concentration, salicylic acid (1%) and boric acid (2%). Sorbic acid was used as preservative, and corn oil, propylenglycol (PG), and emulsifier №1 were used to create an emulsion base (oil / water type).

The antimicrobial activity of this sample was studied in vitro by diffusion to agar («well» method).

This method is based on the ability of the active substances to diffuse into the agar, which was previously inoculated with cultures of microorganisms.

As a culture of microorganisms are used Gram-positive bacterial (Staphylococcus aureus ATCC 25293) and spore (Bacillus subtilis ATCC 6633) cultures of microorganisms, and also a gram-negative culture (Echerichia coli ATCC 25922) and yeast-like fungus of the species Candida - Candida albicans (ATCC 885-653).

The results were recorded by measuring the growth retardation zones of

microorganisms, including the diameter of the wells. The measurement was carried out with an accuracy of 1 mm, while focusing on the complete absence of visible growth.

The diameter of the zones of growth retardation of microorganisms characterized the antimicrobial activity of the experimental samples:

- the absence of growth retardation zones of microorganisms near the well, as well as the delay zone with a diameter of less than 10 mm, was assessed as insensitivity of microorganisms to the sample introduced into the well;

- zones of growth retardation with a diameter of 11-15 mm were evaluated as a susceptibility of microorganisms to the concentration of the active antimicrobial substance;

- zones of growth retardation with a diameter of 16-25 mm were estimated as an index of moderate sensitivity of strains of microorganisms to the sample under study;

- zones of growth retardation, the diameter of which exceeded 25 mm indicates a high sensitivity of microorganisms to the test sample.

Results and discussion. As a result of the studies about the antimicrobial properties of the cream in relation to different cultures of microorganisms, it has been proved that the sample has a broad spectrum of antimicrobial activity, as well as a fungicidal action with respect to the test strains used.

The diameter of the growth inhibitory zones of the gram-positive culture of Staphylococcus aureus was 41.6±0.5 mm; Spore culture of Bacillus subtilis - 33.2±0.4 mm; Gram-negative culture of Echerichia coli - 25.4±0.5 mm and yeast-like fungus Candida albicans - 25.2±0.4 mm.

These results indicate a high sensitivity of microorganisms to the obtained sample of the cream, because the growth retention zones of test cultures exceed 25mm.

Gram-positive bacterial cultures of Staphylococcus aureus and Bacillus subtilis showed the greatest sensitivity to the sample of the cream tested.

Conclusions. The received results of researches have shown that the sample of cream has a wide spectrum of antimicrobial action in relation to gram-positive and gram-negative microorganisms, as well as fungicidal action against the yeast-like fungus of the genus Candida.

Gram-positive bacterial cultures of Staphylococcus aureus and Bacillus subtilis showed the greatest sensitivity to the sample of the cream tested.

Gram-negative bacterial cultures of Echerichia coli and yeast-like fungus Candida albicans showed a lower sensitivity to the sample of the cream, but their growth retention zones still exceeded 25 mm.

FEATURES OF FOR MEN SHAMPOO COMPONENTS CHOICE

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Introduction. Despite the large number of shampoos of various directions in the Ukrainian market, should be noted the absence of such products for men.

The aim of our work was the development of a shampoo for men on the basis of a modern detergents combination with a complex of components with anti-dandruff and fungicidal action.

Materials and methods. Detergents of anionic and nonionic character, pH and viscosity regulators, etc. Determination of pH level (potentiometrically) determination of foaming properties using a Ross-Miles device.

Results of the study. Using modern scientific literature, we have chosen as the main component of the foaming system an anionic surfactant SLES 70% («Sodium Lauryl Ether Sulphate»), possessing the best cleansing properties. In order to impart the foaming agent necessary consumer form, we have introduced a non-ionic surfactant-cocoglucoside-glyceryl oleate («Lamesoft PO 65», «BASF (ex-Cognis)», Germany), which is a viscosity regulator, and also gelling agent «Hydroxy-propyl Methycellulose» («Methocel 400», «Dow», Германия) that helps to thicken the system, and strengthens the foaming ability.

As active substances, with pronounced antibacterial, and antifungal action, we have chosen:

- «JM Anti Care» – a complex, which has a wide spectrum of antimicrobial action, combinable with a large number of components. It is active against a number of gram-positive and gram-negative bacteria, fungi, mold.
- «Octopirox» – a highly effective fungicide and anti-dandruff component, has a wide spectrum of activity not only against fungi and yeast, but also against a number of gram-positive and gram-negative bacteria.

In the course of the work done, we had found that the shampoo developed by us has the following indicators:

- pH (5.5-6.5);
- foam stability 170.8 cu.
- foam value 0.87 mm.

Conclusion. Thus, the developed shampoo meets the requirements of DSTU 4315: 2004. Now, the stability of the developed agent on the above indicators is studied.

CORRECTION METHODS ARE POSSIBLE

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Introduction. Akne is a generalized name for a complex of secondary persistent skin changes that have arisen as a result of a prolonged course of acne and insufficient inadequate or incorrect manipulations used to treat it. However, there are ways to get rid of the consequences of acne.

Purpose of the study. Practical and hardware methods of correction of acne. With acne, additional procedures such as skin cleansing, drying and anti-inflammatory masks, darsonvalization, therapeutic laser, superficial peeling, disinfestation, oxygen therapy, photochromotherapy, photodynamic therapy can be prescribed. Important is the fact that the lack or inadequacy of proper pathogenetic therapy at the time of the beginning of procedures can cause an aggravation of the course of acne.

Materials and methods of research. Various cosmetic procedures and depigmenting agents. With indurative acne with stagnation phenomena, Jacquet massage, oxygen therapy can be recommended. The most common manifestations of post-acne are secondary pigmentation and scars. For correction of cicatricial changes, external means, chemical peelings of various depths, physiotherapy methods, cryomassage and cryodestruction, philling, mesotherapy, microdermabrasion, laser skin resurfacing, dermabrasion, surgical removal of individual scars, excision with laser, electrocoagulation are used. The appearance of miloons can be partly facilitated by dehydration of the stratum corneum in patients with acne. Such patients are shown moisturizers and procedures.

Results. Atrophic scars use methods of philling, mesotherapy, chemical peeling, which helps to smooth the skin, less often - external drugs and physiotherapy, affecting the metabolism of connective tissue. Topical glucocorticosteroids are not indicated in atrophic scars due to the potential risk of additional skin atrophy. With deeper defects, dermabrasion can be recommended. In a number of cases, excision of individual atrophic scars with subsequent peelings or dermabrasion is undertaken. It should also be remembered that the manifestations of melasma become more vivid when oral contraceptives are taken, which are prescribed by such a patient as pathogenetic acne therapy.

Conclusions. It is important to understand that when choosing any method of dealing with post-acne and other consequences of acne, it is necessary to consult first of all a dermatologist and a cosmetologist.

CURRENT TRENDS IN CREATING COSMETIC PRODUCTS FOR DRY SKIN USING POWDERED HONEY

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Introduction. Atopic dermatitis - a chronic allergic disease that develops in individuals with a genetic predisposition to atopy, a relapsing course, the age characteristics of clinical manifestations and characterized by elevated levels of total and specific Ig E in blood serum. Typical clinical manifestations of atopic dermatitis is an eczematous rash and lihenoidic arising from hypersensitivity to specific and nonspecific stimuli.

The aim of the study. Review symptoms of dry skin and studying properties of honey. Symptoms of atopic dermatitis in a child with early disease may manifest Seborrheic scales, accompanied by the appearance of yellow crusts and peeling in the eyebrows, ears, springs on his head, redness of the face, mostly on the cheeks with the advent of keratinized skin and cracks with constant itching, burning, combs.

Materials and methods. Bee honey. Bee honey - one of the most complex natural products, of which revealed more four hundred different components.

The results: Pharmacological properties of honey due to biological nature honey and its complex chemical composition, These include: antibacterial, antitoxic, healing, soothing, immunomodulatory, antiviral, antioxidant, irritating activity.

The most pronounced healing properties of honey can be considered antibacterial activity and stimulating effect. In addition, the combination of antimicrobial activity and the presence of readily available substrates for cell nutrition, underlying the wound healing properties of honey. Honey also has a pronounced dietary properties.

Conclusions. Studied the chemical composition and pharmacological properties of honey, which indicate the feasibility of the development of its new drug for cosmetic use for the care of dry skin. Creation of the cosmetic product will significantly reduce the frequency and quantity of use of drugs for the treatment of atopic dermatitis.

DEVELOPMENT OF HIGHLY EFFECTIVE EXTRACTION TECHNOLOGY OF FLAVOLIGNANS FROM *SILYBUM MARIANUM* FRUITS

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Introduction. *Silybum Marianum* fruits and extraction drugs based on them are widely used for treatment of chronic inflammatory liver diseases. The main active agents in most of these drugs are flavolignans. Thus, improvement and development a new technologies for separation of these substances is a very urgent task.

The **aim** of this paper is to highlight some aspects concerning development of extraction technology of flavolignans from *Silybum Marianum* fruits using filtration type of extraction.

Materials and methods. For extraction we used finely milled *Silybum Marianum* fruits, particle size less than 0.5 mm. The process of extraction was carried out at temperature of 25ºC. As an extragent, we used ethanol at concentration 20, 40, 70, and 96% vol. Hydrodynamic mode of extragent filtration through the plant raw material layer was 0.027, 0.053, 0.11, 0.17, and 0.28 ml/(min·g). Extract outflow relatively to plant raw material was carried out at 1:1 vol:wt, and at total volume of extract to plant raw material of 10:1. For the qualitative and quantitative analysis of extracts, we used HPLC method. For determination of dry residue content, we used gravimetric analysis.

Results and discussion. As a result of the study of hydrodynamic mode, we determined critical velocity with value of 0.28 ml/(min·g), at which compression of plant raw material occurred and the process of filtration stopped. It was also noted, that in case of ethanol use at concentration 20, 40, and 70% vol., the first extract outflow (1:1) was in the form of suspension/emulsion, for segregating which we had to use centrifugation or long-term decantation. This fact shows that for extraction purposes, it is more reasonable to use not the initial plant raw material, but the cake after oil pressing. It should be noted that in case total extract outflow 5:1, the amount of extractive substances transferred from plant raw material to extract was 70% and more at filtration velocity of 0.17 ml/(min·g) and up to 85% at 0.027 ml/(min·g). For maximum flavolignans extraction, the most suitable concentration of ethanol was determined as 70% vol.

Conclusions. The main technological parameters of the filtration extraction process have been studied, the ranges of the optimum filtration rate of the extract through the layer of plant raw material have been described, and the optimal concentration of ethanol has been chosen.

DEVELOPMENT OF EXTEMPORANEOUS MEDICINE FOR INFLUENZA PREVENTION

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Introduction. By frequency and number of cases in the world among all infectious diseases influenza and SARS occupy the first place. According to WHO, influenza and influenza-like illness in the world cause the disease in 5 to 30 % of the population. Respiratory diseases are common pathology in the structure of Ukrainian population morbidity. For the treatment of many diseases the practical medicine widely uses medicines with medicinal plants. For symptomatic treatment and prevention of influenza it is optimal to use medicines that have a wide range of actions, primarily: anti-inflammatory, antibacterial and so on. Such properties are typical for eucalyptus leaves and marigold flowers.

Aim. The aim is to investigate conditions of release of chlorophyll and carotenoids sum from eucalyptus leaves and marigold flowers into non-aqueous solvents for the production of extemporaneous medicine for the prevention of acute respiratory diseases and influenza.

Materials and methods. The objects of research were extracts of lipophilic substances of eucalyptus leaves and marigold flowers composition obtained in different solvents. Study was carried out by the spectrophotometric method of the State Pharmacopoeia of Ukraine.

Results and discussion. In the experiment, the chopped raw of eucalyptus leaves and marigold flowers was extracted with non-aqueous solvent in the infuser on a water bath at 50 ± 5 °C. There were prepared samples of eucalyptus leaves and marigold flowers raw material in the ratio (2: 1) (1: 1) (1: 2) for study. As extractants there were used peach oil, sunflower oil and propylene glycol. The resulting extracts were separated by filtration of plant material in 2 layers of cheesecloth through the press. Plant material was returned to the extraction device, filled with solvent in the ratio (1: 3) and then another extraction under similar conditions was carried out. After a further assertion of solids of the plant material for 2-3 days, extracts were filtered through a layer of filter paper and passed on spectrophotometric determination of active compounds. Research on the development of the extemporal dosage form for the prevention of influenza continues.

Conclusions. Conditions of release of lipophilic substances (carotenoids and chlorophylls) of eucalyptus leaves and marigold flowers composition into non-aqueous solvents were studied. It was established that the selected temperature, the ratio of raw material to solvent, infusion time is optimal.

COMPOSITION DEVELOPMENT OF THE COMBINED OINTMENT FOR PSORIASIS TREATMENT

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Among the modern dermatology issues psoriasis is one of the most widespread dermatosiss. For today there is a great number of theories of origin of psoriasis, to them belong immune, viral, infectious, exchange, genetic, neurogenic, endocrine theories and great number of factors which are instrumental in the origin of dermatosis. Sunblisters, infectious skin diseases, heredity, anomalous formations of keratin, epidermal proliferation, nervosa disorders, defeats of liver, attribute to such factors.

The purpose of our research is an analysis of medications assortment for psoriasis treatment and choice of active pharmaceutical ingredients (AFI) which are more frequent all appointed doctors and which own high pharmacological activity.

There was conducted analysis of medications, incorporated in Ukraine , for treatment of psoriasis three groups are selected: facilities, which are directed on the removal of negative influence of various procatarxiss, citostatichni facilities and immunodepressants and facilities which influence on the correction of differentiation of keratinocytes.

The studying of preparations nomenclature rotined that for psoriasis treatment there widely used the different groups of preparations: gepatoprotectors, adaptogenetics, sedative, anti inflammatory , vitamin facilities, tranquilizers and antidepressants. As a result of facilities differentiation it was possible to mark in relation to a medical form, that for treatment of psoriasis more frequent all apply hard medical forms (45 %), soft (19 %) and parenterally (16 %), rarer liquid medical forms (12 %) and extracts (8 %). Beside this, it is necessary to mark that in the complement of medical forms, at psoriasis treatment often include a medical digister.

For skin psoriasis treatment , doctors use ointments and gels as much as principles of successful purposeful therapy. In the complement of ointments and geley enter operating matters, namely: anti inflammatory, antiseptic, matters, that the regenerations of skin promote.

The conducted researches on the study of assortment of medications for treatment of psoriasis allowed to choose a medical form, namely gels and operating matters for development of composition of the combined extemporal ointment for treatment of psoriasis.

DEVELOPMENT OF DENTAL GEL'S TECHNOLOGY FOR THE TREATMENT OF BABY VIRAL STOMATITIS

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Introduction. To date, in the clinic of therapeutic dentistry it is difficult to find pathology of the oral mucosa, which is similar to acute stomatitis, demands so much attention and wide study. The prevalence of acute stomatitis in children aged from 1 to 4 years is up to 80 % of all cases.

In the pharmaceutical market of Ukraine, the bulk of medicines for the treatment of viral stomatitis are represented by liquid dosage forms. The use of these medicines should be at least 5-6 times a day, which adversely affect patients' compliance. Also listed solutions are alcoholic that often cause locally irritant action. It is therefore soft medicinal forms - dental gels are preferred. However, it should be noted that today range of extemporaneous dental gels is virtually absent.

The aim of our work was to develop extemporaneous dental gel for local treatment of baby viral stomatitis based on natural raw materials.

Materials and methods. After examining the pharmacological properties of medicinal plants used for the treatment of stomatitis, as active ingredients for extemporaneous dental gel for the treatment of this disease, we have chosen dry extract of licorice root and essential oils of sage and peppermint.

In order to choose structural component of gel bases, we investigated the possibility of using as gelling agent Carbopol 934 P, methyl cellulose and sodium alginate.

Considering all experimental data, physical and chemical properties of active substances, namely their solubility (dry extract of licorice root injected into the gel in an aqueous solution and essential oils of sage and peppermint as a solution in ethanol (96 %), we have conducted research on the development of rational technology of extemporaneous dental gel.

Results and discussion. The gel obtained by the developed technology has gel-like uniform consistency with a specific pleasant smell, brown color, pH 7.2-7.4. Study of colloidal and thermal stability proved the stability of proposed system.

Also, we conducted study of developed medicine's stability during storage. Designed dental gel retains its properties during 5 months at two storage temperatures.

Conclusions. Thus, on the basis of the research we have developed technology of extemporaneous dental gel for the treatment of baby viral stomatitis.

SELECTION OF GELLING AGENTS FOR THE DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF THE SOFT MEDICINAL FORM OF GEL FOR NEURODERMATITIS TREATMENT

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Introduction. Among the dosage forms used for the treatment of neurodermatitis, the most interesting are the gel compositions that provide the necessary therapeutic effect of the drug. They have a number of advantages over ointments on lyophilic bases since when applied to the skin they form a very thin membrane that provides prolonged effect and uniform distribution, while not having a toxic and irritating effect. Selection of gelling agent is very important when creation gels, since the gel base determinate rheological properties and can serve as a stabilizer of the disperse system.

Objective. Selection of gelling agent for the development of the composition and technology of the soft medicinal form of gel for neurodermatitis treatment.

Materials. As objects of research of the composition of the soft dosage form for the neurodermatitis treatment, 2% soft dosage form samples were used with the following gelling agents: Aristoflex, Hydroxypropylmethylcellulose (HPMC), Carbopol of Ultrez 10, Sodium carboxymethyl cellulose (Na CMC). Dry plantain extract and liquid marigold extract were used as active substances.

Methods. A complex of physicochemical and technological methods of research was used in carrying out the work.

Results. At the first stage of the work, the thickening power of gell agents was investigated.All samples had a satisfactory consistence, were easily spread over the skin. The addition of a liquid extract of calendula sharply changed the pH to the acidic side (pH 4). As a result, there were a change in appearance and loss of consumer qualities. The most satisfactory characteristics were retained in the sample based on Aristoflex.

Conclusions. In the course of the study, a choice was made in favor of the gel formers Carbopol of Ultrez 10 and Aristoflex. These samples had the most satisfactory results for the spreadability and preservation of the organoleptic properties after the addition of the active ingredients. The use of carbopol as a gelling agent requires a higher concentration of Ultrez 1, the addition of a liquid extract of calendula leads to a sharp decrease in pH and a dilution of the structure of the gel.

THE EFFECT OF QUANTITY OF THE BINDING AGENT ON PROPERTIES OF GRANULES WITH ANTIDIABETIC SOFT EXTRACT

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Introduction. One of a cause of disability, death, cost and a public health problem in the Ukraine is Diabetes mellitus. Therefore, the creation of new antidiabetic medicines in convenient oral dosage forms is relevant.

In the National University of Pharmacy at the Department of Pharmacognosy under the guidance of prof. Kovalev V.N. it has been obtained soft extract from herbal raw material with a hypoglycemic activity. The extract is a dark brown viscous mass.

The composition of granules with soft extract was formulated at Industrial Phamacy department. The research work was supervised by Associate Professor Sichkar A.A.

Aim. The goal of our work was to examine effect of quantity of the binding agent on technological properties of granules with soft extract from herbal raw material.

Materials and methods. Granules were obtained with the using of the wet granulation method. The soft extract was dissolved in a different quantity of purified water for the obtaining of binding agents. Then ingredients from the groups of disintegrants, diluents and moisture regulators were wetted by the binding agent with soft extract. Wet mass was rubbed through the sieve with the size of orifices 1.5 mm. The obtained granules were dried and calibrated through the same sieve.

Results and discussion. The impact of different quantity of the binding agent on technological properties of granules with antidiabetic soft extract was researched (table). Since the extract is an active pharmaceutical ingredient, its amount in the binding agent was constant. Only the amount of water was varied. The granules moisture content after drying was 5±0.9 %. Granules obtained with water 8.5 % by weight of mixture had acceptable characteristics.

Quantity of the water, % by weight of dry ingredients mixture	Technological properties of granules		
	Flowability, g/sec	The bulk density, g/ml	The prevailing fraction
8	5.5±0.6	0.52±0.04	-0.355 mm+0.18 mm (21%)
8.5	7.1±0.5	0.41±0.02	-1.5 mm+0.7 mm (53%)
9	Over-watered mass		

Conclusions. Thus the quantity of the binding agent was determined for the obtaining of high-quality granules with antidiabetic extract from herbal raw material.

JUSTIFICATION OF THE SELECTION OF THE GEL BASIS FOR THE SYPTOMATIC TREATMENT OF ATROPHIC VAGINITIS

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Introduction. Currently a lot of women suffer from a syndrome of vaginal dryness, called atrophic vaginitis. This irritation is caused by thinning of the walls of the vagina and decrease in the amount of natural lubricant released. This condition is extremely often diagnosed during the menopause, due to the fact that it is caused by a deficiency of estrogens. Fifty percent of women experience the symptoms of vaginal dryness 5 years after the beginning of menopause, and after 10 years this figure is increased to 75%. Moreover, the syndrome of vaginal dryness often occurs during pregnancy and after childbirth, due to the changes in the microflora and the endocrine profile. If the hormone imbalance is detected, treatment of vaginal dryness is carried out with the help of medications based on estrogens, it can include oral dosage forms as well as locally administered medication. As secondary therapy, it is possible to use drugs that relieve the symptoms of this condition, containing such active ingredients as hyaluronic acid and tocopherol acetate.

Hyaluronic acid moisturizes and protects the walls of vagina from dryness, participates in the regeneration of tissues and contributes the healing of mucous membrane injuries while eliminating any possible scaring. Tocopherol acetate is known for its moisturizing effects and is a valuable ingredient in many cosmetic products. Intravaginal administration of vitamin E eliminates the symptoms of dryness, increases the amount of moisture and has no side effects.

The main criterion for the development of semi-solid dosage forms, affecting the biopharmaceutical and technological characteristics of the drug, is a scientifically based choice of the basis, since it is the carrier of the drug substance. Possibilities of using a complex base with poloxamers was studied, since this type of bases has thermo-reversible gelling, high occlusive and bioadhesive properties, mucosal indifference, satisfactory release characteristics and compatibility with most ingredients.

Aim. Analyse the literature and experimental data to justify the use of a complex base with poloxamers to develop a vaginal gel for the treatment of atrophic vaginitis.

Materials and methods. Samples were produced based on Poloxamer® 407 (BASF) with a 20% poloxamer, containing hydroxymethylpropylcellulose (Benecel® K100M, Ashland) - 1%; 1.5% and 2%. For each sample, the aggregate stability was studied using the kinetic stability coefficient. Gelation time, gelation temperature, pH, and rheological characteristics have also been studied.

For measuring the gelation temperature 10 ml volume of was transferred to a 20 ml transparent vial. The vial was heated slowly on a water-bath and the gelation temperature was noted. For measuring the gelation time 10 ml of each sample was transferred to a 20 ml transparent vial containing a magnetic stirring bar. The vial with constant stirring at 50 rpm was kept at a constant temperature of 37°C. The time at which the rotation of the bar stopped was taken as the gelation time. The rheological characteristics were determined on a Lamy Rheology RM 200, rotation viscometer with a thermostat. Measuring system - "cylinder in the cylinder", software RHEOMATIK. The measurements were carried out at a temperature of 20 ° C and 37 ° C, corresponding to the storage and application temperatures.

Results. All the bases obtained had aggregate stability (kinetic stability coefficients in the range from 0 to 0.1), pH in the range from 6.0 to 6.3, gelation time from 5 minutes 20 seconds to 7 minutes 30 seconds (gelation time from 4 to 10 minutes is considered optimal), gelation temperature from 27 ° C to 33 ° C (the optimum temperature is from 30 ° C to 37 ° C). Flexural yield stress is in the range from 3.10 Pa to 7.32 Pa at 20 ° C and from 191.2 Pa to 260.4 Pa at 37 ° C. The plastic viscosity according to the Kasson model is from 0 Pa·s to 0.130 Pa·s at 20 ° C and from 0.056 Pa·s to 0.158 Pa·s at 37 ° C. As can be seen from the presented data, as the temperature is raised, the plastic viscosity and the flexural yield stress of the samples increase, indicating that, possibly, there is no leakage of the medication from the place of application and high occlusive properties.

Conclusions. The prospects of using thermo-reversible complex bases with poloxamer and hydroxymethylpropyl cellulose were displayed. These samples have high aggregative stability, optimal pH values, gelation time and temperature, and rheological characteristics.

THE STUDY OF DRUGS FOR PREVENTION OF COLDS

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Introduction. According to the WHO data annually almost 4 million people die from influenza and acute respiratory viral infections in the world; the total number of persons who have had these diseases is up to 100 million per year. Therefore, the problem of prevention of colds, as well as reduction of the overall incidence of influenza is very important for healthcare. The use of preventive vaccination of viral vaccines is not always effective since the influenza viruses are very changeable, and a universal antiviral vaccine has not been currently discovered yet. Along with vaccination for prevention of acute respiratory viral infections drugs with the antiviral activity are often used, they do not allow viruses to penetrate into the body and thus prevent disease. One of the long-known drugs is aminocaproic acid, which is used primarily as a hemostatic agent, but it is also recommended for the treatment and prevention of influenza since it possesses the antiviral activity. To prevent influenza aminocaproic acid is recommended for use internally or for instillation of 5% solution into the nose or as turundae soaked with 5% solution of aminocaproic acid. In the magistral formula of pharmacies the ointment for prevention of influenza is prepared on the emulsion base, it is used for putting into the nose.

Aim. To prepare the aminocaproic acid ointments on various bases and study their organoleptic, physico-chemical and other properties.

Materials and methods. Ointment bases of various types, physico-chemical, organoleptic, biopharmaceutical methods of studying ointments were used.

Results. The aminocaproic acid ointments have been prepared on various bases, organoleptic, physico-chemical and other properties of the ointments obtained have been studied, the project of the processing instruction for preparing the ointment in conditions of pharmacies has been developed.

Conclusions. The possibility and prospects for further studies on development of a drug in the form of the aminocaproic acid ointment for preventing and treating acute respiratory viral diseases have been shown.

INJECTING PROLONGS OF DISULFIRAM

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Introduction. The improvement of quality of life, the preservation of human health, health promotion, the formation of installation on a healthy lifestyle is not easy tasks in world nowadays, in particular in Ukraine. The main problem in the treatment of alcohol and drug dependency are low efficiency of anti-recurrent programs (6-25% of patients, by different resources, had therapeutic remissions). Patients often don't have psychological motivation for a healthy lifestyle. Most of patients can't be able to achieve remission. An alternative is the use of drugs with prolonged action that ensure the continuity of the treatment process and prevent recurrences. Scientists of department of technology of biologically active compounds, pharmacy and biotechnology of National University "Lviv Polytechnic" are dealing with the problem of developing new medicines with prolonged action based on new and known active substances.

Aim. The aim of our study was to investigate the properties of new and already known injectable drugs of prolonged action based on disulfiram.

Materials and methods. Disulfiram–specific drug for treatment of alcoholism of aversive action. Mechanism of its activity is blocking of the acetaldehydedehydrogenase. As result, the oxidation of alcohol is delayed by phase acetaldehyde and aversion to alcohol is formed. Perspective is the use of disulfiram individually or in combination with other agents for the treatment of drug dependence and associated pathologies (alcohol and drug, alcohol and mental disorders, alcohol and related depressions, and HIV-infected patients with concomitant alcohol and / or drug addiction).

Lately, interest to the use of disulfiram for the treatment of cancer is increasing. Disulfiram is used as supporting therapy, such as: orally in dose 125-500 mg per day (to 250 mg in the US), in implant with prolonged action in dose 800 mg. Rational dosage form is injection with prolonged action which contains 250 mg per month. Disulfiram is very poorly melting substance (1 g in 5000 ml), because of this injectable solution in non-aqueous solvents are proposed. For poorly soluble drug substances, suspension of nanocrystals behave themselves similar to solution (for example, in a spray). In order to study the form and size of particles of disulfiram in body fluids the electron microscopy was conducted.

Results and discussion. Crystals of disulfiram - elongated form particles with sizes 1-3 mkm and small particles with sizes less than 100 nm, observed in the

sediment of "Tetlong". These particles sizes lead to the creation of drug stores in muscle tissue, location of which is limited by compartment of injection. The new combined injectable drug of prolonged action based on disulfiram and naltrexone "Naltetlong" for usage in treatment of alcoholism and drug dependence was designed.

The conditions of interaction between polymer and active substance were proposed to preserve the structure of molecules of drugs and to format particles in the form of nanospheres with uniform size from 100 nm to 1 micron, with medical substance in the middle of the polymer membrane that ensures their gradual release. Preclinical studies have shown pharmacological activity and moderate toxicity of a drug. Clinical study of the drug was initiated. The stability of this medical product in conditions of storage appeared to be insufficient. Therefore, we carried out measures to improve its stability.

We conducted research on development of new drugs of prolonged action based on disulfiram, the possibility of obtaining a combined injectable drug based on disulfiram and naltrexone for treatment of alcoholism and drug dependence by encapsulation of the drug using a copolymer of lactic and glycolic acids in organic solvent is being investigated. Obtained preliminary results showed that the method is prospective, because microcapsules containing medicines in the middle of polymer membrane were obtained. Development of optimal composition, choice of excipients and methods of deposition is the prospect of further research.

Since alcohol abuse is often accompanied by a large number of diseases of different systems and organs, we have made predicting the pharmacological activity of the drug “Tetlong” and "Naltetlong" with using of known analytical application “Pharma Expert”. Scientists are interested in immune-stimulating (immunemodulating) action of disulfiram. Famous medical journal «Lancet» appeared a publication (in november 2015) regarding teamwork of US (San Francisco) and Australian scientists on the successful HIV treatment by anti-alcohol drug - disulfiram, which did not cause any side effects.

Conclusions. Therefore, it is obvious that the pharmacological properties of injective drugs with prolonged action based on disulfiram such as "Tetlong" and "Naltetlong" require further study.

DEVELOPMENT OF THE TECHNOLOGICAL PROPERTIES OF MOTHERWORT DRY EXTRACT FOR SOLID DOSAGE FORM

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Introduction. The need to create a medicine based on medicinal plant raw materials for non-hormonal therapy of pre- and post-menopausal syndrome is a small amount of medicines on the Ukrainian pharmaceutical market that have non-hormonal activity and simultaneously have a wide spectrum of action on menopausal syndrome. The modern therapy of menopause includes such elements as: medicines of hormone replacement therapy (HRT); antidepressants; soft sedatives. Motherwort includes flavonol glycosides, mainly rutin, essential oil (traces), saponins, alkaloid stachydrin, tannins, carotene. Medicines based on motherwort are used when nervousness, cardiosclerosis, insomnia, neurasthenia, depression, and venous vascular dystonia, which can result from hormonal imbalance. The present indications for use give the basis to apply dry extract of the motherwort in the development of the dosage form for the complex therapy of climacteric syndrome.

Aim. The aim of the work is to study the powder of the motherwort dry extract, namely, to determine its technological properties, as a promising raw material in the development of solid dosage forms.

Materials and methods. Motherwort dry extract was investigated according to the following technological properties: crystallographic properties, fractional composition, bulk density, flowability, angle of natural slope, moisture content.

For this purpose, the following devices and accessories were used: the “Konus Academy” microscope equipped with the Scope Photo camera programme, the PHARMA TEST (Germany) device for vibration compaction of powders TD, the vibration analyzer for readout of the characteristics of bulk materials VP 12A (MZTO, Ukraine), the sighting ruler and the scale, the device for determining moisture MA 150 by “Sartorius”, State Pharmacopoeia of Ukraine 2nd ed.

Results and discussion. The obtained results showed that the motherwort dry extract complies with SPU requirements for all the claimed technological parameters.

Conclusions On the basis of the findings it can be concluded that the motherwort dry extract is a promising medicinal plant raw material for the development of solid dosage forms that would be used in menopausal syndrome treatment.

CREATION OF SHEA BUTTER CREAM

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Introduction. Shea butter is defined as plant fat extracted from kernels of shea nuts, seeds of shea trees botanically called Vitellaria paradoxa.

Shea butter has long been used in sub-Saharan Africa for medicinal, culinary, and other applications. Shea butter, is a product rich in unsaturated fatty acids. In west african countries Shea butter has long been used by local healers as a treatment for rheumatism, inflammation of the nostrils. Shea butter has also been used for preventing stretch marks in African pregnant women, treatment of different skin and hair conditions.

For treatment of skin infection the most common medicinal form used is creams. The purpose of their use – Act as a barrier to protect the skin from external agent, help to prevent skin conditions as acne, eczema, psoriasis, to maintain or improve the skin moisture, for oily or dry skin. Some creams are specially made for skin lightning. The composition of shea butter cream was formulated at Industrial Phamacy department. The research work was supervised by Associate Professor Sichkar A.A.

Aim. This study aimed to demonstrate the relevance to create and use a Shea butter cream for skin disorders.

Materials and methods. Natural shea butter (Vitellara paradoxa).

Results and discussion. Today among the known medicinal creams that can be used for skin moisturizing and conditions there are no cream made from shea butter.

Shea butter has health benefits due to its abundance of healing ingredients, including minerals, proteins, vitamins and a unique fatty acid profile, and its a superior active moisturizer. Because of its moisturizing properties, shea butter is also an excellent ingredient for creams, lotions and soap.

Using shea butter cream will help with skin conditions and ailments such as extreme dryness, eczema, dermatitis, skin allergies, fungal infections, psoriasis and more. Also it can be use as an anti-ageing of skin due to its protease-inhibiting activity. It acts as a natural sunscreen. The cream can also be used to promote hair growth, when applying regularly it helps to restore hair follicles and the scalp. So it helps to treat hair loss.

Conclusions. From the above it can be concluded that shea butter cream must be created and be among the medicinal creams used for the treatment of skin and hair disorders.

ACTUALITY OF AMIZON ADMINISTRATION TO THE OINTMENT WITH POPLAR EXTRACT

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Introduction. Despite the wide range of drugs for the treatment of purulent wounds inflammation, we conducted a search for combinations of active substances that could be active in all phases of the inflammatory process.

Use with inflammatory wounds lesions of soft medicinal forms, important today because they can create the necessary AFI concentration in the inflammation zone, eliminate systemic adverse events that often occur with oral and injectable routes of administration.

As we know from the literature data, combined soft dosage forms for the first phase of wound healing use should show antimicrobial, anti-inflammatory, analgetic activities and a maximum stimulating effect on the performance of non-specific resistance and immunoreactivity patient body. They must has a high osmotic activity, to provide technologically intensive outflow of fluid from the depth of wounds, necrotic tissue rejection and their removal from the wounds. Equally promising to be considered a development of complex ointments that combine in its composition antiseptic and component anti-inflammatory, immunomodulatory activity. To this aim, we used a Ukrainian NSAID - Amizon.

Aim. The purpose of research is studying Amizon as nonsteroidal anti-inflammatory and immunomodulating component for the technology and composition development of the ointment with poplar extract.

Materials and methods. Due to literary analysis, using agar diffusion method ointment components and their concentration were conducted.

Results and discussion. Introduction Amizon to ointment is important because it helps to stabilize the plasma membrane and lysosomal membranes, slows degranulation of basophilic granulocytes, exhibits antioxidant effect, normalizes the levels of prostaglandins, cyclic nucleotides, normalize metabolism and reduces vascular reactions, so reveals the anti-inflammatory effect. Amizon is low toxic substance with low toxicity the blood and absence of local irritating and mutagenic activities.

Conclusions. Conducted research allowed to argue that amizon in 2.5% concentration not shows negative impact on the antimicrobial properties of the components of the ointment.

SURVEY OF CHOICE FOR PACKING OF THE CURATIVE AND PREVENTIVE MEDICINES «PROPOLIS-DERMA»

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Introduction. In recent years, the proportion of fungal infections in the structure of infectious diseases has increased significantly. According to WHO statistics nearly 20% of adults are infected with fungal infections, and among ukrainians this index reaches 25-30%. Treatment of infectious diseases, including those of fungal etiology, with antibiotics cause difficulties, particularly in cases when the disease is caused by the drug-resistant strains. Overcoming the multiple resistance is a complex and important problem, solution of which is currently possible only by the replacement of drugs, that have lost their effectiveness, with new topical drugs. In previous studies, we have developed a number of curative and preventive medicines of the antifungal, antimicrobial and keratolytic action «Propolis-Derma», such as «Propolis-PSC» (RC № 3320715444-02:2016), «Propolis-PCD» (RC № 3320715444-01:2016) and «Propolis-PNH» (RC № 3320715444-03:2016), designed according to DSTU 4093-2002 «Cosmetic lotions and tonics. Specifications» for the treatment of dermatomycosis, pityriasis versicolor and diseases caused by yeast fungi Candida, and it has been proved that the proposed pharmaceutical compositions do not show side effects and meet the requirements of the State Pharmacopoeia of Ukraine and may be used to treat fungal infections.

The **aim** of the study. Choosing the type of packing for medicines «Propolis-derma» (Propolis-PSC, Propolis-PCD and Propolis-PNG).

Materials and methods. We used a new kind of medical products vials-pencils for storing and applying medicines to the affected part of the skin and its surroundings, which satisfies the requirements of the TS U 25.2-2094621496-001-2004 «Vial-pencil for storage and application of medicines» and is used as part of first-aid kits for personal use in clinical and inpatient departments of health care institutions.

The obtained results. We have conducted tests on the possibility of skin application of alcohol and water solutions of the developed curative and preventive medicines «Propolis-Derma» in and their compliance with TS U 25.2-2094621496-001-2004 «Vial-pencil for storage and application of medicines». The experimental samples of alcohol and water solutions «Propolis-Derma» have been injected into vials-pencils FK-132 and FK-92, which meet the technical requirements set by the specification documentation and sample KLLV 2094621496001 and the standard, approved in the proper manner.

Table 1

Test-trial of the solutions of curative and preventive medicines «Propolis-Derma», introduced into vials-pencils for compliance with TS 25.2-2094621496-001-2004 «Vial-pencil for storage and application of medicines»

Trial name	Specifications TS U 25.2-2094621496-001-2004	Trial results	
		Vial-pencil FK-132	Vial-pencil FK-92
Size test	According to TS	Satisfies the requirements	Satisfies the requirements
Test of the quantity of medicine	The volume of introduced medicine-3 ml	Satisfies the requirements	Satisfies the requirements
Material test	According to TS	Satisfies the requirements	Satisfies the requirements
Test of the surface quality and lack of inclusions	According to TS	Satisfies the requirements	Satisfies the requirements
Impermeability test	According to TS	Satisfies the requirements	Doesn't satisfy the requirements
Package test	According to TS	Satisfies the requirements	Satisfies the requirements
Label test	According to TS	Satisfies the requirements	Satisfies the requirements
Medicine test	Manufacturer: OOO «Apitek-A» (Limited Liability Company) series 010 914	Satisfies the requirements	Satisfies the requirements

Data the table. 1 indicate that curative and preventive medicines «Propolis-Derma», introduced in vials-pencils of FK-132 and FK-92 models for storage and application to the skin according to the indices of trial and quality control, in general meet the requirements set out in TS U 25.2-2094624496-001-2004. However, the experiment have found the insufficient impermeability of the vials-pencils of FK-92 model, and therefore vials-pencils of FK-132 model have been elected for the further investigation.

Conclusions. The original packaging for the new curative and preventive medicine on basis of the substances of antimicrobial and antifungal action and tincture of propolis «Propolis-Derma» in the form of lotions-medical stick (vials-pencils for storage and application to the skin and its surroundings). Most match-purpose the vials-pencils of FK-132 model most closely correspond.

ANALYSIS MARKET OF DRUGS IN THE FORM OF MARKERS IN UKRAINE

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Introduction. Antifungal preparations for topical use ATC classification refers to the group D10A.

The aim of the study. Due to the pharmacological effects of drugs that are created, and it is their activity against a number of pathogens fungal skin lesions purpose is to analyze the market of antifungal drugs for local use.

Materials and methods.

- Calculations standard concentration index (CR $_{3>}$ 70);
- Price of product characteristics Group D01AE;
- Analytical sales of drugs group D01AE.

The obtained results. In Ukraine today there are several drugs in the form of markers. The most famous of them - "Flomed" (Ukraine) containing 5% solution of iodine and "Lekker" (RF), containing a solution of iodine, brilliant green, fukortsyn and where other. Price markers "Flomed" varies from 15 to 25 UAH., The "Lekker" from 35 to 76 USD. Applying the method of pricing based on the prices of competitors, the price of drugs or development should be set higher than the price of the product "Flomed" obrruntuvavshy is its multi-component composition and antifungal effect. At the same time, the price should be lower than the price of the product "Lekker" for competitive advantage.

Given the widespread prevalence of fungal infections and lack of effective antifungal drugs for external use, development of new combination of drugs based on propolis is appropriate. In the segment, which includes medication or development there is competition, the segment is highly concentrated as three brand occupy 81% market share. But the most fierce competition going on among high-cost drugs. Pipeline preparty with reasonable price and will be available to most consumers.

Conclusions. Created drugs "Propolis-PNG", "Propolis-PSC," "Propolis-PCB", according to the preliminary calculations relate to the average price category and will be available to most consumers.

INVESTIGATION IN THE TECHNOLOGY DEVELOPMENT "IBUASCTAMOL" TABLET

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Introduction. Non-steroidal anti-inflammatory drugs are group of drugs that are widely used in clinical practice, many of which can be bought without a prescription. More than thirty million people in the world daily take NSAID, 40% of these patients are over 60 years old. About 20% of inpatients receive NSAID. The great popularity of NSAID is explained by the fact that they have anti-inflammatory, analgesic and antipyretic effects and bring relief to patients with the corresponding symptoms that are noted in many diseases.

Statistics of the pharmaceutical market of the Republic of Uzbekistan, as well as world pharma. Market, shows a growing trend of consumer demand for non-steroidal anti-inflammatory drugs.

One of the classical representatives of this class of drugs is ibuprofen and for almost half a century continues to be appointed by doctors of various specialties as a reliable and proven analgesic. Ibuprofen is a derivative of propionic acid with antipyretic, analgesic and anti-inflammatory properties. Its combination with ascorbic acid and paracetamol increases the activity of the drug in inflammatory processes.

Aim. The purpose of our research work was to study the compatibility of the active substances of the tablets "Ibuasctamol".

Materials and methods. As the subjects of the study used medicinal substances ibuprofen, paracetamol and ascorbic acid, which are offered as a tablet form for the treatment of inflammatory processes. To substantiate the composition and technology of tablets "Ibuasctamol", the technological properties of tablet masses were studied. When creating a multicomponent dosage form, it is first of all necessary to take into account the physico-chemical compatibility of the active components. To determine the possible interaction of components with each other, we used the method of accelerated aging of the mixture. For the analysis, a mixture of ibuprofen + ascorbic acid + paracetamol (0.2 g + 0.2 g + 0.1 g, respectively) was prepared. Part of the mixture is put on accelerated aging at a temperature of 60 ° C and the second half on natural storage.

Results and discussion. Based on the results of the study, a preliminary conclu-sion can be made that ibuprofen + ascorbic acid + paracetamol when combined in a solid dosage form (tablets, capsules) is stable. A study of the compatibility of the above mixture with both natural and "accelerated" aging methods, the above-mentioned qualities of the mixture as appearance, authenticity, solubility and quantitative content of the active substance were positive. During the storage of growth, no foreign impurities were found, and the quantitative content of the main components of ibuprofen + ascorbic acid + paracetamol did not decrease. The quantitative content of active things was determined by spectrophotometry. The appearance of the mass did not change.

As a result of the conducted studies it was established that the mass being studied is a white mass. The results of studying the fractional composition indicate that the bulk of the particles have a size of less than 250 mkm (28,97%), characterized by non-compliant flow (0,501 10-3 kg / s), small bulk density (222, 86 kg /m^3), the angle of a natural slope (54,7 degrees), the values of residual moisture (up to 5,90%) and porosity (80,01%).

The obtained data of the study of technological properties showed that the substances of ibuprofen, paracetamol and ascorbic acid are polydisperse crystalline powders with particles of anisodiametric form. It was found that all the substances studied are weakly flowing materials and have different compressibility, i.e. Practically can not be used in direct compression technology.

Conclusions. The study on the determination of the physico-chemical compatibility of the components of the ibuprofen + ascorbic acid + paracetamol mixture (0.2g + 0.2g + 0.1g, respectively) for the development of a tableted dosage form based on them has proved to be compatible with ingredients in terms of development On their basis tableted dosage form.

THE SUBSTANTIATION OF THE ESSENCE OF SELECTION TECHNOLOGY FOR FAST-SOLUBLE TABLETS WITH ALTEA EXTRACT

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Introduction. One of the most important tasks of modern pharmaceutical technology is the creation of dosage forms that enhance the bioavailability of medicines. This is achieved in various ways, among which the use of special auxiliaries (gas-forming mixtures, superdisintegrants, complexing agents, solubilizers) and technological methods (preparation of solid dispersions, ultrasound and criomicroconisation) that increase the solubility or dispersibility of drug components can be distinguished. Among the group of rapidly dissolving dosage forms, fast-dissolving drugs play a special role, in which the effect of rapid disintegration is achieved through the introduction of gas-forming components. The advantages of fast-dissolving dosage forms include high bioavailability, the possibility of reducing side reactions, combining mutually reactive components and correcting the unpleasant organoleptic properties of medicinal substances. To the instantly soluble it is possible to include solid dosage forms (powders, granules, pellets, microspheres, tablets, capsules, suppositories, etc.) in which the increase in bioavailability is achieved due to the use of auxiliary substances and technological methods accelerating the processes of dissolution or dispersion of medicinal substances .

Aim. The purpose of our research was to study the pharmaceutical aspects of developing and improving the technology of instant tablets with the drug althea extract.

Materials and methods. The following medicinal and auxiliary substances were used in the work: dry extract of drug althea, tartaric acid, citric acid (monohydrate, anhydride), apple acid, succinic acid, sodium hydrogen carbonate, sodium carbonate, sodium citrate, polivinilpirrolidone, starch, methylcellulose, CMC, Sodium-CMC. All technological processes of the experiment were carried out on laboratory and technological equipment: sieving on hand screens, drying in laboratory cabinets, grinding in a PM-1 mill, pelletizing with a hydraulic hand press. The pressing pressure, force and pressure of ejection of the tablets from the matrices were determined on a laboratory hydraulic press at a relative air humidity of 20% to 60%. To this end, effervescent tablets with a diameter of 12 mm were extruded on a manual hydraulic press at a different pressing pressure from 80 to

200 MPa. Then, the influence of the pressing pressure on the gas-forming properties of the recommended tablets was studied. It was also of interest to determine the dependence of the ejection pressure on the compaction pressure at different contents of the auxiliary substances.

Results and discussion. Experimental samples of tablets with an extract of althea medicinal with addition in various ratios and combinations of auxiliary substances were prepared. As a moisturizer, ethyl alcohol and a starch paste of different concentrations (2%, 7% and 10%) were used. The results of the study revealed that low concentrations of starch extend the disintegration time of tablets. At the first stage of the study, the possibility of obtaining effervescent tablets by direct compression was studied. The tablets obtained had a non-uniform surface, chipped at the edges, and they also did not correspond to the strength of tablets and disintegration. In this regard, recommend direct compression, as a possible way to produce effervescent tablets with an extract of althea was not advisable. Therefore, we investigated the options for wet granulation. Based on the results of the study, the recommended gasification tablets increase with increasing pressure of pressing. At a compaction pressure of 80 MPa, depending on the humidity of the room at 60% moisture, the gassing coefficient (kg) is 0.51 and at 20% by 0.90 and at 180MPa 0.45 and 0.81 respectively. In studies, the decrease in the coefficient of gassing with increasing pressure of pressing more than 180 MPa is determined. As follows from the data obtained, the ejection pressure is in direct proportion to the pressing pressure. The minimum ejection pressure was observed for tablets obtained at a compaction pressure of 50 MPa. However, the tablets did not have sufficient strength. With an increase in the ejection pressure up to 180MPa and above, chips and roughness of the lateral surface were observed on the tablets, which is typical for a pressing pressure of 100 MN/m and higher.

Conclusions. Thus, on the basis of the data obtained, the dependence of gas formation in the recommended tablets with the extract of the althaea of the medicinal pressure of pressing and the humidity of the production department was determined. For the further studies, the optimum pressing pressure in the range of 100-180 MPa was established at a shop humidity of 20-60%.

RESEARCH ON THE SELECTION CONDITION OF PRESSING TABLETS "CARBENDACIM"

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Introduction. Tablets from helmints are divided into broad-spectrum drugs, and selectively acting on certain types of worms. Previously, only herbal remedies were used for the treatment of worms - pumpkin seeds, garlic, chenopodia oil from the antihelminth (quite toxic), man's fern extract, etc. To date, the pharmaceutical industry offers synthetic pills for worms in humans that are more Safe, and effective, since they have a higher antihelminth activity. For the treatment of the most common types of helminthic invasions, along with other anthelmintic drugs and carbendacim tablets are used.

Despite the increase in our domestic means, the need to master domestic antihelmint medicinal forms remains an urgent task. This, in turn, will reduce the import from other countries and make it more affordable for the population. In order to develop the country's pharmaceutical industry and to saturate the domestic market with domestic medicines, the introduction of anti-helminthic activity into production and practical use of medicines, as well as an increase in the number of registered generics drugs on the pharmaceutical market of the republic is topical.

Aim. The aim of the research was to study the physicochemical and technological characteristics of active substances and excipients in order to improve the composition and selection of the technology of antihelminthic tablets based on carbendacim.

Materials and methods. Carbendacim-1H-Benzimidazole-2-yl-carbamic acid methyl ester. It is active against intestinal nematodes. The analysis of technological characteristics of carbendacim and auxiliary substances was carried out on the instruments of the firm "Erweka" (Germany) according to the method given in GF XI. As auxiliary substances, sucrose, corn starch, CMC, lactose M-80, lactose M-200, microcrystalline cellulose (MCC), potato starch, calcium stearate, etc. were used.

The study of the shape and size of particles of active and auxiliary substances was carried out with the MBI-15 microscope at an increase of 400

times, which makes it possible to characterize the shape and surface of the particles, as well as the average linear size of the dominant fractions.

Results and discussion. As a result of the conducted studies it was established that the substance studied is white or white with a creamy or pinkish hue, a fine crystalline powder without a smell. Almost insoluble in the water and alcohol. The results of the fractional composition indicate that the bulk of the particles have a size of less than 250 mkm (32.35%), have poor flow characteristics (0.802 × 10-3 kg / s), small bulk density (198.87 kg / m^3), high compaction factor, angle of repose (58.7 degrees), is not high values of residual moisture (up to 3.45%).

The obtained data show that the carbendacim substance is polydisperse fine crystalline powders with anisodiametric particles. In studies it was determined that the shape of carbendacim powders is small rectangles, with a particle size of up to 11 μm, a flowability of 1.9 ± 0.04 g / s and a compressibility of 21.2 ± 0.5 N.

From the results obtained, it can be concluded that the carbendacim substance has poor flowability and, at the same time, quite satisfactory compressibility. It was found that the substances studied can not practically be used in direct compression technology.

Conclusions. Thus, the shapes and sizes of particles of active and auxiliary substances that will be used to improve the tableted form of carbendacim have been studied, and the technological characteristics of the pulverulent mass have been experimentally determined. The preparation of a tableted dosage form of carbendacim by direct compression is not possible, so it was decided to use the wet granulation method and the introduction of auxiliary substances.

PROSPECTS OF USING THE SUNFLOWER EXTRACT IN THE TREATMENT OF DERMATOLOGICAL DISEASES

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Introduction. Drug products topically administered via the skin fall into two general categories, those applied for local action and those for systemic effects. Local actions include those at or on the surface of the skin, those that exert their actions on the stratum corneum, and those that modulate the function of the epidermis and/or the dermis. Common products in the former category include creams, gels, ointments, pastes, suspensions, lotions, foams, sprays, aerosols, and solutions. Creams, ointments, and gels generally are referred to as semisolid dosage forms.

Aim. The aim of our work was to develop a sunflower extract ointment for topical use.

Materials and methods. The objects of the study were examples of ointments with sunflower extract.

Results and discussion. Pharmaceutical preparations for treatment of conditions such as rashes, skin irritation, stings, fungal infections etc. are normally supplied in the form of a cream or ointment as this provides an effective means of delivering the active ingredient directly to the required area. Products can be either a water in oil (w/o) or oil in water (o/w) emulsion, consisting of waxes, emollients and lubricants dispersed in an oil phase, and a water phase containing emulsifying, stabilizing and thickening agents, preservatives and in some cases, colorant. Active ingredients are dispersed in either phase or added when the emulsion has been formed and allowed to cool.

Sunflower is very rich in medicinal properties. Sunflower seeds in their composition contain a large amount of vitamin D, A, B, F, amino acids, tannins, minerals. In the flowers of sunflower there is alcohol, acid, glycosides, bitterness, choline and betaine.

Conclusions. The delivery of drug through the skin has long been a promising concept because of the ease of access, large surface area, vast exposure to the circulatory and lymphatic networks, and noninvasive nature of the treatment. Among the three formulations (oil, cream and gel) prepared, on the basis of pharmaceutical parameters creams formulation loaded with herbal extracts give the considerable results. Hence this herbal cream formulation was utilized for further pharmacological studies.

INVESTIGATION OF PHYSICOCHEMICAL AND TECHNOLOGICAL PROPERTIES OF DIHYDROQUERCETIN

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Introduction. In the pathogenesis of vascular diseases, an important role is played by changes in the microcirculation of the blood. Therefore it's extremely important to search for new drugs that help improve microcirculation. Such medications include drugs based on dihydroquercetin - bioflavonoid, obtained from Siberian larch wood. It exerts a stimulating effect on the tissue bloodstream and stabilizes the barrier function of microvessels. Dihydroquercetin also reduces the permeability of the capillary walls and thereby helps to reduce congestion in microcirculatory way.

Objective. The research of the physicochemical and technological properties of Dihydroquercetin

Materials. The substance of Dihydroquercetin was used as a research object.

Methods. Physicochemical and technological methods of investigation were used to select the auxiliary substances.

Results. In the course of studying the physicochemical properties, it was found that Dihydroquercetin is a white crystalline powder, odorless, with a weak bitter taste. The results of microscopic analysis indicate that the particles of Dihydroquercetin are in the form of rods with a linear size of 0.2-1 / μm. The form factor is 0.1, which allows to assign Dihydroquercetin to powders with an anisodiametric form. The melting point is 220 ± 2 ° C, the residual humidity is 8.61%. A study of the solubility of Dihydroquercetin in water showed that it depends on temperature. The results of the study of technological characteristics indicat that the flowability of the powder is very low (0.52 g / s), the angle of the natural slope is 47.6 °, the bulk density 0.23 g / ml, the compression ratio is 0.73 g / cm. The study of moisture absorption at 40 and 100 relative humidity showed that the substance is hygroscopic. The study of the fractional composition showed that the fraction with a size of 0.5 to 1.0 mm predominates in the powder.

Conclusions. Dihydroquercetin can be considered as an effective treatment for vascular diseases. The results of the study of physicochemical and technical properties indicate that the powder has unsatisfactory technological characteristics and it is expedient to use auxiliary substances from the group of binder and fractional ones in the composition of tablets.

COSMETICS FOR DIFFERENT SKIN TYPES

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Introduction. Healthy skin is our best decoration. The type of skin depends on the work of the sebaceous glands, manifests itself during the puberty of a person and can change with age. Specialists distinguish several basic types of skin: normal, oily, combination, dry. Also emit fading and sensitive skin. There are age and gender characteristics of the skin. The skin of the newborn is covered with curd cheese-like grease. There are features in the baby's skin - the density of sweat glands is 5-7 times higher than in adults. Baby skin is more sensitive to the effects of ultraviolet rays. The skin of men is thicker than the skin of women by 20%, the high content in the dermis of collagen leads to later aging. For each type of skin, a certain care and special cosmetics are necessary.

Aim. Learn how to determine the types of skin and choose cosmetics for certain types of skin.

Materials and methods. 15 questions were prepared, questionnaires were conducted among students and pharmacy respondents for knowledge of the features of existing skin types, determining the type of skin at home, the use of cosmetic products recommended for certain types.

Results and discussion. The survey involved 57 students aged 16-20 years, pharmacy respondents: 37 women aged 30-45 The results of the experiment showed that 64% of students know what the type of skin depends on. The combined (42%) and fatty skin types (34%) prevail among the students. Respondents in pharmacies are fading (30%) and dry (25%) type. Most respondents consider their skin type when choosing cosmetics. Students prefer micellar water, tonics, scrubs, cream. Respondents of pharmacies – serums, masks, gels. 65% of students had skin problems, and they consulted a doctor, but 25% did not apply to a specialist. Only 20% of students and 60% of pharmacy respondents know about the gender characteristics of the skin and take them into account when buying cosmetics. 78% of students systematically take care of the skin. Among women of mature age, 43% regularly visit a cosmetologist and systemically take care of the skin. The questions on skin care that concerned students and pharmacy respondents and recommendations were clarified.

Results and discussion. Skin is responsible for the formation of an attractive appearance. Skin care should be systemic. Cosmetic means should be selected according to the type of skin, depending on the age. Recommendations for skin care, which take into account the problems of respondents, are formulated.

DEVELOPMENT OF EXTEMPORANEOUS SOFT MEDICINAL FORM OF HEALING ACTION WITH METHYLURACIL

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Introduction. The problem of treating purulent-inflammatory diseases, which is one of the oldest in surgery, remains acute today. A large clinical experience and experimental data conclusively prove that local medical treatment of wounds should be built strictly in accordance with those processes that occur in different stages of the wound process, helping their natural course and not hindering it. The medicines used in practical medicine for local treatment of wounds do not fully meet the increased medical requirements, since they are often created without taking into account the phasing of the wound process.

The aim of our work was to develop extemporal liniment of methyluracil for the treatment of wounds.

Materials and methods. In the development of composition and technology of soft medicinal form with wound healing action, we were guided by the following main provisions: medicines should have a high therapeutic activity, minimal side effects, provide maximum release of biologically active substances and the prolonged action. Selecting of research objects carried out on the basis of clinical advices and analysis of the literature data. Selection of auxiliary components produced based on the order to provide the desired therapeutic activity of medicines.

Results and discussion. Taking into account the results of studying the influence of various factors on the structural and mechanical properties of the liniment's bases and using the traditional approach, we proposed rational technological scheme of the liniment with methyluracil production. The first step (preparation of the base): the known amount of arespol placed in a container with water and allowed to swell, followed by adding of sodium hydroxide as a neutralizing agent. The ingredients are mixed thoroughly. The second stage involves the preparation actually of the liniment. Weighed amount of methyluracil administered, then the emulsifier tween-80 added to the resulting gel on the first stage and emulsified. The resulting emulsion base is mixed with castor oil. Agitation and a thorough homogenization are carried out.

The final product should be a homogeneous mass without mechanical impurities, white, and with a specific smell.

Conclusions. On the basis of the conducted research technology of extemporal liniment of methyluracil for the treatment of wounds was developed.

TECHNOLOGY AND EVALUTION OF QUALITY OF "DERMOSTOP" OINTMENT

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FS) –the most frequent and severe complication of diabetes mellitus , which occurs in The development of purulent-necrotic process against the background of the diabetic Complex treatment and prevention of DFS is an urgent task in endocrinology. Our republic has a rich raw material supply of natural raw materials. Therefore, studies aimed at expanding the range of anti-inflammatory application phyto-preparations are relevant.

Research objectives: development of composition, technology and evaluation of the quality of anti-inflammatory ointment of comlex composition «Dermostop».

Materials and methods. Scientists of the Tashkent Pharmaceutical Institute have developed the formulation «Dermostop», consisting of flowers of calendula, nettle leaves and white mulberry, of milfoil herb and chicory roots, recommended for external therapy of various etiology dermatoses, the formulation has astringent, antiseptic, antimicrobial, anti-inflammatory and wound healing effect.

On the basis of «Dermostop» preparation, a liquid extract (1:1) was obtained by the method of three-stage fractional maceration with circulation, and its standardization was carried out. The pharmacological studies carried out showed high efficiency of the natural complex of polyamidoamino acids - Glypil produced from waste of silkworm cocoons in prevention and external therapy of DFS and other dermatoses on the background of diabetes mellitus.

The obtained results. In the course of the research, the following composition of the «Dermostop» ointment was suggested: glypil 5.0 g; a liquid extract of «Dermostop» 5.0 g; boric acid 3.0 g; menthol – 0.5 г; emulsion base – up to 100.0 g. Technology: the ointment is prepared under aseptic conditions. Vaseline with the T-2 emulsifier is alloyed by stirring in a water bath, hot water (90-95 %) is gradually added and mixed again until the temperature lowers to 30° C, then cooled to room temperature. Menthol is introduced into the base and stirred. In the mortar glypil with the liquid extract «Dermostop» is grinded and gradually by 2-3 stages added emulsion consistency base, then the ointment was homogenized for one hour with a mechanical MI-2 stirrer until a homogeneous mass was formed. The finished ointment is packed in 30.0 g in tubes. Evaluation of «Dermostop» ointment quality was carried out according to appearance in a creamy ointment with a characteristic pleasant odor; homogeneous, pH 6.5-6.8 (potentiometrically); the study of thermal

and colloidal stability showed that the ointment is stable at temperature drops (from -20 to $+45^0$ C) and centrifugation for 5 minutes at a speed of 6000 r/min. In determining the rheological parameters of the ointment, the effective viscosity was studied, the shear stress and the plastic viscosity of the preparation were carried out on a Reotest-2 instrument using a cell consisting of a cylinder system S/S1 with a constant Z=5.6. The determination of the effective viscosity (η_{eff}) at different gradient rates (γ) for the preparation was carried out a shear flow at 25^0 C. The instrument reading α was fixed in mode II at a different value. On the basis of the obtained data, two graphs were constructed: the first for determining the effective viscosity of preparation, Fig.1 (a), the second for determining the shear stress limit preparation Fig.1 (b).

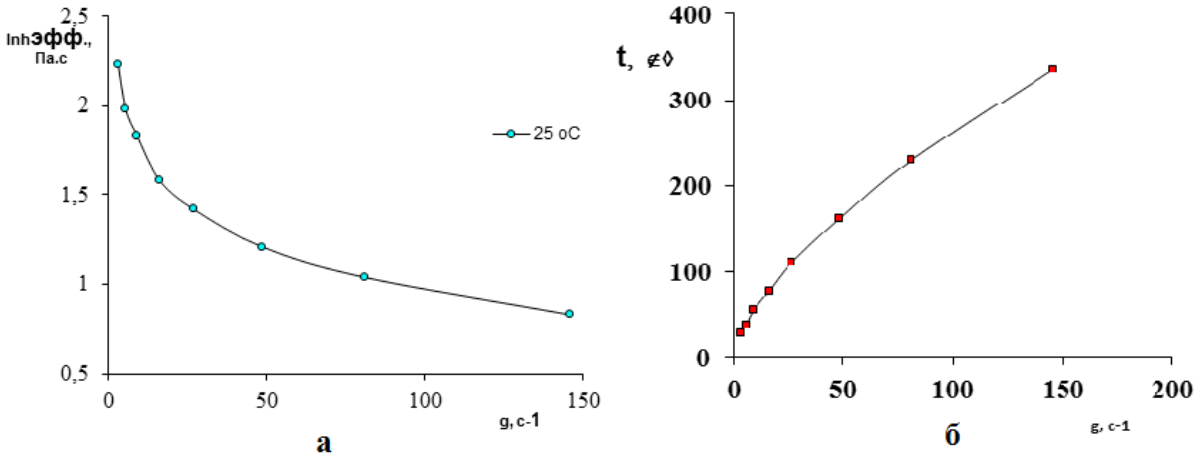

Fig. 1 (a) – dependence of the effective viscosity (ln $\eta_{эфф.}$) on the gradient of (γ) the drug at 25^0 C; b-dependence of the shear stress (τ) on the gradient of the speed (γ) for the preparation.

From fig.1 (b) at $\gamma \to 0$ the ultimate shear stress of the preparation is $\tau_{пр} \approx 25$ Pa. To determine the plastic viscosity (plasticity) (η_p) we used the formula of Shvedov-Bingham: $\tau = \tau_{пр} - \eta_p\gamma$;

$\eta_p = (\tau - \tau_{пр})/\gamma = (78.4 – 25)/16.2 = 3,3$ Pa·c

The effective viscosity of the preparation, the shear stress and plasticity indices satisfy the requirements, therefore, in general the preparation has the optimum consistency from the consumer point of view.

Conclusion: studies have been carried out to develop the composition and technology of the anti-inflammatory ointment «Dermostop» of complex composition and studied their qualitative indices.

DEVELOPMENT OF SUPPOSITORIES COMPOSITION AND TECHNOLOGY WITH AN EXTRACT OF BROCCOLI

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Introduction. The lowest section of the intestinal tract is the 16-20 cm-long rectum, which is moistened by about 1-3 ml mucus and the pH value of which varies between 6.8-7.9. Anastomoses are found between the arteries and veins of the rectal area. The absorbed drug is transported by blood in two different directions. From the anal region the absorbed drugs enter the blood circulation bypassing the liver, which yields useful advantages in certain cases: on the one hand the onset of the effect is very rapid, it can equal even the speed of an intravenous injection, and on the other hand drugs enter the organism bypassing the first-pass metabolising effect of the liver, which can be a therapeutic advantage in the case of liver diseases and also in the case of drugs which are biotransformed by the liver into ineffective products. Consequently, an alternate route of administration to avoid or minimize the above side effects is preferred in form of suppositories.

Aim. The aim of our work was to investigate stability of modeling samples of ointment suppositories bases for preparation them with dry extract of broccoli.

Materials and methods. The objects of the study were examples of suppositories bases. Suppositories were made by the melting method. Accurately weighed amount of the respective bases were melted on the water bath and maintained at 55°. The extract was then added to the melted mass and thoroughly mixed. The melt was then poured into the 1 g suppositories moulds and set aside for cooling for 15 min. The suppositories formed were taken out from the moulds and stored in refrigerator.

Results and discussion. Prepared suppositories were further kept for freeze thaw and accelerated temperature conditions to study the stability of the prepared formulations. Suppositories with extract of broccoli were prepared by using water-soluble and oil soluble suppository bases. Release rate was good in water-soluble suppositories bases in comparison to oil soluble suppositories bases. When stability studies were performed on the prepared extract of broccoli suppositories it was found that suppositories made by water-soluble base had no significant changes while suppositories prepared by oil soluble bases, had some signs of instability.

Conclusions. In view of the fact that the melted (or dissolved) rectal suppository spreads in the rectum, the lower few centimetres of which are not separated sharply from the pelvic upper part with respect to blood paths either, if a drug is administered rectally into the body, the rate of a drug administered in the form of an intramuscular injection can be expected.

DEVELOPMENT OF CAPSULES WITH ACORUS CALAMUS DRY EXTRACT FOR ULCEROUS GASTRIC DISEASE TREATMENT

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Introduction. Peptic ulcer is a common disease of the XXI century, whereas before it occurs much less frequently. Statistics show that the total number of people in the world who have gastric ulcer is about 25%. Despite advances in diagnosis and treatment of gastric ulcers, the disease continues to amaze more and more young people, without showing a tendency to stabilize or reduce the incidence.

In today's world herbal medicinal products continue to occupy a significant place in the treatment of pathologies of the gastrointestinal tract. A wide range of therapeutic action of the biologically active substances Acorus calamus extract and a limited number of drugs based on it, point to the relevance of developing drugs based on this raw material.

Aim. The aim of our work was the development of the composition of the encapsulated drug for the treatment of gastric ulcer with a dense extract of Acorus calamus.

Materials and methods. On the basis of exploratory research, the potential activity of Acorus calamus for the therapy of peptic ulcer has been established.

Results and discussion. Acorus Calamus, commonly known as Sweet Flag, or simply Calamus, is a wetland reed plant that grows indigenously throughout Asia. Despite safety concerns, calamus is used for gastrointestinal (GI) problems including ulcers, inflammation of the stomach lining, intestinal gas, upset stomach and loss of appetite.

The choice of an appropriate hard gelatin capsule is mainly based on the capsule size. The determining factors are the minimum amounts of drug active and excipients required. It is possible to achieve a smaller capsule size by increasing the density of the formulation through granulation or compression, or to arrive at a larger size by increasing the amount of excipients. Usually, only a limited number of excipients are necessary, and these are simply mixed with the active and directly filled into the capsules. For the development of hard gelatin capsules with a thick extract of Calamus we should use two capsule sizes 0 and 1 with a capacity of 0.68 and 0.5 milliliters.

Conclusions. The choice available in terms of capsule type, the range of sizes and the capsule's colour or combination of colours, as well as the possibility of printing directly onto the capsule, means that patient compliance, product recognition and product differentiation can be markedly improved.

DEVELOPMENT OF THE COMPOSITION OF EXTEMPORAL MEDICINAL PLANT SPECIES FOR THE COMPLEX TREATMENT OF HYPERTENSION

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Introduction. Arterial hypertension is a common disease. In case of mass measurements of blood pressure 20 – 30 % of subjects show the elevated figures. In the implementation of the stage-by-stage examination method of arterial hypertension, this disease is diagnosed, on the average, in 65 % of cases, while in 35 % symptomatic forms are found.

Medicinal plants, which have diuretic, sedative, hypotensive effect, are widely used in the treatment of hypertensive disease

Aim. The purpose of our research was the study of technological parameters of medicinal plant raw material in the development of extemporal species for the complex treatment of hypertonic disease.

Materials and methods. The orthosiphon leaves, birch leaves, peppermint leaves, motherwort herb, mountain ash fruits, valerian rhizomes with roots were selected as the objects of research, based on their chemical composition and pharmacological properties.

Determination of the moisture content was carried out on a Sartorius MA-150 moisturemeter. The shape, size and nature of the surface of the powder particles were determined with the use of the Item PB-2610 microscope equipped with a micrometer grid at a magnification of 1000 times. The determination of the fractional composition was carried out according to the procedure given in SPU. Technological parameters (specific, bulk, voluminous, angle of natural slope) of the raw materials were determined according to the methods of Vetrov, given in the literature. Based on the obtained results, the porosity of the raw material, the variability and the free volume of the layer were calculated.

Results and discussion. Such technological parameters of the medicinal plants and the developed extemporal species humidity, fractional composition, shape and particle size, wettability, hygroscopicity, bulk, variability, specific mass were studied; porosity and variability values of raw material and free volume of the layer were calculated.

Conclusions. The results of the conducted studies allowed offering extraction conditions and predicting the choice of packaging of the extemporal phytomedicine for the complex treatment of hypertensive disease.

RESEARCH OF CHOOSING OPTIMAL BASIS FOR SOFT PHARMACEUTICAL FORM

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Introduction. In the process of developing soft pharmaceutical form particular attention should be paid to selecting optimal basis whose purpose is providing of maximum releasing medical substances and their bioavailability. Also the basis must provide structural and mechanical properties and stability of the prepared pharmaceutical form.

Aim. A choice of optimal ointment basis for creating soft pharmaceutical form and a definition of biological availability of active substance were the aim.

Materials and methods. The active substance of soft pharmaceutical form that is created is water-soluble protein polysaccharide complex (WSPPC) of Pleurotus ostreatus mushroom. As constituents parts of the basis for soft pharmaceutical form approved for use substances were used.

We made the choice of components of the basis for the pharmaceutical form based on the compatibility with the active substance and taking into account its physical and chemical properties.

We evaluated releasing WSPPC from the basis by the method of dialysis through semi-membrane «in vitro».

The quantitative determination of WSPPC was carried out by the photocolorimetric method because of saturated brown color of aqueous solution of WSPPC. Purified water was used as comparison solution. The optical density was determined according to a wavelength of 440 ± 2 nm in a cuvette with a layer thickness of 5 mm.

Results and discussion. During research it was revealed that the releasing of WSPPC was the most dynamic and complete from ointments on emulsion basis. Linear dependence of the optical density of WSPPC concentration in the dialysate was obtained. The discreteness was 0.9711.

Conclusions. The composition and compatibility of ointment basis components with active substance significantly affect its release and bioavailability. The emulsion basis of the o/w type was most promising one. The WSPPC release was the most full from them.

MARKETING RESEARCH EYE DROPS, PRESENTED ON THE MARKET OF UKRAINE

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Introduction. Eye diseases - organic and functional damage to the human visual analyzer, limiting its ability to see, as well as affection of the eye adjuvant. Ophthalmic diseases are widespread among different strata of the population.

Aim. Analysis of the assortment of eye drops presented in the pharmaceutical market of Ukraine. By appointment, modern eye drops are divided into the following groups:

- Antimicrobial eye drops are used to combat all kinds of infections.
- Anti-inflammatory eye drops are intended for the treatment of inflammatory lesions of the organ of vision and its appendages of non-infectious nature.
- Eye drops used for treating glaucoma, which is a persistent increase in intraocular pressure, leading to severe consequences up to the irreversible loss of vision.
- Antiallergic eye drops, intended for the treatment and prevention of allergic reactions. - Eye drops used with cataract.
- Moisturizing eye drops or "artificial tears."
- Diagnostic eye drops and eye drops used during surgical interventions.

Materials and methods: The eye drops.

Resultsa and discussion. A result of the marketing research of drugs represented in the Ukrainian pharmaceutical market, is installed: the main share among eye drops manufacturers occupied by foreign pharmaceutical companies.

Conclusions. It is necessary to search for new medicinal products, more focused on the development of drugs with high bioavailability.

THE TECHNOLOGY OF OBTAINING ANTIHYPERTENSIVE MEDICINES ON THE BASIS OF FRITILLARIA PSKEMENSE

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Introduction. Fritillaria pskemense is a genus of perennial herbaceous plants of the Lily family. Stem erect, glabrous, thick, pale green. The leaves are covered with a bluish bloom. Bulb globose, yellow, 3-5 cm in diameter. They contain alkaloids, acting on central nervous system and heart. Fritillaria pskemense has long been widely used in folk medicine as a remedy antihypertensive. The development of technology for medicine from the bulbs of Fritillaria pskemense is an urgent task.

Aim. The development of technology for antihypertensive medicine on the basis of Fritillaria bulbs pskemense.

Material and methods. Object of this researching was bulbs of Fritillaria pskemense which was harvested on April of 2016th year from the mountains Pskom.

Dig the bulbs are best when the aboveground part of the plant begins to turn yellow and dry up, it's in April-may. After we dug up 10 kg of bulbs of Fritillaria pskemense should be carefully inspected to remove the remaining dry film and rinse. Then you need to remove in the Central part of the onion core. Then chop the onion. The resulting mass is necessary to survive and to separate the liquid part. Then the liquid part is immersed in the water and leave for 1-2 days. Thus, the white mass is accumulated. You need 3 times you need to change the water to eliminate ballast substances. After filtered and received the white precipitate then carefully poured into water and the separated white mass. After that you need to dry.

Results and discussion. In the end of the process was obtained 1.3 kg of powder(moisture 8%). The yield of 13%. 10-15kg bulbs Fritillaria pskemense get 1-2kg of white powder.

Conclusions. First developed technology of obtaining antihypertensive medicines on the basis bulbs of Fritillaria pskemense were the optimum conditions for the process and succeeded in obtaining a substance with a yield of 13%.

JUSTIFICATION OF COMPOSITION OF TABLETS FOR CORRECTION OF BODY WEIGHT

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Introduction. Overweight and obesity are one of the most important problems of modern medicine, which is associated with psychological discomfort and the emergence of all sorts of problems whit many systems and organs of the body.

Aim. The purpose of our work is to justify the composition of tablets to correct body weight.

Materials and methods. Objects of research – API (bromelain and dry extract of green tea) and excipients from adsorbents, glidants, lubricants and fillers. We used physicochemical (shape and particle size, moisture) and pharmaco-technological (fluidity, angle of repose, strength tablets) methods.

Results and discussion. As API, we selected components of natural origin - dry extract of green tea and bromelain, which will promote the splitting of fatty deposits, prevent their deposition in the body, reduce appetite, accelerate metabolism, etc. In order to establish a rational composition and technology of tablets we decided to explore their properties, which will determine the type and required amount of excipients. Based on the results of the crystallographic analysis, was established the polydisperse composition of the API powders. Studies of the moisture-absorbing capacity of the samples indicate their hygroscopicity. So, we have decided to include substances that regulate humidity such as the Aerosil 380, Syloid® 244FP, Neusilin®. They were injected into the mixture APIs in a concentration of 1% and after that we investigated the kinetics of moisture. The best results have shown Syloid, and as a further step was to study kinetics of a mixture of API at different concentrations with the Syloid. According to the results, the best capacity for water absorption and turnover has tabletting mass of 1,5% Syloid. As filler we chose MCC, that reduces the digestibility of fats, cholesterol, carbohydrates, causes a rapid sense of satiety, reduces appetite and is used as an independent additive to correct obesity. Due to a lack of fluidity of tabletting mass and different particle size of the active substances and excipients, which can lead to weight heterogeneity and its stratification, we can not get tablets by the method of direct compression. As binders, was chosen an alcohol solution of PVP and ethanol in concentration of 96%, because use of aqueous humectants led to partial dissolution of the mixture. The best in appearance and processing properties turned out granules obtained with 96% ethanol. As a lubricant, was chosen calcium stearate and its optimal concentration was set at 0,75%.

Conclusions. In this way, on the basis of physicochemical and pharmaco-technological research was established the final composition of the tablets for correction of body weight and the need for prior granulation.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF ANTI-INFLAMMATORY GEL FOR THE TREATMENT OF THE MUSCULOSKELETAL SYSTEM DISEASES

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Introduction. One of the most urgent social problems of healthcare of the nation are the musculoskeletal system diseases, which occur because of degenerative processes of conjunctive tissue and injuries or wounds of various etiologies with subsequent inflammation, diagnosis and treatment of which often causes significant complications. According to the State Register of Pharmaceutical drugs the assortment of drugs of the group «M02 – local action medicinal products usage for joint and muscular pain» is presentenced on the Ukrainian market only by some substances which produce just short – term anti – inflammatory effect and indirectly affect the pain syndrome oppression. First of all this applies to Nonsteroidal anti-inflammatory drugs, in particular diclofenac sodium and its derivatives, which can not provide polyvalent pharmacological effect and effective recovery of conjunctive tissue and pharmacotherapy of these pathologies to the full extent. Therefore, the development and introduction of drugs to treat diseases of the musculoskeletal system based on new highly – effective substances is essential for maintaining the health of our population.

Aim. Substantiation of composition and the development of technology of anti-inflammatory and analgesic action gel for treatment of injuries and pathological states of the musculoskeletal system.

Materials and methods. The objects of research were active pharmaceutical ingredients – propolis phenolic hydrophobic drug (RC № UA/4505/01/01, Order Ministry of Health of Ukrainian № 337 from 07.06.2011 p.), local anesthetic, menthol, essential oils, additive agents for medical use adjuvants, the rational concentration of which was established in accordance with the analysis of modern literature and experimental research and gel of anti-inflammatory and analgesic action. The paper uses the organoleptic, physical, chemical, pharmaceutical and technological, graphical and statistical research methods that enable assess the quality of the developed drug objectively.

Results and discussion. The technological properties of substances were studied and rheogoniometry with the aim to find the rational basis for the new gel was conducted and the choice of gelling agent and neutralizing agent and their concentration was proved and the indices of quality of the developed drug were defined.

Conclusions. The composition of anti-inflammatory and analgesic action gel was theoretically proved. The technology of production of the gel was developed. The set of experimental studies was conducted and retention samples of the gel were put up in order to study its stability and its period of validity.

RESEARCH STUDY RESIDUAL MOISTURE IMPACT ON DEVELOPMENT FLOWING MIXTURE IN CAPSULES "API-IMMUNO-VIT"

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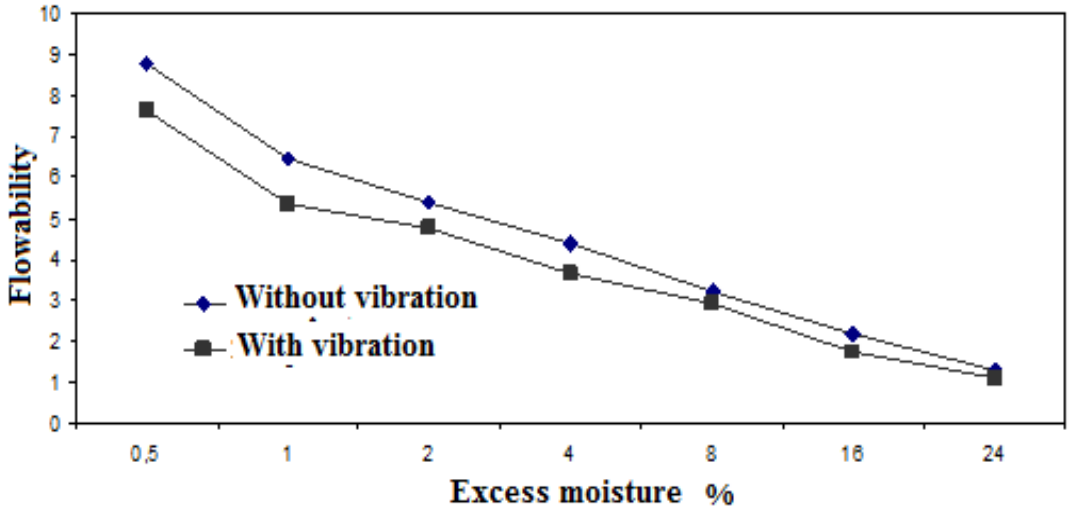
Introduction. Development efficient production technologies capsules "Api-Immuno-Vit" and the definition of residual moisture to flow mixtures of active substances with adjuvants.

The aim of the study. Due to the physical, physicochemical and pharmacological properties of individual action technological substances that are part of the drug "Api-Immuno-Vit" was necessary to study the effect of residual moisture on the flow mixes in the development of this drug.

Materials and methods. We were prepared mixture model chosen composition with different relative humidity and fractional composition granules and then studied the effect of residual moisture and fractional composition of granulate mixtures for technical performance and quality investigated capsules.

The obtained results. Analysis of experimental data regarding the impact of residual moisture to flow mixtures for filling capsules showed that an increase in residual moisture of the granulate mixtures flow decreases. Especially pronounced decrease the flow rate granulate mixtures with a moisture content of 1.5%, which can affect the quality capsules.



Conclusions. Thus, analyzing the results of the study expedient to conclude that in the preparation of the drug "Api-Immuno-Vit" is necessary to prevent increase in residual moisture.

DEVELOPMENT OF COMPOSITION OF HYGIENE PRODUCTS FOR DRY SKIN

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Introduction. Features of hygienic care of dry skin is a gentle cleansing and moisturizing, carried out through the use of soft hygiene products that do not contain anionic surfactants, and also have properties to soften the skin and supply the missing lyophobic components to water-lipid mantle of the skin. As dry skin is sensitive, prone to micro traumas, its owners frequently use diphase tonic to remove makeup. Market analysis of hygiene products in Ukraine showed the absence of the domestic diphase hygiene products, while imported products are represented in a wide range in pharmacies and stores.

Aim. The aim of the work is the development of the diphase cosmetic hygiene product for the care of face and neck dry skin.

Materials and methods. There were used methods of systematic, structured, logical analysis, method of data summarizing. The method of percolation was used, physical and chemical,technological properties of silicone fluids were studied. To obtain the silicone extract the maceration method and medicinal plants that meets the SPU requirements – chamomile flowers, calendula flowers, sage leaves – were used. The composition of the extract obtained was confirmed by thin layer chromatography.

Results and discussion. As dry skin features a high reactivity and sensitivity to aggressive environmental factors, the chamomile, calendula and sage extracts were introduced in tonic. The active pharmaceutical ingredients of these plants (essential oils, coumarin, phytosterol, apigenin, carotenoids, etc.) have anti-inflammatory and weak antiseptic properties and are traditionally used in folk and official dermatological practice. The extract of medicinal plants was obtained by maceration at 42 °; the ratio of raw material-extractant was (1:10); the used extractant was cyclopentasiloxane DC 245. The specified silicone fluid is able to extract lyophobic biologically active substances and improves consumer properties of hygiene product. The tonic aqueous phase is isotonic sodium chloride solution. The oil phase stabilizer is polysorbate monooleate (tween-80), that also has antiseptic and soothing effect on the skin. All concentrations were determined on the basis of literature analysis.

Conclusions. Composition of diphase tonic based on silicone extract of medicinal plants is processed. The remedy is recommended for hygienic care of face and neck dry skin.

DEVELOPMENT OF DERMATOLOGICAL OINTMENT'S TECHNOLOGY FOR THE TREATMENT OF ALLERGIC DERMATITIS COMPLICATED WITH FUNGAL INFECTION

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Introduction. Allergic skin diseases are widely prevalent disorders in the world and in the last decade have attracted increasing attention of doctors. In Ukraine, on all kinds of allergic dermatitis suffers 40 % of adults and children.

Today at the pharmaceutical market of Ukraine there are many industrial produced ointments for the treatment of allergic dermatitis complicated with fungal infection with different compositions and mechanisms of action. Preferably, these medicines are mono-medicines based on synthetic substances. As for the extemporaneous ointments, the most of them are represented by medicines with relatively narrow focus of pharmacological action that is why diversification of extemporaneous medicines is important by creating a new combined soft dosage form with integrated antiallergic and antifungal action.

The aim of our work was to develop extemporaneous ointment for the treatment of allergic dermatitis complicated with fungal infection.

Materials and methods. After examining the pharmacological properties of medicinal plants and synthetic substances used for the treatment of allergic dermatitis complicated with fungal infection, as active ingredients for extemporaneous ointment for the treatment of this disease, we have chosen dry extract of licorice root, essential oil of lavender and terbinafine hydrochloride.

Considering all experimental data, physical and chemical properties of active substances, namely their solubility (dry extract of licorice root injected into the ointment as an aqueous solution, essential oil of lavender as an oil solution in corn oil and terbinafine hydrochloride as a solution in propylene glycol), we have conducted research on the development of rational technology of extemporaneous ointment.

Results and discussion. The ointment obtained by the developed technology has uniform consistency with a specific pleasant smell, light-brown color. Study of colloidal and thermal stability proved the stability of proposed system.

Also, we conducted study of developed medicine's stability during storage. Designed ointment retains its properties during 5 months at two storage temperatures.

Conclusions. Thus, on the basis of the research we have developed technology of extemporaneous ointment for the treatment of allergic dermatitis complicated with fungal infection.

THE CHOICE OF ACTIVE SUBSTANCES FOR DEVELOPMENT OF COMBINED PESSARIES FOR GENITAL HERPES THERAPY

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Introduction: Recently, in connection with the increase of the number of diseases of genital herpes (GH), there is a need to create new combined drugs for local treatment of GH.

The aim of the study is to select the composition and the optimal ratio of the active substances to create and obtain combined pessaries for GH therapy, due to its different mechanisms of action.

Materials and methods: To develop the composition, physical, chemical and technological methods were used during the research, as well as mathematical methods of statistical processing to evaluate and analyze the data.

One of the most widely recognized active substances for the treatment of the herpes virus is acyclovir. Drugs based on acyclovir or its derivatives occupy a leading place due to its studied pharmacological action in the pharmaceuticalmarket and in clinical practice. Therefore, in experimental studies we used acyclovir substance as an active pharmaceutical ingredient (API) for pessaries, which completely meets the regulatory requirements of SPhU 2.0. Recently, various essential oils are widely usedin developing of various combined dosage forms.

The combination in one dosage form both substance of synthetic origin and essential oils gives the following advantages: the possibility of reducing the dose of each of the ingredients in comparing to their standard dosage within the monotherapy to achieve an equivalent effect (increasing the safety of treatment); the possibility of expanding the therapeutic spectrum and indications for use in comparison with monotherapy.

During the development, we chose the most optimal concentrations of essential oils of tea tree and thyme, which have antiviral, anti-inflammatory, immunomodulating action, and show the most pronounced activity with GH. Optimum basis in connection with the biomedical indicators of this disease for the developed drug form was selected Witepsol. The conducted studies on antiherpetic activity prove that the developed pessaries effectively inhibit the reproduction of the second type of herpes virus. Additional studies have shown that essential oils in pessaries contain antibacterial action of a wide spectrum.

Conclusion: Based on the studies carried out, a compound for combined pessaries for the treatment of genital herpes was developed.

RESEARCH OF TECHNOLOGY FOR OBTAINING OIL EXTRACTS

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Introduction. Today is an acute issue of expanding the range of domestic medicines based on raw materials of plant origin by many advantages.

Aim. Development of technologies for oil extracts from medicinal plants celery (Apium graveolens L.) and parsnip (Pastinaca sativa L.).

Materials and methods. Analysis of the literature, organoleptic analysis of the sample of oil extracts, thin-layer chromatography.

Results and discussion. Oil extracts are widely distributed in the range of medicines past centuries. Although in most cases the rational use of polar extractant as alcohol (which eliminates the need for addition of antiseptics and preservatives), but if necessary, to conduct extraction of lipophilic substances such as chlorophyll or carotenoids, it is better to use vegetable oil.

The objects were used by us in subsequent studies were fragrant herb celery (Apium graveolens L.) and parsnip (Pastinaca sativa L.).

An analysis of published data we know that the grass celery contains such biologically active substances such as asparagine, tyrosine, nicotinic acid, chlorophyll, essential oils, B vitamins, vitamins C and E, carotenoids, and Pasternak - furocoumarins, flavonoids, chlorophylls.

Therefore, medicinal herbs contain both hydrophilic and lipophilic substances. Through the selection of extractant can vary the content of various substances in the extract. Where necessary to get from raw whole range of substances the raw can moisten by alcohol before extraction.

For oil extracts and further research, we chose corn oil, which has established itself as emollients with relatively high extractive capability.

After oil organoleptic analysis of the extracts we were determined all samples were a homogeneous liquid oil with a specific smell, green. However, samples of previous wetting ethanol had a rich green color, indicating a more complete extraction of chlorophyll.

Qualitative composition was determined by thin-layer chromatography.

Solvent system hexane – isopropyl alcohol – water solution of sodium carbonate in the ratio 50: 5: 0.25 used for chlorophyll and carotenoids.

A result of conducting of thin-layer chromatography spots of chlorophylls, carotenoids and feofityn were found.

Conclusions. Based on the results of the studies we found that the oil extractants advisable to use if necessary to get lipophilic substances from medicinal plants.

THE SELECTION OF METHOD OF INCLUSION OF DRY CALENDULA EXTRACT INTO A SOFT DOSAGE FORM FOR PSORIASIS TREATMENT

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Introduction. Soft dosage forms are widely used in psoriasis treatment. During ointment application maceration occurs, which helps penetration of active pharmaceutical ingredients into derma. Therapeutic effect from application of soft dosage forms directly depends on the kind of the basis, their components and the methods of inclusion of active substance into them.

Aim. Selection of method of inclusion of dry calendula extract. Study of its solubility in water, after jojoba oil, hydrophilic non-aqueous solvents.

Materials. As the study subject the following materials were used: jojoba oil, dry calendula extract, glycerin, propylene glycol, PEO-400, water, 96% alcohol.

Methods. The solubility research was conducted in accordance to GPU 2nd ed. and with use of microscopic method. The results of the research show that calendula extract is practically insoluble in the researched solvents.

Results. Solubility according to National Pharmacopoeia of Ukraine shows that calendula extract is practically insoluble in all samples of solvent. According to the results of microscopic analysis it was established that addition of purified water to the extract causes significant size decrease of the particles (up to 0.1 micrometres) with uniform distribution across all the field of view. Addition of alcohol, propylene glycol, PEO-400 or glycerin to the extract caused no change in linear size and form, however full moisturisation of powder particles was observed. The sample of the extract with jojoba oil showed that moisturisation of particles by edge type was caused along with decrease of size and form.

Conclusion. From the results of the research it can be concluded that the most optimal option in manufacturing of soft dosage forms of dry calendula extract is using jojoba oil as a supplement.

THE DEVELOPMENT OF SUPPOSITORY FORMULATION WITH ANTI-INFLAMMATORY ACTION ON THE BASIS OF *SAMBUCUS NIGRA* EXTRACT

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Introduction. Prostatitis is the most common urological disease in men in the age of 20-50 years. A great danger of prostatitis is that it could lead to sexual function disturbances and new growth processes in the testicles of male germ cells, so to infertility. Among medicinal preparations of this group the drugs based on natural components as well as synthetic, and combinations thereof are used. However, in Ukraine, most of these drugs are foreign-made, which in most cases are more expensive than domestic ones. Hence, we suggest that the development of new effective domestic preparations for local treatment of prostate diseases is an important task of modern pharmaceutical technology.

The aim of the study is to choose the composition and to develop the technology of suppositories for the treatment of prostate diseases.

Materials and Methods. The subjects of the study were the dry extract of medicinal plant (*Sambucus nigra*), the technological features of suppositories containing dry extract, auxiliary substances and formulation of the dosage form suppositories by using them.

Results. The studies on developing optimal composition and manufacturing technology of rectal suppositories for the treatment of urological diseases (prostatitis) have been carried out. An effective action of drug substances in suppositories depends on many factors, but one of the most important – is optimally selected suppository base. As optimal suppository base the polyethylene oxide (PEO) with a ratio of PEO-1500 to PEO-400 as 70:30 was chosen. The study of osmotic activity of suppository mass revealed that it has sufficient osmotic properties to reduce inflammation, inherent in urological diseases. Determination of the dependence of structural and mechanical properties of suppository mass and base on the temperature allowed to select optimal temperature regime of manufacturing process for the suppositories.

Conclusions. On the basis of conducted studies, the optimal composition and manufacturing technology of rectal suppositories containing *Sambucus nigra* extract have been developed.

ELABORATION OF TECHNOLOGY OF EXTEMPORAL SUSPENSIONS AND EMULSIONS

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Introduction. The interest in personal medicine recent years is growing. Modern pharmacies in Ukraine many medicines by prescriptions are doing.

Aim. Analyze of the number and content of prescriptions in pharmacies had to make. By type of dosage forms of the medicines should be classified.

Materials and methods. Take of prescriptions in pharmacies and classification by the types of dosage forms.

Results and discussion. This analysis revealed a large number of prescriptions for suspensions and emulsions that contain components with different properties. Suspensions are the dosage forms that make it possible to include insoluble medicines. This achieved firstly by careful grinding of dry ingredients and subsequent dispersion with a small portion of the solvent.

Dispersing the drug with the solvent makes, it possible significantly increase the dispersion of ingredients and thus makes it possible to improve their therapeutic activity. When we were preparing the suspension, we used Deryagin rule. The results of our biopharmaceutical research confirmed the effectiveness of this method.

Emulsions are mixtures of two immiscible liquids, but add emulsifier uniformity of their distribution in each other makes it possible. The combination of polar and non-polar solvent enables the introduction into the emulsion composition ingredients with different solubility. The hydrophilic substances recommended dissolved in polar solvent and the hydrophobic substances dissolve in non-polar solvents. It known that dissolved medicines have higher bioavailability than non-dissolved state.

Thus, the emulsion is multifaceted and promising dosage form, comprising a combination of components with different solubility. In developing emulsion technology, we chose the best emulsifier, which would ensure the stability of the product during the period of its use.

Conclusions. Our studies allow us to recommend optimal technology for certain suspension and the best emulsifier for certain emulsion. Using the proposed technological methods and excipients will provide stable and high-quality liquid medicines.

ANALYSIS THE RANGE OF EMULSIFIERS FOR TECHNOLOGY OF COSMETIC SOFT MEDICAL FORMS

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Introduction. Nowadays emulsion ointments and cosmetic creams are the most common in the pharmaceutical and cosmetic markets due to their high efficiency. Emulsion system is thermodynamically unstable. To improve the stability of the soft emulsion tools used emulsifiers.

Aim. To analyze of emulsifiers for preparing cosmetic soft drugs.

Materials and Methods. Emulsifiers – surface-active agents that promote the formation of emulsions. They must meet the following requirements to ensure formation of a stable emulsion; be chemically indifferent; not detect toxic action, including not irritate the skin; have no odor. Emulsifiers are as follows: they are concentrated on the border of the liquid phase, creating a protective layer and reduce interfacial tension. In the emulsifier molecules containing hydrophilic and lipophilic poles that allow the molecule to attract both phases simultaneously. Physical manifestations of aggregate instability of emulsions can be avoided by stabilizing systems using surfactants of different nature and concentration. The dispersion medium is the phase in which the emulsifier is mostly dissolved.

The **results**. Depending on skin type emulsifiers are classified: a) an emulsifier for oily skin: sucrose stearate; b) for sensitive skin: sodium alginate, stearic acid; c) for dry skin: guar gum, beeswax.

Lecithin - a natural emulsifier, which is very beneficial for the skin. Lanolin – a wax of animal origin, derived from sheep's wool. The most common base or emulsifier – Glyceryl monostearate used for the production of ointments and creams has antiviral effect. Lamekrem – a natural emulsifier, which bind moisture and create a pleasant sensation on the skin. Ksilians – wheat emulsifier, provides good texture tools wash, creams because it does not separate. These cosmetics are stored for a long time and do not change their consistency on for the duration of use.

Polavaks (wax emulsion) – perfectly moisturizes and softens skin, long retaining the original look of the cream. Sucrose stearate – a natural emulsifier, which has moisturizing and antimicrobial properties. Beeswax emulsion system adds softening and anti-inflammatory properties.

Conclusion. Based on the analysis proved that the modern pharmaceutical market a wide range of emulsifiers that meet the requirements and needs of the modern pharmaceutical and cosmetic industries.

DEVELOPMENT OF HERBAL VAGINAL GEL FORMULATION AND TECHNOLOGY

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Introduction. The herbal vaginal gel extracted from herbal material can be used to treat bacterial vaginosis, vaginal dryness caused by yeast infection and/or in women with experiencing post-menopausal stage.

This medicine of local action will quick up the treatment and because it possesses plant material, this is an advantage on the therapeutic effect.

The composition of herbal vaginal gel was formulated at Industrial Phamacy department. The research work was supervised by Associate Professor Mansky A.A. and Associate Professor Sichkar A.A.

Aim. The aim is to successfully formulate a gel that will have optimal healing properties for bacterial vaginosis infections.

Materials and methods. Tea tree oil (melaleuca alternifolia), sage oil (salvia officinalis), calendula oil (calendula officinalis).

Results and discussion. Among the medicinal plant material that we will use to make the gel for vaginal vaginosis are sage, tea tree oil and calendula. Pot marigold or C. officinalis, calendula comes from the latin word calendae ‘’little calendar’’. It is from the asteraceae family with genus of 15 to 20 species traced way back to ancient Egypt to have rejuvinating properties. It has great anti-inflammatory action, inflamed and itchy skin conditions.

Bacterial vaginosis main side effect is unpleasant fish - like vaginal odor, discharge when present sometimes appears white or grey and thin in appearance. Tea tree oil because of its antimicrobal and antifungal effects will help in the treatment by selective control of pathogenic microflora enclosing Candida albicans infections.

Sage or salvia from the Lamiaceae family expresses or promotes the toxin elimination hence natural way of body’s purification used several thousands years ago.

The choice of the gel agent to create a stable gel system with a complex of herbal oils have been theoretically substantiated and experimentally confirmed. Composition and rational technology of the gel with a complex of essential oils have been designed.

Conclusions. The medicinal plants substances used in the creation of vaginal gel for the treatment of bacterial vaginosis are tea tree, sage and calendula oils. The action of these three herbal oils may bring mucosal restoration, soothing and protective properties.

THE RELEVANCE OF DRUG DEVELOPEMENT OF SUSTAINED RELEASE CAPSULES WITH SIMVASTATIN

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Introduction. Simvastatin is used to control hypercholesterolemia. Simvastatin is derived from a synthetic modification of a fermentation product of Aspergillus terreus. Simvastatin contain a lactone ring within their structure. Simvastatin is a prodrug that is administered in its inactive lactone form and converted in the body to an active beta-hydroxy acid metabolite. The mechanism of action for simvastatin is competitive, reversible inhibition of HMG CoA reductase, the rate-limiting enzyme in cholesterol synthesis. Simvastatin is administered orally for the treatment of two hypercholesterolemia. Doses of simvastatin used to treat hypercholesterolemia are 5, 10, 20, and 40 or 80 mg/day. Initial effects occur within 1–2 weeks, with the maximal effect noted within 4–6 weeks. The major adverse effects associated with simvastatin, as well as with other statins, are an increased risk of myalgia and rhabdomyolysis. The relevance of development of sustained release capsules with simvastatin was formulated and the research work was supervised by Associate Professor Sichkar A.A. (Industrial Phamacy department).

Aim. The relevance of drugs development of sustained release capsules filled with simvastatin pellets. Simvastatin capsules are to use together with a proper diet to treat high cholesterol and triglyceride (fat) levels in the blood. This medicine may help prevent medical problems such as heart attacks, strokes caused by clogged vessels and to reduce the amount of cholesterol in the blood by blocking an enzyme that is needed to make cholesterol.

Materials and methods. It was used comparative, systematic, and logical analysis of data generalization in this work.

Results and discussion. There are several classes of antihyperlipidemic agents. They may differ in both their adverse effects and impact on the cholesterol profile. The prevalence of hypercholesterolemia and other forms of dyslipidemia and the risks associated with atherosclerosis and coronary heart disease determine the relevance of the search and creation of new oral lipid-lowering drugs. Nevertheless, for a majorety of drugs, there are significant limitations in the use, because of the risk of side effects. Sustained drug delivery technology is a practically promising way to enhance the therapeutic efficacy of drugs.

Conclusions. The results of data generalization and frequency of mentioned diseases present of the necessity of the new medicines development using simvastatin with lesser side effects.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF THE EXTEMPORANEOUS OINTMENT FOR TREATING URTICARIA

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Urticaria is the common name for the group of diseases. Its main clinical symptom is transient itchy wheals of various sizes, which are clearly structured and formed above the surface of the skin. Cold-induced urticaria is one of its types. The range of drugs of domestic and foreign production for treating dermatitis, namely urticaria, has been studied. The results have shown that there is a very small range of drugs to treat urticaria.

The aim of our work is to develop the composition and technology of the extemporaneous combined ointment for the treatment of cold-induced urticaria. Extemporaneous compounding of medicines makes possible an individual approach to a patient, which takes into account the peculiarities of the organism, the course of the disease, the symptoms of the disease and its stage. This is the main principle and advantage for preparing drugs in pharmacies.

Based on the literature and consultations with dermatologists of Kharkiv the formulation for the treatment of cold-induced urticaria has been selected. It is expedient to include the following active pharmaceutical ingredients (APIs) to the formulation: loratadine, lidocaine hydrochloride, methyluracil, salicylic acid and zinc oxide, which meet the requirements of the SPhU. The methods for testing the ointment are listed in the SPhU "Soft dosage forms". As a base for the ointment the emulsion base was used.

According to the studies conducted the technology of the ointment in pharmacies has been developed. The shelf life of ointments prepared *ex tempore* is 10 days; however, it does not correspond to the period of symptomatic therapy of cold-induced urticaria since its treatment can last up to one month. Therefore, extemporaneous compounding of the ointment has been conducted according to the requirements of Good Pharmacy Practice, which includes appropriate preparation of premises, APIs and excipients. The flowchart for preparing the ointment for the treatment of cold-induced urticaria has been developed. The study of organoleptic indicators of the samples of the combined ointment has been conducted. The stability of the ointment samples obtained by the direct inoculation method has been studied. Based on the results of the microbiological studies it has been found that the ointment samples are stable for 30 days, it allows defining the shelf life of 30 days.

DESIGNING OF A DAILY SUNSCREEN ON THE BASIS OF SNAIL`S SECRETION (MUCUS) ACHATINA FULICA AND WALNUT OIL

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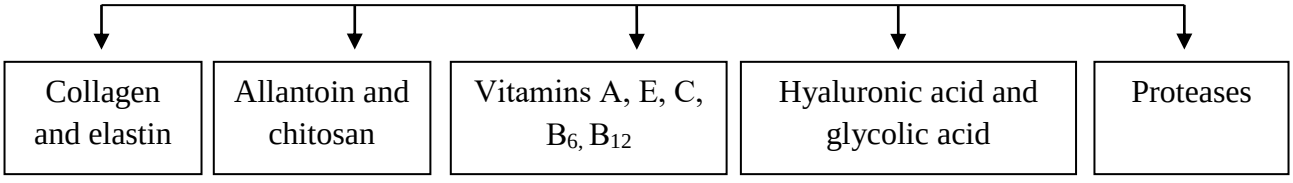
Introduction. A modern person is increasingly becoming a fan of a healthy lifestyle paying attention to appearance, the health of skin and hair. The skin condition reflects the general physiological condition of the body, so promising is the use of cosmetic products that provide optimal protection from harmful ultraviolet rays. New ingredients based on vitamins, herbs, animal products are used in cosmetology every year. Innovative technologies make possible to improve the formulation and improve the appearance of cosmetics. Excessive ultraviolet radiation is harmful to our skin, it leads to premature photo aging, unwanted pigmentation (freckles), dryness, and severe burn.

Aim. The aim of our work (which is a continuation of the research work of department Technology of Biologically Active Substances, Pharmacy and Biotechnology about creating drugs from natural raw materials) is the designing of a daily sunscreen based on snail’s secretion (mucus) *Achatina fulica* and walnut oil.

Materials and methods. The secretion of snail`s slime contains mucin, which protects the skin from ultraviolet radiation, slows down aging, reduces wrinkles, evens relief, accelerates healing, improves skin conditions with rosacea and dermatitis. Mucus of shellfish is rich in vitamin E, which nourishes the skin, giving it moisture and protects against free radicals.

The structure of snail’s slime glands secretion belongs:



This set of ingredients, which is in slime, is very useful for skin and hair, so snails are widely used in cosmetics. Walnut oil contains polyunsaturated fatty acids that have regenerative properties. There are vitamins A, E, C and B. These substances restore, moisturize, nourish, and tonify the skin, make the skin soft and silky. It has the ability to cool and soothe irritated and inflamed skin.

In addition, walnut oil contains minerals and trace elements such as iodine, calcium, iron, phosphorus, cobalt, selenium, magnesium and coenzyme Q10. This useful cell component prevents free radicals and participates in cell regeneration and slows aging.

Through this walnut oil can be used to produce cosmetics for any skin type.

We have developed recipes of daily sunscreen for skincare containing snail's slime extract, lanolin, beeswax, vitamin E, walnut oil and peach butter. During our work, we use the snails of Ahatina fulica's genus which we grow at home and provide proper care, feed them zucchini, cucumbers, pumpkins, apples, carrots and spinach. We grow these snails at home and provide them proper care. There are zucchini, cucumbers, pumpkins, apples, spinach and carrot in its diet. For their supply we also use any dry food for aquarium fish. Locations to give eggshell chalk and food, which are a source of calcium, which require extremely *Ahatina fulica.*

For receiving secretion, snails were subjected to physical effects (rotation and shaking) in the laboratory under the strict control. It makes snails' glands vigorously excreting secretion. Emanating secretion was taken away with the help of a large amount of water, filtered and passed through the centrifuge for purification of various contaminants. This process does not cause any harm to snails and does not affect the therapeutic properties of secretions.

The resulting extract was used to create daily sunscreen for skin care.

Purified water was added to the extract of snail's slime. The received result was constantly emulsify with lanolin and wax. Walnut oil, peach oil, vitamin E was added to the melted wax.

Results and discussion. As shown by laboratory studies with the cream component composition protects the skin from ultraviolet radiation, restores skin elasticity.

Conclusions. We are continuing to learn the physical - chemical and microbiological properties of this daily sunscreen; its further cosmetic investigations are scheduled.

REASONING OF CREATING OF NASAL GEL ON A NATURAL MATERIAL

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Relevance: Rhinosinusitis is a bacterial or viral infection, which is accompanied by inflammation of the mucous membrane of the cavity and paranasal sinuses. Despite the large assortment of medicines of industrial production, it is important to development extemporal drugs, because they have several advantages: providing an individual approach to the treatment of patients, the absence of preservatives and stabilizers in theirs composition, accessibility of low cost.

Aim: To analyze the assortment of medicines for the treatment of acute rhinosinusitis. Development of a nasal gel based on natural origin raw materials for the treatment of acute rhinosinusitis.

Results and its discussion. When we analyzing the pharmaceutical market in Ukraine, we was found that the medicine for the treatment of acute rhinitis are classified as ATC-classifier for: sympathomimetics simple drugs (36.2%), sympathomimetics in combination with other substances (except corticosteroids) (13.3%), combined medicines (10.5%), other medicines for the treatment of diseases of the nasal cavity. Among the range of medicines in the form is predominate drops and spray. Soft drugs (in the form of nasal ointment and gel) occupy only 4% of the market. This indicates an little assortment of herbal medicines.

To develop a new extemporal drug we chose nasal gel form , since the gel has a more prolonged action, has a moisturizing effect, thus reducing the likelihood of dryness of the nasal mucosa. As active substance it was used an aloe extract which has antiseptic, antimicrobial effect, increases trophic and tissue regeneration.

As a gelling agent was chosen a carbopol of grade 934 P, which minimum amount of residual solvents and is intended for applications to the mucous membranes. Systems with the necessary viscosity were formed by neutralization of carbopol with trometamol, which, unlike other amino derivatives, is a non-toxic substance. So the selected composition will provide a wide range of pharmacological activity of the developed gel with minimal side effects, which will allow it to be effectively used in the treatment of acute rhinosinusitis, including for children.

Conclusions. It was selected the composition of the extemporal gel, which will make it possible to use for the effective treatment of acute rhinosinusitis.

RELEVANCE OF THERAPEUTIC SHAMPOO COMPOSITION DEVELOPMENT

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Introduction. Analyzing the range of therapeutic and prophylactic shampoos represented in the pharmaceutical market of Ukraine, it was found that from numerous assortment of shampoos, which are available on the shelves of pharmacies only shampoos of line "Fitoval" are classified as medicinal shampoos containing extracts from herbal drugs and included the State Register of medicines. VRM possesses invaluable resources and on its basis many highly efficient drugs have been developed, and its potential is inexhaustible. Since ancient times, decoctions of medicinal plants are considered healers in matters of hair and scalp treatment. A shampoo should have good cleaning properties and in doing so should be soft, harmless to health. This means that a number of detergents must be chosen very carefully. Modern foamy basis is preferably to thicken with natural or semi-synthetic thickeners (xanthan, guar gums, cellulose derivatives, etc.), and the addition of electrolytes that can overdry skin should be avoided.

Aim of the study. Therefore, the aim of our work was to develop therapeutic shampoo containing plant extracts for the treatment of seborrheic dermatitis.

Materials and methods. To develop a soft foamy shampoo bases the following substances were used: Polyquaternium 7, Hydromoist O, CTAC 30 KC, Dynagen, Stearic acid, Gluadin, WQ Vipirox Piroctone olamine, Lamesoft Care, Betaine, AHA extract 44, ProtectagenLosmalol AES 70-2 -24, Nutrilan I 50 BP Keravis PE-LQ-(WD), Cocamidopropyl betaine 30 HI, Zetesol 270 / N. The quality of model shampoo samples evaluated according to State Standard 4315: 2004 "Cosmetics for cleaning the skin and hair."

Results of the study. Shampoo samples were studied on such quality indicators as organoleptic properties, pH, kinematic viscosity, foam value and dry residue. Determination of pH was carried out preparing a 10% solution of the shampoo, foaming property - 3% solution of the shampoo. As a result it was found that the shampoo has foam number of 175 mm, foam stability - is within acceptable limits and is 0.8-1.0 units. pH - 5,5 ± 1,0. The data obtained have shown stability of therapeutic shampoo on physical and chemical parameters.

Conclusions. Research has been carried and the shampoo composition has been offered that meets the requirements of State Standard 4315: 2004 "Cosmetic for cleaning the skin and hair."

STUDY OF THE ABSORPTION OF PUMPKIN OIL BY EXCIPIENTS

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Introduction. The use of vegetable raw materials in pharmaceutical industry allows expansion of assortment of drugs through creation of new effective drugs with minimal side effects. Drugs based on extracts are inconvenient in use and have unsatisfactory consumer properties. Thus, the actual task in farmacy is development of composition and technology of drugs that have satisfactory consumer properties.

Aim. Research of the absorption of pumpkin oil by excipients used in manufacturing.

Materials. Pumpkin oil, microcrystalline cellulose (MCC) 102, 103, 302, Neusilin, β-cyclodextrin, Cellect and granule samples were used as research objects.

Methods. For selection of excipients physico-chemical and technological research methods were used.

Results. Absorbing capacity was studied by the rate of oil's penetration of excipients layer, by mass fraction and depth of oil's penetration into the layer of absorbent. The achieved results show that by mass fraction of absorbed oil MCC 102, Neusilin and MCC 302 have the best indicators (69.49%, 68.21%, 64.05% respectively). The biggest depth of layer penetration of oil goes to MCC 102 (5.0 cm), Cellect (4.8 cm) and Neusilin (4.7 cm). The best indicators of oil's penetration rate go to MCC 102 (1.4 cm/min), Neusilin (1.1 cm/min), β-cyclodextrin (0.9 cm/min). During the course of the work sample granules containing these supplementary substances and pumpkin oil were acquired, which had organoleptic properties. Sample granules with Neusilin had solid white texture with oil being not prominent. Sample granules with MCC 102 and Cellect were not matching organoleptic properties as the acquired granules did not have solid mass, had leaking oil and stuck in perforated plate's openings.

Conclusions. The acquired results of the research show that MCC 102 (69.49%) and Neusilin (68.21%) have the best absorbing capability. Sample granules based on them exhibited different organoleptic capabilities. The most satisfactory results were shown by the tableting mass based on Neusilin. It can be concluded that the optimal option in manufacturing of solid dosage forms with inclusion of pumpkin oil is the usage of Neusilin as the excipient.

DEVELOPMENT OF OBTAINING TECHNOLOGY FOR DENSE EXTRACT OF CARDIOLYTIC ACTION AND TABLETS ON ITS BASE

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Introduction. Cardiovascular diseases occupy the first place among the most widespread and dangerous diseases of our time. There are many reasons for this, but the genetic predisposition and wrong way of life are considered basic. One of the most acute problems of modern health is myocardial infarction, and its incidence curve is steadily creeping up. Despite all the achievements of world medicine in this field, so far mortality from myocardial infarction ranks first in all economically different countries, including Ukraine, 2-3 times exceeding the death rate from cancer.

As a result of the analysis of the pharmaceutical market in Ukraine, the following were selected as research subjects: hawthorn fruits, the therapeutic effect of which is to increase myocardial tone, slightly increase cardiac muscle contractions, reduce myocardial excitability, eliminate vascular spasms, and enhance blood circulation in the vessels of the heart and brain.

Herb of Leonurus – regulates the functional state of the central nervous system, has a calming effect, reduces the increased nervous excitability. Melissa herb – indications for the use of Melissa herb remedies are: neuroses, mild form of hypertension, mild forms of coronary heart disease, tachyarrhythmias.

Hop cones have a calming, spasmolytic, analgesic and anti-inflammatory effect.

Aim of the study. Substantiation of technology for obtaining a thick extract and tablet mass with its content.

Materials and methods. To achieve the goal, physico-chemical and pharmaco-technological methods of analysis have been used.

Obtained results. The first stage of our studies on the way to obtaining a complex thick extract was the choice of the extractant, which would extract the BAS from the VRM as much as possible. The extracting activity of water-alcohol solutions of different concentrations was investigated. The criterion for evaluating the extracting activity was the amount of extracted extractives.

As a result of the research, it was found that 70% ethanol extracts the

maximum amount of extractives for all types of plant material.

The preparation of a thick extract initially involves obtaining a liquid extract and its further evaporation. To obtain liquid extraction, we have chosen the percolation method as the most rational and widely used in pharmaceutical industry. To substantiate the extraction rate, we studied the dynamics of the extraction of individual plant raw materials and at combined extraction of a mixture of VRM.

To obtain tablets containing a complex thick extract, model compositions of tablets were produced. For the preparation of tablets, lactose was used as a filler, sodium croscarmellose (disintegrant), microcrystalline cellulose (binder), talc and magnesium stearate (antifriction substances).

The tablets were prepared by wet granulation. As humidifier, alcohol 70%, 3% aqueous and alcohol solution of PLASDONE 25K were used. The complex thick extract was added to the bulk solids, previously dissolved in the humectant solution. Tablet masses were subjected to the study of pharmaco-technological properties.

Quality indicators for tablets were determined according to the requirements of the State Pharmacopoeia of Ukraine for such indicators: description, average tablet weight, crush resistance, friability, disintegration time.

Conclusions. The technology of a thick extract obtaining has been substantiated and the composition of tablets with its content has been developed.

STUDY OF THE RHEOLOGICAL PROPERTIES OF THE VAGINAL GEL WITH HYALURONIC ACID

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Introduction. Currently, the use of hyaluronic acid is becoming increasingly popular in the treatment of various diseases. Due to highly moisturizing, anti-inflammatory and reparative actions using of hyaluronic acid is justified in the treatment of urogenital smptoms during the menopause. This period is accompanied by changes in the urogenital system of the woman. At this time noted: frequent inflammatory diseases of genital organs; painful and frequent urination, vagina itching and dryness, itching of external genitals. Also, the use of hyaluronic acid is possible during preparing the cervix for childbirth in gestation period. We are developing a vaginal gel for the treatment of urogenital symptoms during menopause and for softening the cervix in preparation for childbirth.

Aim. The purpose of our study is to study the rheological options of a vaginal gel using various gellants. The studies were carried out using gellants: Carbopol Ultrez, Aristoflex AVC, Seppimax Zen, Sepinov, Methocel, Hydroxyethylcellulose in different concentrations. The rheological options of the samples were determined using the rheostest Myr.

Results and discussion. In the course of the study, samples containing 0.1% hyaluronic acid were used. Comparison of 9 samples with gellants of different concentrations was carried out: Carbopol Ultrez 2%, Aristoflex AVC 1%, Aristoflex AVC 2%, Sepimax Zen 2%, Sepinov 1%, Methocel 2%, Hydroxyethylcellulose 2%, Hydroxyethylcellulose 3%. According to the results of the study, the best rheological options had samples with gellants Aristoflex AVC 1%, Sepinov 1%, Sepimax Zen 2%.

Conclusions. For further research, samples with gellants Aristoflex AVC 1%, Sepinov 1%, Sepimax Zen 2% were chosen.

STUDY OSMOTIC PROPERTIES OF SOFT DRUGS WITH DRY PINE EXTRACT FOR USE IN GYNECOLOGY

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Introduction. Infectious inflammatory diseases of female genital currently occupy first place (55-70%) in the structure of gynecological pathology and is one of the reasons for the disruption of many organs and systems of the female body. The urgency of this problem is due to not only the high frequency of this disease, but severe adverse effect on her sexual and reproductive function of women.

Today the pharmaceutical market of Ukraine a wide range of synthetic drugs for the treatment of this disease, which may make alternative modern herbal. Accordingly, the actual problem is the development of technology and soft drug with anti-inflammatory and antimicrobial activity of dry extract of pine.

Aim. The aim of our work was to investigate osmotic activity modeling samples of ointment bases, followed by the establishment of dependence degree of fluid absorption from the type of foundation.

Materials and methods. The objects of the study were typical model examples of ointments with dry pine extract on hydrophobic, hydrophilic, emulsion type o/w, emulsion type w/o, emulgel and gel bases. Osmotic activity of ointment bases determined by dialysis through a semipermeable membrane. The study was conducted at 37±0,1 ^{0}C.

Results and discussion. Osmotic activity is an important specific parameter that characterizes the properties of soft drug for external use. It is believed that detection of an osmotic activity of the drug anti-inflammatory action promotes dehydration in the area of inflammation, which reduces swelling and speeds up the metabolism in tissues. Based on the medical and biological requirements of drugs that are used in gynecology, the drug should have a moderate osmotic activity and prevent local irritating action.

Study depending osmotic activity of the drug with dry pine extract showed its dependence on the nature of the base. During experimental studies found that osmotic activity of hydrophilic bases twice above than hydrophobic, moderate osmotic activity has emulsion type o/w and emulgel bases.

Conclusions. Based on experimental studies for further analysis we selected emulsion type o/w and emulgel bases for subsequent development on the base of it a soft dosage form with dry extract of pine for the treatment of gynecological diseases.

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Due to statistics in Ukraine there are about 10-14 million persons suffer from sharp respirator viral infections (acute respiratory disease) a year, that is 25-30 % from all morbidity. One of the most widespread diseases in our time is acute respiratory disease or cold.

Acute respiratory disease is the complex of symptoms, which is characterized running nose, by Ringos, sinusitis, pharyngalgia, fever and cough. Acute respiratory disease in most cases arises up because of infection of man respirator viruses, which count more than 200 exciters. One of the most widespread symptoms is a cough.

A cough (tussis) is a reflex act, playing a large role in self-wiping of respiratory tracts both from foreign bodies, gettings from outside and from endogenously appearing products (mucus, blood, pus, products of tissue disintegration).

Studying literary sources and analysing the assortment of medicinal preparations at the market of Ukraine for treatment of acute respiratory disease and cough concluded that now, not enough preparations for treatment of acute respiratory disease and cough for children from 3-meses. In addition, more senior. In our time, the problem of application of effective and safe preparations for treatment of cold for children becomes actual.

Basic advantages of the extemporal compounding is the individual going near every patient and absence of conservants, emulgators, stabilizators and other harmful compounds in composition preparation. The amount of pharmacies, engaged in preparation of extemporal of medications, diminishes with every year. To date in Ukraine the problem of maintainance and improvement of production pharmacies costs sharply.

Conducting the analysis of samples of writing in a pharmacy № 9, Kharkov has shown that today children have not enough medicinal preparations for treatment cold diseases and cough by age from 3 months and more senior, as an amount of children with a chronic cough in the last few years from data of literature considerably has increased from 10 to 38 %.

The purpose of our work is development of composition and technology of child's syrup for treatment of cold diseases on the basis of digester. In spite of considerable progress of modern organic chemistry, that provides the production of high-quality synthetic bioactive matters, which are used in pharmacy, popularity of

vegetable preparations in the whole world not only does not fall but also grows steadily.

In the practice application of child's medications from a digester is inalienable part of pharmacotherapy. The assortment of LP for treatment of diseases of breathing organs for children is presented by preparations of synthetic and vegetable origin

Most often in the complement of preparations paracetamol enters for cough treatment and acute respiratory disease. Paracetamol is medication, analgesic and febrifuge from the group of anilids, renders a febrifuge action. It is wide-spread central nonnarcotic analgesics, possesses enough weak anti inflammatory properties (and does not have the side effects characteristic for NPVP related to them)

The mechanism of action and type of safety of paracetamol is well studied, his efficiency is clinically approved, in this connection this preparation is included in the list of major medications of Worldwide organization of health protection (WHO Model List of Essential Medicines, 16th list. WHO (March 2009).

Althaea of root an extract is dry – contains vegetable mucus, pectin matters, asparagine, starch, betaine, which in a complex possess secret motorial, by emollient, mucolytic, bronchiolitis and coughing up actions.

Thyme an extract is liquid - 0,8-1,2 contains % essential oil of thyme , basic components of which are Thymolum and carvacol, cymene and caryophyllene., use as a coughing up and antibacterial mean. An extract is able to strengthen the secretion of bronchial glands, dilute a sputum and accelerate evacuation of products of inflammation and mucous the masses.

And cough syrup which paracetamol and vegetable extracts enters in the complement of is offered: root of althea and thyme liquid. As sweetener it is suggested to use glycerol which possesses a less allergen action and can be recommended for people with saccharine diabetes. A sweetness of Sorbitol is approximately 60 % from the sweetness of saccharide, and calorie content of glycerol in 1,5 time less calorie content of sugar.

So on the basis of the conducted researches there was developed by composition and technology of extemporal syrup for treatment of ORVI and cough for children from 3 months and more senior, which paracetamol and vegetable extracts enters in the complement of: root of althea and thyme liquid. .

DEVELOPMENT OF THE COMBINED MEDICATION COMPOSITION FOR SYMPTOMATIC PSEUDORHEUMATISM TREATMENT

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A pseudorheumatism (RA) is a chronic disease which has an immune inflammatory nature that leads to proof deformations of the staggered joints and their functional ability violation . Treatment of RA consists in application of two types of preparations: anti-inflammatory and basic.

Due to the information of State form of Ukraine seventh edition by medicinal preparations (LP) which influence the locomotory are anti inflammatory : non-steroid locomotorium preparations: (selective and unselective inhibitors of COG–1 and COG–2) but corticosteroids : betametazon, methylprednisolonum, prednizolon.

To base LP belong: cytostatics; biological preparations which influence on a specific albumen; antimalarial preparations; sulfanilamidums and penicilamin.

The purpose of our research is an analysis of assortment of LP and choice of active pharmaceutical ingredients (AFI) for development of complex composition of soft medical form for symptomatic treatment of RA.

A pharmaceutical market of Ukraine industrial production analysis rotined on 1.03.2017, has shown that an assortment for RA treatment is enough various . For RA treatment uses monocomponent (45) and combined (5) medications which have a different medical form: ointments and gels are 45 % from the general amount of preparations, pill, 32 %, solutions for injections – 12 %, supositorio and capsules – 5 %.

Non-steroid anti inflammatory medications which have an anti inflammatory, analgetic and antipyrogenic action enter in the complement of these preparations. Traditional basis of medical therapy is made by Non-steroid anti-inflammatory medications.

Among medical forms which are used for treatment of RA soft LZ are let in on the ground: possibility of achievement of high therapeutic action of ointments and geley due to combined AFI and them rapid freeing; relative simplicity and unconcern in application by comparison to other by medical forms; economy and technologicalness; comfort and local use.

Thus, the conducted researches allowed to choose active pharmaceutical ingredients for development of the combined gel ofextemporal production for symptomatic treatment of pseudorheumatism.

METHOD OF THE DIRECT PRESSING IN THE TECHNOLOGY OF TABLETS "MELTIAZID"

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Introduction. The people are firmly kept, passing from generation to generation, information about the methods of healing various diseases, as well as about medicinal plants. A medicinal plant contains one or several substances that, in the presence of known conditions, can exhibit certain healing properties in the human body and animal. Compared with synthetic drugs, medicinal plants are known to be less toxic. Therefore, in modern pharmacy to create a medicinal product based on medicinal plants is an urgent task. It is known that vegetable raw materials serve as a source of obtaining more than a third of all medicines. Most patients suffering from hypertension, to reduce blood pressure to safe digits, should take at the same time 2-3 types of tablets. A single drug effectively lowers the pressure in no more than 20-30% of patients with hypertension. The remaining 70-80% of patients need combination therapy, ie, several different drugs at the same time. Combined drugs for hypertension – such as those containing 2-3 active substances in a single pill are widely used in medical practice.

Potassium-sparing diuretics have little effect on the level of sodium and fluid in the body, as well as on blood pressure per se. They are not self-important in the treatment of hypertension, but are often used in combination with other diuretics to enhance their action and avoid excessive loss of potassium by the patient's body.

In connection with the foregoing, the question of creating an easy-to-use, standardized combination form of "Methylthiazide", which has sufficient bioavailability and storage stability, became topical.

Aim. The aim of this work was the development of an easy-to-use drug based on medicinal plants. The studies were carried out in the field of tablets production by the method of direct pressing.

Materials and methods. As the subjects of the study, the medicinal substances used were the dry extract "Meliflos" obtained by our recommended technology and dichlorothiazide, which are first proposed for the creation of a combined tablet form for the treatment of hypertension. Dry extract "Meliflos" – is

a dry hygroscopic, finely dispersed powders from red to dark brown with a specific smell. Dichlorothiazide is white or white with a yellowish tinge crystalline powder. Very little soluble in water, little in alcohol, easily in solutions of caustic alkalis. The analysis of the technological characteristics of the dry extract and auxiliary substances was carried out on the instruments of Erweka (Germany), the particle size was assessed by microscopy using the VideoTest program. For the development of tablets, we tested compounds with various compositions of auxiliary substances and their ratios. The main requirements for this group of excipients are storage stability, good compressibility, the ability to quickly and completely release the active substance and form strong tablets. The analysis of the tablets was carried out according to the current regulatory documentation.

Results. obtained by direct compression of the tablet "Melthiazide". Experimental samples of "Methyliazide" tablets were prepared with the addition of auxiliary substances in various ratios and combinations. The composition of the tablets includes auxiliary substances, taking into account the physicochemical and technological characteristics of the substance (dry extract), ensuring sufficient flowability of the tablet mass, its good compressibility and homogeneity of filling the matrix of the tablet press, and hence the uniformity of the distribution of the active substance in the dosage form. Tablets obtained by the method of direct compression did not meet the requirements for tableted dosage forms. Therefore, we decided to use the wet granulation method for tabletting.

Conclusion: Thus, it is not possible to obtain the tablet form of the extract under study by the method of direct compression, as a result of which it was determined to use the wet granulation method and the introduction of auxiliaries into the complex. When choosing auxiliary substances and tabletting by wet granulation, it is necessary to take into account the properties of the kinetics of moisture absorption (hygroscopicity) of the dry extract.

RETURN OF OLEUM TEREBINTHINAE FROM NIHILITY TO PHARMACEUTICAL PRACTICE IN THE FORM OF EMULGEL

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Introduction. The history of application of coniferous trees resin, of which turpentine is now produced, has thousands of years. Currently, purified turpentine as a curative and restoring remedy has found wide application in officinal and folk medicine. The most widely purified turpentine is used in preparations for local administration in sciatica, neuralgia, myositis, rheumatism, gout and other inflammatory diseases, as well as for the preparation of recovery baths. The disadvantage of most topical preparations (ointments and liniments) is their hydrophobic nature, as well as insufficient dispersion of turpentine as a hydrophobic substance in water when preparing baths - on the water surface it is in the form of a film.

Aim of the study was the development of chemist's technology of turpentine emulgel для for its subsequent use in the composition of therapeutic baths, and also as a basic dosage form to obtain complex preparations of this natural remedy, which production will be carried out according to the prescriptions of doctors in pharmacies with a production function, the number of which in Ukraine increases year after year.

Materials and methods. In the work, such materials have been used: turpentine purified (*Oleum Terebinthinae rectificatum*), gelling agents (carbomer 934P and sodium carboxymethylcellulose (Na-CMC)), oleic and stearic acids, 10% solutions of ammonia and sodium hydroxide. As emulsifiers in the work have been used oleates and stearates of ammonium and sodium, obtained during the interaction of the acids and alkalis used. The quality of obtained emulsions and emulgels was evaluated by their thermal and colloidal stability, and also microscopically.

Results and discussion. Due to the fact that the production of stable concentrated turpentine emulsions by a common method of dispersion at heating was complicated because of turpentine volatility, in our study we have used the method of physical-chemical dispersion at room temperature, in the course of which the acid (oleic or stearic) neutralization reaction by alkali (ammonia or sodium hydroxide) occurs simultaneously, the result of which is the formation of salts, which are emulsifiers of emulsions of the o/w type. Preparation of emulsion systems is done by active agitation in a closed vessel of acid solution turpentine with alkali solution or gel pH>8,0. The main problem to be solved in the development of the method was

determination of the ratio of mutually reacting acid and alkaline ingredients. The problem was solved using calculation method from reaction:

$$C_{17}H_{33}COOH + NH_4OH \rightarrow C_{17}H_{33}COONH_4 + H_2O.$$

The acid and alkali, participating in the reaction should be used in equimolecular quantities with a little excess of alkali, that might me controlled by the value of pH.

To increase the stability of the emulsions obtained, a gel former (carbopol 934P or sodium carboxymethyl cellulose) has been introduced into their dispersion hydrophilic medium. The introduction of the gelling agent is carried out at the stage of preparation of the hydrophilic phase. When using carbomer as a gelling agent, the amount of alkali used should be increased to neutralize its carboxyl groups, which is also controlled by the pH value.

The obtained stable emulsions of turpentine of type o/w with a content of 20-70% of the hydrophobic phase are well diluted with any amount of water (in the preparation of baths), and can also be used as a base for the preparation of combined preparations containing essential oils, analgesics, nonsteroidal anti-inflammatory agents, etc.

Below is given an example of the preparation of 200 g of the emulgel containing 50% turpentine purified and 1% carbopol in the hydrophilic phase: 2 g of oleic acid are added to 100 g of purified turpentine and the mixture is stirred until uniform (hydrophobic phase).

In another container, a dispersion of 1 g of carbopol in 45 ml of water is prepared, to which a calculated amount of 10% NH4 OH (or NaOH) solution is then added.

Both phases are combined and emulsified at a speed of 3000 rpm until a homogeneous white mass is obtained.

In the absence of mixing devices in a pharmacy (blender, mixer, etc.) the emulsification stage might be performed in a vial having it closed tightly and shaking vigorously for 2-3 minutes. The last stage to be conducted is deaeration, that is removal of air bubbles that were emulsified at vigorous shaking. The presence of these bubbles influences the volume of the emulgel and its texture. This operation is by vacuumation of the container with prepared product.

The most favorable storage conditions of the prepared emulgel are as follows: at temperature 8-15°C in a dark place. At dispension from a pharmacy the preparation is additionally labeled “shake before use”.

Conclusions. The technology for producing turpentine emulgel with a content of this product 20 to 70% has been developed. As emulsifiers, have been used salts of oleic or stearic acid, obtained as a result of the interaction of the acids used with alkalis. To increase the stability of the emulsion systems obtained, their dispersion medium is thickened with gelling agents.

QUESTION OF THE DEVELOPMENT COMBINED ORAL PREPARATION FOR COMPOSITION PIRACETAM WITH CINNARIZIN

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Introduction. The recommended medicine is a combined medicine preparation with pronounced nootropic activity based on piracetam and cinnarizine. The creation of new medicines requires large financial costs. An alternative to the improvement of medicamentous therapy is the development of new dosage forms with various combinations of drug substance based on already known medicines. Improvement of the technologies for the production of the new dosage forms is possible only by modifying the pharmacokinetic parameters of drugs. Despite the relatively large number of nootropic drugs used in various nosological in adults and children, it remains relevant for the pharmaceutical science to the develop new effective nontoxic drugs that improve cerebral circulation. The effectiveness of combined forms of drugs is achieved by changing the pharmacokinetic profile, which provides more stable concentration of the drug with an increase in the minimal effect in the dosing interval. The indicator of the maximum concentration of the drug in the blood for such dosage forms is of less importance, which is associated with a decrease in the maximum effect. This makes taking new dosage forms safer, which is very important.

Aim. Research in the field of development of the composition and conditions for the manufacture of a tablet dosage forms based on piracetam and cinnarizine for the treatment of craniocervical trauma and elimination of psycho emotional overloads.

Materials and methods. As the objects of the study, industrial samples of the substance of piracetam and the substances of cinnarizine were used.

Piracetam is nootropic drug, chemically it is a pyrrolidone-2-oxo-1-pyrrolidineacetamide derivative. Cinnarizine is a drug, a derivative of diphenylpiperazine, 1- (diphenylmethine-4-(3-phenyl-2-propenyl) piperazine, which improves microcir-culation in the brain vessels. As auxiliary substances, local raw materials such as sucrose, lactose, microcrystalline cellulose, Potato starch, calcium stearate. The role of binders was performed with purified water, starch paste and ethyl alcohol of various concentrations. The experimental

samples of piracetam-based tablets And cinnarizine using various auxiliary substances The auxiliary substances different in appearance and used in the amount of auxiliary substances The technological properties of the composition and the technological characteristics of the recommended tablets based on piracetam and cinnarizine were further studied. Technological parameters of the mixtures of the compositions were determined for selection. The most promising composition by known methods. Mixing of active and auxiliary substances was carried out in the laboratory mixer SL-APM-30. The compression of the tablets was carried out on a manual press at pressure of 120 MN / m^2. The quality of the obtained tablets was evaluated by appearance, disintegration, strength in accordance with the requirements of GF XI.

Results of the study. The obtained tablets is white, flat-cylindrical, with a facet and a risk, appearance meet the requirements of GF XI. By disintegration and abrasion resistance, composition №5 ensures the production of tablets with good performance. Thus, due to the combination of the processability of the formulation of auxiliary substances, a tableted form according to the recommended composition (No. 5) (piracetam, cinnarizine, hydroxyethyl rutoside, lactose, potato starch and calcium stearate) is obtained with positive quality characteristics.

Conclusions.

1. Based on the theoretical and experimental studies carried out, the composition is proposed and conditions for direct pressing for tablets of nootropic action are developed.

2. The obtained samples of tablets correspond to the quality indicators required for the given dosage form.

IMPROVEMENT OF EXTEMPORANEOUS OINTMENT WITH WOUND HEALING ACTION

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Introduction. Wounds healing is a very complicated matter, treatment must conform wound type, phase of healing and the overall level of reactions to the resulting damage and all its consequences. The use of modern drugs for the topical treatment of wounds reduces systemic antimicrobial therapy terms, avoid the development of side effects, significantly reduce the cost of antibiotics, to avoid of resistant to antibiotics microflora formation.

Aim. Theoretical, experimental and biopharmaceutical researches for the composition improvement of combined ointment proposed for purulent wounds treatment.

Materials and methods. Advantages of drugs made in pharmacies by prescription, are obvious. Analysis of industrial production medicines for the purulent wounds treatment showed that their relatively high cost in low solvency of the population does not allow to meet the needs of patients. We analyzed the range of extemporaneous preparations for topical application, used for wounds curing. It was found that most of the traditional ointments prepared on lanolin - vaseline base. Analyzed published data on the polyethylene oxide base use for the treatment of festering wounds of different origin and location suggest that these bases are highly effective and safe. Pronounced therapeutic effect in this group of drugs due to the high-dehydrating effect, broad antibacterial activity spectrum can be considered as drugs for the first phase purulent wounds local treatment. As the object of study was selected following composition extemporaneous ointment used for wounds with purulent necrotic content treatment. To achieve a specific therapeutic effect was proposed to study the influence of replacing vaseline base and emulsifiers using for increasing rate and extent active ingredients from ointments release. As the investigated base polyethylene oxides 1500/400 (7: 3) and №1 and T- 2. emulsifiers were chosen.

Obtained results. In vitro experiments proved the active substances intensity increase on hydrophilic bases with emulsifier №1. Thus it can be concluded that the replacement of traditional hydrophobic ointment base leads to an increase the therapeutic effect of the drug.

Conclusions. Based on technological and biopharmaceutical research was selected following composition extemporal ointment for the symptomatic treatment of wounds with purulent necrotic content.

DIFFICULT CASES IN EXTEMPORANEOUS PRESCRIPTIONS

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Introduction. Despite the variety of industrial produced medicines, extemporaneous prescriptions have not lost their significance. The interest in personal medicine is growing. Modern pharmacies in Ukraine are preparing a lot of medicines according doctor's prescriptions.

The aim of our work is to conduct an analysis of the extemporaneous prescription of different pharmacies.

Results and discussion. Preparation of each prescription requires a serious and thoughtful attitude from the doctor, since an improperly prescribed prescription can cause difficulties and a delay in the preparation and, consequently, in the dispensing of the medicine to the patient. However, there are cases when ingredients that make up the medicine form new substances during their interaction. Sometimes such interaction does not disrupt the therapeutic effect of the medicine, since substances that formed have the same therapeutic properties as the original ones.

The receipt in pharmacies of incompatible prescriptions prescribed by doctors is explained by the fact that in the modern recipe the quantity of complex dosage forms is continuously increasing. Often, doctors complicate already known prescriptions by introducing newer, more effective medicines in their composition without taking into account their compatibility with the rest of the ingredients. Doctors do not always take into account the possibility of drug's interactions in the human body.

In addition, when several medicinal substances are introduced into the body, the interaction between them effects the change of various functions of the organism. As a result of the various effects of several substances on cells, tissues, organs, functional systems, and the body as a whole, there may be a weakening of the desired therapeutic effect of the substance or its complete absence. Therefore, the knowledge of those physical phenomena and chemical reactions that can occur in the body when taking medicines, gives an ability to find a rational way to eliminate difficulties or incompatibilities with a view to giving the patient a high-quality medicine.

Conclusions. The analysis of the extemporaneous prescriptions of three pharmacies in Kharkiv was conducted. Difficult casers in prescriptions had been identified, the development of which technology will be the subject of our next research.

WAYS TO REVIVE THE EXTEMPORAL PHARMACEUTICAL COMPOUNDING IN PHARMACIES OF UKRAINE

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Introduction. In the 90^{s} of the last century, the number of medicines that were prepared according to individual prescriptions fell sharply. Most of the pharmacies in Ukraine have turned into outlets on sales of ready-made medicines, while production pharmacies have been massively closed. Doctors did not have an individual approach and alternatives in the pharmacotherapy of diseases with ready-made or extemporal medicines. All this has led to a decrease in the quality of providing the population with highly effective, inexpensive and non-toxic medicines. Nowadays, the situation is gradually changing; there is a tendency to increase the range of the extemporal formula and the number of pharmacies that produce it. The revival of the extemporal formulation is an urgent issue of pharmacy and pharmacotherapy of various diseases in our country.

Aim. The purpose of this work was the analysis of the extemporal prescriptions of Ukrainian pharmacies, the identification of the medicines compounding on individual prescriptions and ways to overcome them.

Materials and methods. There were analyzed the extemporal formulation in a number of cities of Ukraine (Kiev, Kharkov, Dnepr, etc.), and also the literature sources on this issue were studied.

Results and discussion. One of the primary problems is the need to expand the range of medicines that are prepared in pharmacies according to individual prescriptions. Despite the growing need for aseptic medicines, they are rarely prepared, mainly eye drops in limited quantities. There are certain problems in the acquisition of substances and auxiliary substances that are necessary for the pharmaceutical compounding in pharmacies. In Ukraine, they are mainly imported. One of the significant problems is the licensing of production pharmacies. To expand the range of the extemporal medicines, Ukraine has created the necessary regulatory framework (pharmacopeia, MH orders, Standards for technology and quality, etc.).

Conclusions. Analysis of the extemporal formulation in a number of Ukrainian pharmacies has been carried out. Problems with the preparation of extemporal medicines and ways to overcome them have been identified. The questions of import substitution of substances, the pricing of the extemporal medicines, and the expansion of the regulatory framework for pharmaceutical compounding require solutions.

COMPOSITION ANALYSIS OF THE EXISTING PRESCRIPTIONS BASED ON MEDICINAL PLANT MATERIAL AND EXTEMPORAL MEDICINES FOR HELMINTHIASIS TREATMENT

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Introduction. Phytotherapy largely reflects the perennial experience of folk medicine in the field of medicinal herbs usage. There is an enormous quantity of folk medicine remedies for helminthiases of digestive system treatment.

Aim. The aim of research was to analyse the existing prescriptions of herbal remedies and extemporal medicines which are offered in helminthiases treatment.

Materials and methods. The literature data of digests of folk medicine and non-traditional methods of treatment, phytotherapy digests and digests of extemporal medicines were analysed.

Results and discussion. Such medicinal plants as tansy flowers, wormwood herb, wormseed flowers, elecampane rhizomes and roots, pumpkin seeds, buckthorn bark, garlic bulbs, valerian rhizomes and roots, chamomile flowers, fern rhizomes, aspen bark, ginseng rhizomes, centaury herb, gentian roots, birch buds, carnation buds, buckthorn bark are the most frequently met in the composition of anthelminthic folk remedies. Wormwood herb, wormseed flowers garlic bulbs, wild carrot seeds, quinoa herb, mistletoe leaves are also used separately.

Extemporal digests offer powders with thymol and sugar and phytotherapy digests recommend fitovit (in the form of tablets), gelmin (in the form of internal drops) and multicomponent species.

The available dietary supplements for helminthiases treatment, which are popular today, are “Vormil phyto” (by Mili Healthcare Limited, the UK) and “Antihlyst” (by Farmakom, Ukraine).

The frequency of medicinal plants usage was calculated and the further PASS-analysis of their biologically active substances was carried out.

Conclusions. Development of new domestic anthelminthic medicines of herbal origin is one of the priority tasks of the modern Ukrainian pharmacy. On the basis of the obtained results of biblosemantic and PASS-analysis the following composition of the medicinal plant material is offered for the creation of new phytomedicine for the complex helminthiases treatment: tansy flowers, buckthorn bark, wormwood herb, wormseed flowers, elecampane rhizomes and roots, ginseng rhizomes, centaury herb, pumpkin seeds, buckthorn bark, valerian rhizomes and roots, chamomile flowers.

DEVELOPMENT OF EXTEMPORANEOUS SPECIES TECHNOLOGY FOR THE TREATMENT OF BRONCHOPULMONARY DISEASES

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Introduction. Recently respiratory diseases occupy a significant place in the total diseases rank and are likely to develop under the direct influence of environmental factors, which include strong fumes and dust, high content of harmful toxins in the air, etc.

For the treatment of dry cough are used antitussive agents of centrally acting and antitussive agents of peripheral acting. Modern Ukrainian pharmaceutical market has a lot of medicines based on herbal substances.

Herbal medicines are more effective and safe in long-term treatment of chronic diseases, less toxic, chemical composition makes rich multivalency action, and they are more affordable and accessible than synthetic medicines.

The aim of our work was to develop extemporaneous species technology for the treatment of bronchopulmonary diseases and cough in particular.

Materials and methods. In order to justify the optimal composition of the extemporaneous species to treat bronchopulmonary diseases with overwhelming mucolytic, anti-inflammatory and antiseptic action we have studied and analyzed published data regarding medicinal plants, which are often used in the treatment of bronchopulmonary system.

They are flowers of lime, herb of thyme, leaves of andromeda, herb of violet, leaves of plantain, herb of oregano.

Results and discussion. In order to develop the extemporaneous species technology we studied the technological characteristics of plant raw material, which are the part of the species: specific, volumetric, bulk weight, porosity, sponginess and free volume of the layer.

Also we studied the influence of the time and infusion method and the type of packaging material for release of extractives substances from the investigated species.

It was found that the optimal output of hydroxycinnamic acids and polysaccharides had a species, embedded in the filter bags and infused after processing with boiling water at the room temperature for 20 minutes.

Conclusions. On the basis of the conducted research technology of extemporal species for the treatment of bronchopulmonary diseases and cough particularly in filter bags was developed.

STUDY OF OIL-IN-WATER TYPE EMULSION STABILITY

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Introduction. The use of emulsion systems in the development of semisolid drugs provides rapid release of the active substances due to physiological affinity with structural elements of skin cover. Penetration of these systems occurs through sweat and sebaceous glands due to the presence of functional groups of hydrophilic and hydrophobic nature. In the development of these systems much attention is givento methods of stabilization and study of physical stability. Stabilization of emulsion system is achieved using surfactants or high-molecular substances. The physical stability of emulsions is estimated based on the results of structural and mechanical studies and research of their colloid and thermal stability.

In order to develop a medicinal cream to treat cuperosis has been developed a number of formulations of first kind emulsions stabilized with emulsifiers PEG 75, Lanolin and Cetearyl Alcohol 50/50 of different concentrations: №1 - 7% / 3%; №2 - 4% / 10%; №3 - 8% / 8%; №4 - 12% / 6%; №5 - 16% / 4%; №6 - 20% / 2%.

Emulsions were prepared by high-temperature method with high-speed emulsification at a speed of 10,000 rev / min. for 10 minutes using Polytron®System homogenizer PT 2500 E ("Kinematica AG", Switzerland).

Aim. Study of the first kindemulsion colloidal stability.

Materials and methods. For the test laboratory centrifuge with a set of tubes was used. Test tubes filled 2/3 of the volume with investigated samples and weighed to the nearest 0.01 g.Then the tubes were placed in a water bath at a temperature of (42,5 ± 2,5) ° C for 20 min., and then placed in the centrifuge slots. Centrifuged for 5 minutes. at a speed of 6000 rev / min. Samples were considered stable if, after centrifugation in test tubes was observed no separation. If at least in one of the tubes was observed sample separation or isolation of sediment analysis was performed again with new portions. If during the repeated test found at least one tube with separation, the sample was considered unstable.

Results of the study. According to the results of the first kind emulsion colloidal stability study it has been established that all proposed formulations withstood the test of colloid stability.

Conclusions. Thus for further physicochemical and structural-mechanical studies can be used all the proposed samples of emulsion systems.

DEVELOPMENT AND RESEARCH OF GEL "MUMIYO-ASIL"

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Introduction. Mumiyo is a versatile, naturally occurring biological regulator, which exerts a favorable effect on metabolic processes and on the human immune system. It is a unique biologically-active substance with striking healing effects and protective influence on the human body.It is also used as a general strengthening and tonic remedy.

Mumiyo has a wide spectrum of pharmacological activity. But, official medicine is familiar with it only as food additive.

Aim. Study of physical and chemical properties of gel "Mumiyo-asil".

Materials and methods. The most optimal option was 5% gel with carbopole. To prepare this gel by calculation for 200 grams, it takes 10 grams of carbopole powder and 190 ml of distillated water. All components are thoroughly mixed. In order not to form lumps, the powder is added in small portions. The dishes are tightly closed with a cork and left in a cool place for one day. The formed gel has a specific structure and odor. To increase the viscosity of the gel, the necessary amount of alkali (NaOH) is added.

To make a solution with mumies, take 15 grams of the substance, crush and pour 30 ml with distillated water. The solution is regularly stirred until the mumiyo completely dissolves in water. Using filter paper, we filter solution.

We collect 187.5 g of gel base and 12.5 ml of solution with mumies and gently mix in porcelain dishes.

Gel research.

1) Determination of colloidal stability. We take 2 tubes and fill it with 2/3 of the volume of the gel. The test tubes are put on a water bath at a temperature of 42-45 grays for 20 minutes. We take out the test tubes, wipe them dry and install them in a centrifuge at a speed of 100 s-1. After 5 minutes, take out the test tubes and determine the stability of the gel.

2) Determination of thermal stability. 3 tubes are filled into 2/3 of the volume of the gel under study so that no air bubbles remain in the emulsion. Tightly close the tubes with a stopper and place in a water bath at a temperature of 40-42 degrees for 5 minutes.

3) Determination of homogeneity. Take 4 samples of gel to 0,02-0,03 grams,

placing them on 2 slide glasses. Covered by a second slide and tightly pressed to form spots, up to 2sm in diameter.

4) Potentiometric determination pH of gel in accordance with the requirements of the XI State Pharmacopoeia of the Uzbekistan.

5) Method of identification of mumies. 0.5 grams of mummy is dissolved in 5 ml of distillated water. A few drops of a solution of chloride of oxidized iron are added. The result is a dark green color.

6) The method of checking the quality of mumies. Take in the hands of the mummy and a good mash.A poor quality mummy will remain firm and will not soften from the temperature of the hand.

Result and discussion. We got the gel, which is the corresponding provisions of this dosage form. The gel has a brown color and specific smell of wood tar. According to the structure of the gel is uniform, without visible particles, stable and resistant to high temperatures. Furthermore, the gel has a pH close to the skin.

Determination of colloidal stability had shown thatin both tubes with gel, there is no separation of the emulsion and the evaporation of the aqueous phase.

The result of determining the thermal stability is that no aqueous phase was detected in any of the 3 tubes. This shows that the emulsion is stable to high temperature.

When examining the result of the determination of gel's homogeneity, no visible particles were found on any glass.

The gel has a pH of 6.5.

When checking the quality of the mumies, it is easily softened.

All research have shown that the our gel “Mumiyo-asil” complied with all the requirements of the XI State Pharmacopoeia of Uzbekistan.

Conclusions. As a result of this work we can draw the following conclusions:

- the resulting gel has a pH close to the pH of the skin,which makes it extremely promising dosage form.This gel is distributed evenly on the skin, it does not clog pores. In addition, it is important that the resulting formulation is quite has retained all the beneficial properties of the mumiyo.

DEVELOPMENT OF NON-AQUEOUS SOLUTION TECHNOLOGY FOR STOMATITIS TREATMENT

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Introduction. One of the most topical problems in Ukraine is a state of health, including its component – dental health. Among dental diseases occupy a special place processes associated with lesions of the oral mucosa. Increased interest in science researchers and practitioners of this pathological-nology explains the frequent occurrence of diseases oral mucosa, large differently-manitnistyu of forms, a wide range of etiological factors, rather warehouse them, and in many cases poorly understood mechanism of pathogenesis for disease. When treating stomatitis using frequent rinsing of the mouth, antiseptics, topical treatment is used in a various antifungal, antiviral, anti-inflammatory and others drugs. Medicines of industrial production are not always has influence to all aspects of oral mucosa pathogenesis. Proceeding from these extemporaneous formulations for the oral mucosa treatment and prevention actively developing.

Aim. Is development of extemporal non-aqueous solution for the stomatitis treatment.

Materials and methods. To select research objects an analysis of formulations which are prepared extemporaneously in industrial pharmacies in Krakow (Poland) for the dental diseases treatment were carried out. We selected prescriptions that are often repeated among them. The results of this study found that most formulations has unidirectional action it is a significant reason for the development of new combined medicines. For the extemporaneous preparations development novocaine and tannin were selected. As a solvent glycerin and purified water were chosen.

The active substances are readily soluble in the solvent components, but compatible dissolution forms chemical incompatibility, so we should carry out researches on the rational technology to prevent active pharmaceutical ingredients destruction.

Results and discussion. The results of the technical studies has shown that for tannin destruction prevent necessary to change half amount of purified water to 70% ethanol and choose a special active substances dissolution sequence. The solution obtained by the proposed technology was stable in 30 days of storage.

Conclusion. Based on complex research complex solvent composition and rational technology that prevents the formation of chemical incompatibility between prescription ingredients were chosen.

EXPERIMENTAL DETERMINATION OF THE OPTIMAL CONCENTRATION OF SWEETENER IN THE COMPOSITION OF MEDICATED CHEWING GUM

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Introduction. One of the most important characteristics for oral dosage forms is taste characteristics. The use of taste correctors – is one of the main ways to mask the unpleasant flavour of drugs and provide them with a pleasant taste. This component of dosage forms significantly affect on the perception of drug and patient adherence. During choosing taste correctors it is important to assess their corrective potential.

Aim. The aim of the research is to choose the optimal sweetener and determine its concentration during the creation of medicated chewing gum (MCG) with proteolytic enzymes.

Materials and methods. To confirm the appropriateness and correctness of the choice of concentration of taste correctors was suggested consistent application of evaluation panels and taste scoring system by A. Tentsova. In developed mix of active pharmaceutical ingredients with the base, glidants, lubricants, flavours and moisture-absorbing agent, was injected sweeteners in different concentrations – sorbitol, xylitol, sucralose and then, we studied their impact on the taste of MCG.

Results and discussion. As taste correctors were taken sweeteners - mannitol and sorbitol and chlorinated derivative of ordinary sugar - sucralose, sweeteners which have non-carious nature. Following the method by A. Tentsova 2 groups of 20 persons each carried out organoleptic assessment of MCG samples in compliance with all tasting rules with different concentrations of correcting agents and without it. According to the results we have withdrawn the main indexes of taste and flavor as the average of the sum of all indicators, divided by the number of people participating in the study. Comparative evaluation of corrective actions showed that when sucralose added to MCG, it had high index of basic taste and flavor, but gum was very sweet (lusciously) and while chewing was felt a metallic taste. Duration of sweetness sensation – about 4-5 min. At the end, was felt a little bitterness. Better characteristics had MCG with the addition of xylitol and sorbitol, which, in addition to approximately the same values of numerical codes taste and basic taste, had a pleasant cooling flavour. Chewing gum with xylitol had lowest taste duration (about 2 min.). The highest masking potential showed MCG with 0,3% concentration of sorbitol, because numeric indices of taste and flavour were close to the maximum value, and a sense of sweetness lasted approximately 4-4.5 minutes.

Conclusions. We carried out a comparative assessment of sorbitol, xylitol and sucralose corrective action in different concentrations allowed to choose the optimal sweetener and its concentration, which prolongs the intense sweet of MCG. The results of the experiment determined that best corrective substance was sorbitol at a concentration of 0.3%.

TO THE ISSUE OF PARENTERAL NUTRITION EMULSION COMPOSITION DEVELOPMENT

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Introduction. One of the tasks of infusion therapy is to ensure the body's need for energy materials. In some pathological conditions, there is a need for parenteral nutrition - intravenous administration of drugs containing a balanced mixture of amino acids, glucose, fat emulsion for the prevention of protein deficiency and provision of energy needs of the body. The analysis of the assortment of preparations for parenteral nutrition has shown that amino acid solutions and fat emulsion to Ukraine are supplied by foreign companies.

Aim. To conduct research on the development of the composition of domestic fat emulsion for parenteral application.

Materials and methods. This group of infusion drugs is designed to introduce into the body fats, which are a source of energy and a supplier of higher unsaturated fatty acids, involved in the construction of cell membranes. For the creation of finely dispersed stable emulsions, as the oil phase used fractionated and highly purified vegetable oils - soybean, cottonseed, sunflower, coconut, olive, corn; fish oil; As an emulsifier used egg lecithin (i.e. phospholipids of egg yolk). The dispersion media of fatty emulsions were solutions of glycerin and sorbitol, which ensure the osmolarity of the preparation. As antioxidants, preventing the oxidation of fats during storage, tocopherol and methionine were used.

Model samples of emulsions of various compositions were prepared by mechanical dispersion using a high-frequency electromagnetic stirrer. Emulsion studies were carried out according to SPU requirements.

Results and discussion. Samples of fat emulsions for infusions containing 10% and 20% of specially purified vegetable oil, 1,2% of egg phospholipids, carbohydrate additive for osmolarity, antioxidants and purified water for injections were obtained using the mechanical dispersion method. The diameter of the microparticles of the oil phase in the emulsions, measured by means of an immersion microscope, was 0.8-1 μm.

Thermostability, frost resistance, pH value of emulsion samples were monitored. At present, the stability of emulsions is checked by centrifugation.

Conclusions. Since Ukraine does not produce fat emulsion for parenteral nutrition, research in the development of the formulations and technologies of these pharmaceuticals is extremely important and necessary.

DIRECTIONS FOR THE IMPROVEMENT OF REVERSE LOGISTICS AT PHARMACEUTICAL COMPANIES

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In recent years, there has been a deterioration in public health in Ukraine. This is largely due to the unfavorable environmental situation in the country. Production processes in industrial enterprises are the main causes of increased pollution of the environment. This occurs as a result of non-compliance with the standards of workplaces; low level of environmental consciousness of the society, high specific gravity of resource-intensive technologies, low efficiency of treatment facilities, imperfection of legal and economic mechanisms for environmental protection. The specific weight of the influence of these factors on the health of the population reaches 40%. In this regard, there is a need to improve the environmental policy of pharmaceutical enterprises. The use of optimal waste management methods is one solution to the problem

The purpose of the reserch is solving the problems of reverse logistics at pharmaceutical enterprises.

Research methods: content analysis, method of analysis and synthesis.

Results. The main reasons for the ineffective use of reverse logistics in pharmaceutical companies are: insignificant attention from the leadership (67% of respondents); deficit of financial resources (65% of respondents); insufficient (obsolete) production technology (56% of respondents); imperfection of the regulatory framework (56% of respondents); underestimation of the importance of reverse logistics (45% of respondents); deficit and imperfection of information systems (13% of respondents); deficit of knowledgeable logistics approaches, environmental aspects and pharmaceutical specificity of personnel (7% of respondents).

The development of work algorithms and the description of business processes that show work and their hierarchical order in the tree of business processes, the sequence of work and their interrelations, and the movement of information and material flows are a prerequisite for improving the performance of pharmaceutical enterprises

Conclusions. Building business processes is necessary for conducting qualitative analysis and optimization of the company's activities.

REVIEW OF ABRASIVES FOR THE DEVELOPMENT OF THERAPEUTIC AND PREVENTIVE TOOTHPASTES

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Introduction. Currently, the most common oral hygiene product is toothpaste. The share of dental and oral care products accounts approximately 20 % of the total volume of manufactured cosmetic products. In addition to hygienic purposes, toothpastes are effective and economical means of preventing diseases of the teeth and oral cavity. The main ingredients of toothpaste are abrasive substances. Abrasives effectively fight tooth plaque and promote teeth whitening. The most important requirements for abrasives are chemical indifference, controlled abrasive ability in relation to tooth enamel, low adsorption capacity of the other components of toothpaste, good wettability, etc.

Aim. The assortment of abrasives in our time is very diverse, so the aim of the work was to analyze range of abrasives that are used in modern toothpastes.

Material and methods. There were used methods of systematic, structured, logical analysis, method of literature data summarizing.

Results and discussion. The most traditional abrasive is chalk, but currently, calcium carbonate is rarely used, as it has a high abrasion effect and cannot be combined with therapeutic additives. In our time, mono- and dihydrate of dicalcium phosphate, anhydrous dicalcium phosphate, tricalcium phosphate, sodium metaphosphate, aluminum hydroxide, silicon dioxide, zirconium silicate, aluminum silicate, polymeric compounds of methyl methacrylate are used. Many of them are not only abrasives, but also have additional properties, for example, contribute to the remineralization of enamel. Silicon dioxide is safe, well compatible with all components of toothpastes, does not reduce the activity of fluorine-containing components and surfactants, antibacterial additives, vitamins, has controlled abrasiveness, which allows creating pastes with a wide range of specified properties. It provides the optimal pH – 7. In addition, silicon dioxide synthesis provides a substance with the required degree of dispersion, taking into account the index of abrasion. So, the optimal abrasion of toothpastes is: pastes for children – 20-30, pastes for adults – 80-100, pastes for smokers – 120-150.

Conclusions. Thus, when choosing an abrasive, it is necessary to take into account its indifference to the other components of the paste, the ability to react with the hard tooth tissues, adsorb the components of the caste, to be wetted with the water-glycerol solution of the gelling agent and economic accessibility.

Section 5.

MODERN BIOTECHNOLOGY

THE MICROORGANISMS ANTIBIOTIC RESISTANCE AND ITS MECHANISMS

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Introduction. The microorganisms antibiotic resistance phenomenon appearance is an actual worldwide problem, which has a negative influence on the human health and on the control over the majority of important diseases. This leads to the decrease of the causal infectious diseases treatment efficiency. The microorganisms capacity to endure great concentrations of antibiotic drugs is called the microorganisms resistance.

Aim. To study the bacterial antibiotics resistance mechanisms.

Results and discussion. The microorganisms antibiotic resistance mechanisms are complicated and diverse. They are preconditioned by a number of factors which include the drug active form transformation under bacterial fermentative activation and modification; the absolute deprivation of the cell wall permeability to the separate drug; the change of the bacterial cell genome as the result of spontaneous mutations.

The microorganisms resistance mechanisms are divided into natural and acquired. Mycoplasmas that do not have cell walls can serve as an example of the natural mechanism because they are susceptible to all drugs acting at this level. The acquired resistance is characterized by genetic bases, when the resistance to drugs is defined by resistance genes (r – genes) and conditions facilitating their proliferation in germ populations. The acquired resistance can arise as the result of the occurring mutational changes in the bacterial chromosome with the following mutant selection. The mutation process proceeds easily under the presence of the drug, it is exactly under these conditions when the mutants get advantage over all other cells of the population. The mutations can be occasional and multiple; the transposition of the R–plasmids. These plasmids code the cross – over resistance to certain families of antibiotics. β – lactamase coded by the TEM – 1 plasmid can serve as an example of this cross – over resistance; the carrying r – genes transposons transposition.

Conclusions. It is almost impossible to prevent the bacteria antibiotic resistance development but it is necessary to use these antimicrobial drugs so that they could not facilitate the resistance development and proliferation. That is why narrow antibacterial drugs spectrum must be taken, the drugs administration for preventative reasons must be prevented, the drug must be taken according to the indications only.

STUDY OF THE STABILITY OF PROBIOTIC CROPS TO ANTIBIOTICS AND THE ACTION OF BILE

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Disruption of the microbiota of the gastrointestinal tract is associated with many pathological conditions. Understanding the mechanisms of action of probiotic drugs and knowledge of the evidence base is important for gastroenterologists, therapists and general practitioners who support their use in practice.

Probiotics are living microorganisms and substances of microbial origin, which with the natural method of administration have positive effects on the physiological, biochemical and immune responses of the host organism through the stabilization and optimization of the functions of its normal microflora. So, the positive effects in the treatment of rheumatoid arthritis, some infections of genitourinary ways, pyoinflammatory complications in surgical practice, gynecological diseases of infectious nature and many others. Such diverse effects of probiotics is determined by the original mechanism of action. Soon after taking the drug begin to stand out of bioactive substance and function of the system of microbial cells, which could have a direct effect on pathogenic and conditionally pathogenic microorganisms and is mediated by the activation of specific and unspecific protection systems of the organism. In this same time period, bacterial cells of a probiotic, which can be considered as biocatalysts of many vital processes in the digestive tract, actively produce enzymes, amino acids, antibiotic substances and other physiologically active substances that complement the comprehensive medical and preventive action.

Depending on the time of creation and improvement there are several generations of probiotics:

- the first generation – classic monocomponent preparations, consisting of one strain of microorganisms – the typical inhabitants of the intestine;
- the second generation – smolinerwien antagonists;
- third generation – multi-component drugs consisting of several (2 to 30) of the strains of bacteria or multiple species of bacteria
- the fourth generation – a combination of drugs (synbiotics), consisting of strains of bacteria and ingredients that contribute to their growth, reproduction and metabolic activity
- the fifth generation multi-component combination therapies, consisting of several types of bacteria and ingredients that contribute to their growth, reproduction and metabolic activity.

Probiotics contain live cultures of bacteria that are characteristic of the gastrointestinal tract of a healthy person. These include, first of all, *Lactobacillus acidophilus* and *Bifidobacterium bifidum*. Probiotics positively influence the balance of microflora in the intestine, suppressing the growth of pathogenic microorganisms, participating in the process of cavitary digestion, stimulating antimicrobial immunity. However, it is established that the range of indications for the use of probiotics in clinical practice can be substantially expanded.

The aim of this work is to study antibiotic resistance and bile resistance of probiotic cultures.

To date, basic requirements have been formulated to select strains for medicines and to prove their effectiveness and safety in clinical trials: microorganisms included in the preparation must be alive; The content of microorganisms in the preparation should be approximately the same concentration throughout the shelf life, minimally vary in different batches of the drug; Microorganisms must be resistant to low acidity, organic and bile acids, antimicrobial toxins and enzymes produced by pathogenic microflora.

Such characteristics of strains as resistance in acid medium to bile salts obtained during in vitro studies should confirm the feasibility of further development of the probiotic preparation.

The sensitivity of probiotic strains to antibiotics

The sensitivity of the production probiotic strains to antibiotics is determined in accordance with the procedure "Determination of antimicrobial activity of antibiotics by the diffusion method in agar".

Studies on the evaluation of antibiotic susceptibility are subject to pure cultures of the tested microorganisms, belonging to a certain species is confirmed by pheno- and genotypic methods of investigation.

Determination of the resistance of the production probiotic strain to the action of bile

Production strains should be resistant to the action of gastric juice, bile, increased salt and alkali content when passing through the gastrointestinal tract to preserve the viability of the cultures that have become part of the probiotics. If these properties are not detected or reduced in the recommended strain, and the culture is characterized by the production of unique biologically active substances with a therapeutic effect, studies should be carried out for the selection of auxiliary substances or dosage form (for example, acid-fast capsules, tablets with protective coating, etc.) Maximum preservation of the viability of probiotic cultures.

To date, the department of biotechnology is conducting studies to determine the resistance of probiotic strains widely used in the production of probiotic drugs, antibiotics, and also to the action of bile.

CONIFERS RESISTANCE MECHANISMS TO THE CAUSATIVE AGENT OF ROOT ROT

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Introduction. Resistance to basic biotic and abiotic stresses is one of the main requirements that are imposed on modern varieties of cultivated plants. A major damage to forestry is caused by the pathogenic fungus Heterobasidion annosum, causing the death of many hectares of coniferous forests. Infection of trees is transmitted by basidiospores. Settling on the stumps, spores germinate, and the mycelium passes into the roots. The further contamination of plantings in the areas results by contact or fusion of diseased and healthy trees. The root rot leads to decay and a decrease in the protective properties of the trunk. The plant resistance mechanisms study will help to create the resistant to this pathogenic fungus coniferous plantations.

Aim. The aim of this work is the coniferous tree species resistance to the root rot pathogen mechanisms and factors study.

Results and discussion. In the plants protection from infectious diseases phytoncides take part. The phytoncidal effect is due to so-called enzyme poisons, which act when they come into contact with the pathogen. The plants resistance is also provided by phenolic compounds found in the root system. They fall into the soil and exert a certain influence on the microflora (inhibit spore germination and growth of the phytopathogenic fungi hyphae). When injured plants exudate oleoresin. Root rot is a highly pathogenic fungus in different conditions. It was shown that different coniferous tree species have a variety of antibiotic activity. This is manifested in the fungus germination intensity and parameters. Empirically established that the extracts of wood with greater antibiotic activity can inhibit the root rot mycelium growth and with less activity stimulate its growth. Exudates of most coniferous plants have a stimulating effect on H. annosum; however, among them there are species that inhibit the spores germination (Pinus ponderosa, Pseudotsuga menziesii). The pathogenic fungus growth is also affected by soil microorganisms. Their groups in the root zone of trees which vary in a root rot resistance degree differ significantly. Metabolic activity of the fungus is also limited by the temperature and wood condition.

Conclusion. Studied the root distribution in conifer plantations and characteristics of pathogenic fungus on samples of pine wood. Further in-depth studies of the conifers resistance mechanisms to root rot will be important for the control of phytopathogenic fungi on the territory of Ukraine.

TECHNOLOGY OF PREPARATION OF HOMEMADE FERMENTED MILK PRODUCTS AND STUDY THEIR MICROFLORA

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Cultured milk products are one of the essential components of a proper diet. They have revitalizing and healing properties, help to improve metabolism. Cultured milk products produced from pasteurized milk or cream which it is ripened by the introduction of lactic acid bacteria or yeast.

The aim of this work is to consider the technology of preparation of homemade fermented milk products, to study their microflora.

In researches milk were used as a raw materials that must be pasteurized to prevent the development of extraneous microflora. Pasteurization of milk was carried out at 80 °C for 30 minutes. Starter culture for clabber and boiled fermented milk served dairy products to make kefir in the role of the starter culture was used kefir fungus. Kefir, obtained in the result of the activity of kefir fungus is a product at the same time and lactic acid fermentation and alcoholic fermentation. For the production of clabber in a sample of warm milk sour cream made. The sample was being repined at 30 °C for 8 hours. For production homemade kefir, as a ferment kefir fungus was used which is a symbiosis of lactic acid bacteria, acetic acid bacteria and yeast. Milk, with added milk fungus was being repined at a temperature of 20-22 °C for 24 hours. For production boiled fermented milk it is necessary to prepare a sample of baked milk obtained by heating milk in a water bath for 8 hours. In a sample of baked milk were made pre-prepared clabber. The fermentation process lasted 8 hours.

As a result of study were obtained samples of clabber, kefir and boiled fermented milk, which were investigated for the presence of microorganisms of the genus *Lactococcus*, *Streptococcus*, *Acetobacteraceae, Saccharomyces, Lactobacillus* and organisms of the genus *Escherichia* and *Staphylococcus*. In the process of studying the microflora of cultured milk products the following methods of staining were used: simple staining with methylene blue, a complex Gram staining. Stained fixed preparations were examined using a light microscope to determine the morphology of the cells. In the sample of cultured milk products were discovered the estimated micro-organisms, except bacteria of the genus *Escherichia* and *Staphylococcus.* Pathogenic microflora was not detected. Studies on the development of formulas and technologies of cultured milk products with potential therapeutic properties continue.

HETEROBASIDION ANNOSUM MICELIUM CULTIVATION IN THE PURE CULTURE

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Introduction. The root and stem rot etiologic agent (Heterobasidion annosum, Fomitopsis annosa) is a xylotrophic basidiial fungus from the group of aphyllophoroid hymenomycetes. It affects conifers (spruce, pine), as well as some deciduous (birch, alder). The root rot became a world problem, the disease covered huge areas of coniferous plantations, that causes great damage to forestry. Sources of infection are diverse - basidiospores, conidiospores, fungus mycelium. The pathogen distribution is affected by soil category and planting density. The search for reliable means to root rot control is one of the important problem of forestry. The main methods of root rot preventing and control are various forestry measures for the sustainable plantations cultivation (selective sanitary felling, the mixed populations formation; the use of antiseptics for the stumps treatment or removal; the introduction of chemicals into the soil; biological methods of infection control etc.).

Aim. Selection of optimal nutrient media and cultivation conditions for obtaining a pure culture and accumulation of H. annosum mycelium.

Materials and methods. To obtain the H. annosum mycelium, the conventional culture-morphological and physico-chemical methods were used. The fungus pure culture was obtained from basidiomes, which were previously purified from contamination by 3% H_2O_2 and 70°ethanol, cut into 0.7 x 0.7 cm fragments and transferred to the nutrient medium (Czapek's, wort and Sabouraut agar) surface. Primary isolations were incubated in the dark at (23-25)°C, subcultivation was carried out at (16-20)°C.

Results. In primary platings on the semisynthetic Czapek's medium H. annosum mycelium grew less intensively than in other media. Also, the mold fungi intensive growth was observed. The mycelium grew more intensively in solid and liquid wort nutrient media (6° Balling degree). It was found that H. annosum isolation and biomass accumulation can be carried out at (16-20)°C on standard Sabouraut medium. Growth of fungus on natural substrates was more intensive on wood and bark of pine than on birch materials.

Conclusion. Studies of phytopathogenic fungus H. annosum in the laboratory, selection of optimal parameters for cultivation and biomass accumulation are necessary for obtaining new knowledge that will help to improve available and to develop new root rot preventing and control measures.

THE ROLE OF PURIFICATION METHODS IN BEER MANUFACTURING TECHNOLOGY

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Brewing is one of the dynamically developing branches of biotechnology in the world. Beer is a low-alcohol beverage obtained by alcoholic fermentation of malt mash with the addition of hops. To date, beer is the third most popular drink after water and tea, but in the last decade the volume of beer production in Ukraine has decreased, which is associated with a drop in material provision of the population and a reorientation of the consumer to cheaper brands. The technology of beer includes the following stages: preparation of production, raw materials, obtaining malt, its crushing, mashing, filtering of mash, hopping, fermentation, beer ripening and filtration, carbonization, bottling and packaging. It should be noted that the quality of the ready product depends on the raw materials used, the recipe and, the modes of conducting the technological process. The critical stage in the production of beer is the clarification, during which suspended colloid particles, mechanical inclusions, yeast cells are extracted, which increases the stability of the ready product during storage and prolongs its expiration date. Clarification can be carried out by centrifugation and filtration. Centrifugation can extract only large particles and yeast cells, so it is ineffective, while properly selected filtration conditions allow to achieve high biological and protein-colloidal stability of beer without impairing its organoleptic properties. For filtering various filters are used: precoat filter, filter presses and membrane filters. The latter is used only for beer that has undergone complete preliminary and basic clarification by other methods, since the pore sizes of the membranes are rapidly clogged, which makes their use not rational. Plate-type filter presses based on cardboard are cumbersome, non-automated and labor-intensive in maintenance. The most widely used for clarification of beer are precoat filters (candle, disk, sheet and frame). Structurally, such filters involve the deposition of various particle sizes of auxiliary material (kieselguhr or perlite) into special partitions. Despite the high quality indicators of beer obtained by filtration through precoat filters, their high productivity, ease of sterilization, it is necessary to point out the inefficiency of natural materials and the additional expenses associated with the irrecoverability of use and their subsequent utilization. Thus, the development of new ways of clarifying beer and beer mash is quite actual for biotechnology. At the department of biotechnology NUPh, a feasibility study is being conducted of using ftroplastic filters to purify beer from yeast and suspended colloidal particles.

INFLUENCE OF WASTE VEGETABLE OIL QUALITY ON THE SYNTHESIS OF MICROBIAL POLYSACHARIDE ETHAPOLAN

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Introduction. Microbial exopolysaccharides (EPS) due to the ability of their solutions to gelation, emulsification, suspending and changing rheological properties of aqueous systems are widely used in various industries, agriculture and medicine. Usually, products derived from sugar beet: molasses, sugar syrup, sucrose or corn: starch, hydrolyzed starch, glucose syrup, glucose, maltose are used as substrates in production of EPS. Industrial wastes can be used as substrates to improve the economic efficiency of microbial synthesis technology. Waste (fried) vegetable oils are cheap and available in quantities necessary for use in microbial technologies.

In our previous studies, the ability of strain *Acinetobacter* sp. IMB B-7005 for the synthesis of EPS ethapolan on wide range of C_2-C_6 mono- and mixed substrates, and also on sunflower oil (refined and waste after frying meat and potatoes) was shown.

It is known from the literature that toxic substances are forming in oil in process of frying at temperature above 180°C, the amount of which depends on the oil composition, in particular on the ratio of mono- and polyunsaturated fatty acids. For example, sunflower and corn oils are characterized by a high content of polyunsaturated acids. Under these oils heating, their molecular structure changes with formation of toxic aldehydes and lipid peroxides.

Olive and rapeseed oils of cold pressure during frying form much less aldehydes, as they contain more monounsaturated and saturated fatty acids, which are less oxidized under heating. In addition, the quality of waste oil depends on the product which is frying. Formed aldehydes and peroxides can be potential inhibitors of the target product growth and synthesis.

Previously, we noted that up to the present time in the world there is practically no information about synthesis of microbial polysaccharides on waste oils, and furthermore no data about quality and composition effect of such oils on the synthesis of the target product.

Aim. To study the synthesis of microbial exopolysaccharide ethapolan on

Материалы и методы. Cultivation of *Acinetobacter* sp. IMV B-7005 was carried out in a liquid mineral medium of such composition (g/l): KH_2PO_4–6.8;

KOH–0.9; $MgSO_4 \times 7H_2O$–0.4; $CaCl_2 \times 2H_2O$–0.1; NH_4NO_3–0.6; $FeSO_4 \times 7H_2O$–0.001, pH 6.8–7.0. In additionally yeast autolysate (0.5%, v/v) and multivitamin complex "Complevit" (0.00095%) were added to the medium as growth promoter and source of pantothenate, respectively.

Refined and waste after frying potato and meat oils: sunflower (TM Oleina, Ukraine), corn (TM KAMA, Ukraine), rapeseed and olive oil of cold pressure (TM Salvadori, Italy) at a concentration of 5% (v/v) were used as a source of carbon and energy.

. Quantity of inoculum was 10% from the volume of the medium.

Cultivation of *Acinetobacter* sp. IMV B-7005 was carried out in flasks (750 ml) with 100 ml of medium in shacker (320 rpm) at 30ºC for 120 hours.

Results and discussion. At the first stage, a comparative analysis of ethapolan synthesis on sunflower and corn waste oil, which are similar in polyunsaturated fatty acids content, was performed. In these studies inoculum was grown on the corresponding refined oil.

Thus, experiments showed that the highest concentration of EPS (11.2–14.4 g/l) was observed under the strain IMB B-7005 cultivation on waste after frying meat oils (both sunflower and corn).

At the same time, when the ethapolan producer was grown on olive and rapeseed oils, characterized by a high content of monounsaturated fatty acids, the content of EPS was slightly lower (7.7–9.0 g/l), that can be explained by the presence of phenolic compounds in such substrates.

On the next stage, waste oil was used in inoculum obtaining and EPS biosynthesis to reduce the cost of the target product. However, in this case, regardless of waste oils type, insignificant decrease in EPS synthesis was observed compared with using refined oil for inoculum preparation.

Conclusion. Thus, in result of the work it was shown for the first time the possibility to use not only waste sunflower, but also corn, rapeseed and olive oil for the synthesis of the microbial polysaccharide ethapolan.

Obtained results showed that oil of any composition and quality can be used to produce EPS ethapolan, which allows to develop universal technology for its production, independent of the region, type and supplier of waste oil.

STUDY OF MEDICAL PRERATIV SUPPOSITORIES FOR FURHER RESERCH

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The actual problem of modern pharmacy is the search for new effective and safe drugs of a wide spectrum of action. A special role among medicines belongs to herbal preparations, thanks to a balanced complex of biologically active substances with a minimum of possible side effects. In the pharmaceutical market, medicines for the treatment of proctological diseases based on plant raw materials are represented by a narrow range of names. The aim of the work is to analyze rectal suppositories containing biologically active components. To evaluate of the composition of suppositories, medicinal and auxiliary substances, determination of their optimal content in a dosage form. To date, for the treatment of dysbiosis in children and adults, there are many drugs belonging to the group of probiotics. Between themselves, they can differ in terms of storage, form of release, price and rules of the tricks. This category of suppository is intended for the treatment of intestinal dysbiosis in adults and children. The effectiveness of such medicines at the local level remains extremely high, while the negative impact on the body is almost completely absent. Such preparations for adults and children include:

- antifungal and antibacterial. Such a category of suppositories are medicines based on local antiviral, antifungal agents and antibiotics. Often in their composition, you can see glucocorticosteroids to reduce the inflammatory process in the rectum. As already mentioned above, they have a minimal amount of side effects, they are good at coping with the early stages of the disease, but are contraindicated in the presence of pregnancy. Among effective rectal suppositories of this type are: kipferon, ginkor procto, nipagin, aurobine, anuzole, levomycetin, prostipin, apis, geneferon, viferon;

- probiotic. These drugs are necessary for direct delivery to the intestines of microflora in the form of bifido-, lactobacilli and enterococci directly into the rectum, bypassing the gastrointestinal system.

- quickly in the intestine. Popular candles of this category: lactobacterin, bifidumbacterin, lactonorm, biphonorm +.

Among the various dosage forms of greater interest are suppositories and accordingly, the rectal route of administration of medicines, which has a number of advantages over others. Proceeding from the foregoing, the creation of suppositories with probiotic microorganisms is a very actual and promising task of practical pharmacy.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF THE MATSUN DAIRY DRINK

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Matsun – is a drink of the Caucasian origin, is rich with useful sour-milk microflora which is even called "youth bacteria". It is prepared on the basis of boiled cow's, sheep, goat milk or their mixture. The production technology consists in souring of milk by means of lactic streptococci and the bacillus of Massol. At a temperature of 37C the mix is placed into a special device designed to keep heat where it should be maintained about 3-4 hours.

Useful properties of matsun. Regardless the preparation method of matsun – the drink slakes thirst and hunger what is urgent for people with active lifestyle. Using of matsun is very useful in sport, with low caloric content (about 55 Kcal in 100 g) the product is rich with digestible proteins promoting rapid growth of muscle bulk.

The sour-milk microorganisms contained in matsun promote control pathogenic microflora in intestines, what influences well to general health, and, according to some information, promotes prolongation of youth. Thanks to a special method of preparation of yogurt and properties of the ferment which is its part, the product perfectly stimulates appetite, promotes blood circulation improvement, normalizes activities of intestines and improves work of a liver and kidneys.

The purpose of this work is the reason for choice of ferment for development of technology in dairy drink matsun in vitro. For receipt of drink matsun different types of ferments are used, for example: LbS ferment of 22.11 K, 22.11 KF (Such microorganisms - *Streptococcus thermophilus, Lactobacillus casei* are a part of microflora of this ferment); LbS ferment 22.11 V (*Streptococcus thermophilus, Lactobacillus bulgaricus, Lactobacillus acidophilus, Lactobacillus casei*). In case of cultivation of lactic microorganisms for ferments the special dairy environment with active growth factors of bacteria is used. Cultivation of lactobacilli in this sphere not only allows to adapt them for the subsequent souring of milk in a production process of fermented milk products, but also increases efficiency of souring, reducing a log phase to 30 min. At the expense of its risks of development of pathogenic microflora are minimized that guarantees high degree of safety – microbiological purity of products. Using the listed ferments and dairy components, available to our region, at department of biotechnology researches on development of a compounding and technology of dairy drink matsun are conducted.

AZOTOBACTER CHROOCOCCUM BIOLOGICAL PREPARATIONS INFLUENCE ON THE PLANTS GROWTH

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Introduction. Bacterial species Azotobacter chroococcum is a typical member of free-living soil microorganisms, that are nitrogen fixers. They have a pronounced antagonistic activity against wide range of phytopathogenic microorganisms, and are characterized by a number of positive effects on the plants development. Biological products derived from this bacteria designed to improve crop yields and increase plants resistance to various diseases. Such preparations are an integral part of modern agricultural activities, agrobiotechnology and microbiology. These preparations are used to increase phytobacteriology nitrogen-fixing symbiosis capacity implementation in agrocenoses.

Aim. The aim is to study the effect of biologicals containing Azotobacter chroococcum on the pumpkin plants growth parameters.

Materials and methods. We used a biopreparation Azotophyte-r® (manufacturer: private enterprise"BTU-Center"Ukraine, Vinnitsa region, Ladyzhyn) and studied the effect of Azotobacter chroococcum pure cultures, isolated from it, on pumpkin variety Hokkaido seeds germination, germination energy and growth of seedlings. Research methods – microbiological, laboratory agrobiological and statistical.

Results and discussion. Object of the study is pumpkin variety Hokkaido. Pumpkin flesh has a stable consistency, contains a large amount of beta-carotene (provitamin A), vitamins B1, B2, B6, C, E, folic acid, magnesium, iron and phosphorus. Biopreparation Azotophyte-r® contains Azotobacter chroococcum cells and micro - and macronutrients, enzymes, amino acids, vitamins, phytohormones. To biologicals obtaining Azotobacter culture was grown on solid Ashby medium, over 96 h at $(29\pm1)^0$C, pH 6,8-7,0. The living culture suspension was standardized by the viable bacteria number. Germination energy and seed germination, seedlings mass and linear growth parameters were calculated according to GOST 12038-84.

Conclusion. The plants nitrogen nutrition efficiency is due to forms of nitrogen compounds and the conditions of their application. Currently to enrich the soil with nitrogen and increase plant yield new harmless to human health and environment biological preparations are used. The results obtained in the study can be used for the bio-fertilizers and biologicals quality improving in olericulture.

STUDY OF THE AGARICUS BISPORUS STRAIN A-15 GRAIN SPAWN OBTAINING METHOD

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Introduction. The basidiomycetes species Agaricus bisporus cultivation relevance is their high nutritional value. Chemical studies show that the mushrooms have a large amount of easily digestible nutrients. Due to the high content of proteins (64.66 % of the total proportion of PFC (the ratio of proteins, fats, carbohydrates)), mushrooms can be compared with the meat quality. Mushrooms contain 18 amino acids of the known 22. The mushrooms benefit is that they also contain no less important for proper functioning of the human fats and carbohydrates (1 gram of fat and 0.1 gram of carbohydrates in 100 g fruiting bodies). The quantity of minerals and vitamins (percentage daily intake per 100 grams: vitamin B2 25 %, vitamin B5 - 42 %, vitamin PP - 28 %, potassium - 21.2 %, phosphorus - 14.4 %, iodine - 12 %). Mushrooms are similar to the fruit, and the phosphorus content brings them to several types of animal products such as fish. Japanese researchers found that the mushrooms in high quantities amino acids such as lysine and arginine that have a beneficial effect on the development of mental abilities and memory. The protein from fungi is digested for 70-80%. Thus, the mushrooms chemical composition shows that their nutrients content is not less than the other necessary for complete nutrition products, and certain nutrients in the mushrooms are even more. The mushrooms biological value the high minerals, vitamins, essential amino acids content. Physiological value is due to the presence of BAS (biologically active substances) of the antibiotic nature, and extractive substances that promote gastric secretion.

Mushrooms have medicinal properties. Mushrooms can purify the body, remove heavy metal salts. Also the mushrooms consumption can reduce cholesterol level and prevent atherosclerotic plaque formation. Studies shown that people who frequently consume these mushrooms blood cholesterol is below 34% compared to those who do not eat mushrooms. Therefore the risk of developing heart attack and atherosclerosis reduces. Low caloric value mushrooms can be used in various slimming diets. While a person does not lose the necessary vitamins and other nutrients. The healing properties are preserved in the dried mushrooms. They can be consumed to those who have stomach ulcers and hepatitis.

Methods of biotechnology allow to obtain high yields of this valuable food product.

Aim. The aim of this work is to study the Agaricus bisporus mycelium cultivation technology and growth speed in order to obtain grain spawn.

Materials and methods. The object of the Agaricus bisporus strain A-15 mycelium, which was isolated from compost mycelium of commercial production. Research methods - cultural, microscopic, and photographic documentation of the obtained results.

Results and discussion. When mushrooms are grown up compost or grain spawn are used as a seed material. Grain spawn is a boiled and sterilized grain, developed by pure culture of the fungus. Grain mycelium is suitable for most fungi reproduction and also has a good nutrients supply. Compost mycelia is compost (the result of biological oxidation of the mixed organic materials with added to them mineral substances such as phosphorus, nitrogen), seeded with mushrooms mycelium, obtained in an artificial environment. The fungus strain A-15 matrix culture was obtained in laboratory conditions on the Wort agar medium and its morphological and cultural characteristics were studied. It was established that the mycelium hyphae appearance is like a fluffy thread of white color. The structure of the mycelium is in the form of hyphae growing in a chaotic direction, hyphae have septate structure. The mycelium has an active grows at $(24\text{-}26)^0$ C on Sabouraud and wort agar. The growth rate of mycelium, which was determined by linear measurement, is 1.5 cm/day.

The grain spawn preparing method is consists of several stages.
You must boil the grain (wheat or another cereal culture) with its subsequent drying. Add gypsum and chalk to control pH and prevent grain adhesion. Prepared grain is placed in 0.5 l capacity and is sterilized at 0.5 atm pressure and 121^0 C for 20 min.

The prepared substrate is inoculated by the mushroom pure culture. Cultivation should be carried out in the dark at ambient temperature $(24\text{-}26)^0$C to fully exploit substrate by the mycelium. During cultivation of container-growing mycelium periodically review is needed. When green, brown or orange fungal contaminants at the grain stains are detected, such containers should be immediately removed from the thermostat for repeated sterilization in the autoclave at a pressure of 2,0-2,5 atm for two hours. After receiving the mycelium should be stored at a $(4\text{-}5)^0$C for 6 months (optimal retention time is 3-4 months).

Conclusion. As a result of the work in the laboratory condition the Agaricus bisporus strain A-15 mycelium pure culture was obtained on the solid nutrient medium, and the method of grain spawn obtaining was studied. This practice opens the prospects for further laboratory research in the field of basidiomycetes cultivation for the optimal grows conditions, storage time and the yield of mycelium identification and the isolation and the biologically active metabolites activity estimation methods selection.

THE FERMENTED BEVERAGES BASED ON HONEY

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Nowadays, the consumption of fermented drinks from unconventional raw materials is gaining popularity among the population. A special place is drinking honey – fermented beverage based on honey, which positively affect the health of the human organism through biological active substances. The main ingredient, honey, contains the following useful ingredients: invert sugar (fructose up to 54%, glucose - to 44%); organic acids (formic, malic, grape, pyruvic); proteins; enzymes; mineral substances; vitamins (group B, ascorbic, pantothenic, folic acid). Chemical composition of honey depends on its origin (floral, mixed or honeydew), plant raw materials (lime, eucalyptus, coriander) and the climatic conditions of cultivation of melliferous plants. Also drinking honeys include aromatic raw materials: ginger (vitamins A, C, choline, gingerol); peppermint (essential oils, tannins); sage (alkaloids, camphor, flavonoids); galangal (gum, catechin) etc. For the preparation of liquid honey it is important the quantitative ratio of vegetable raw materials and water, which affects not only the sensory characteristics of the beverage, but also on the completeness of the fermentation of sugars, and the qualitative chemical composition of the finished product. "Poltorak" (the ratio of water and honey 1:2), "dvoynyak" (1:1), "troynyak" (2:1) and "quarter" (3:1) are distinguished among drinking honey. With the increase in the number of sugar-containing raw materials decreases the completeness of the digestion, and the duration of the process increases, which significantly increases the cost of the technology makes it economically advantageous. Thus, the most promising for the development of a new fermented beverage based on honey are patterns of production "troynyak" and "quarter", which include the preparation of water (heated to 40°C), weighing honey in an appropriate concentration, boiling (temperature of 80°C), making seed yeast, fermentation in anaerobic conditions, clarification, bottling and ripening in sealed containers within 3 months. This technology allows to obtain a fermented beverage, rich in bioactive ingredients and contains 12% to 14% ethanol. Important technological aspect is the choice of the type and quantity of seed. Traditionally, for the manufacture of drinking honeys used baking yeast *Saccharomyces cerevisiae*, however, today in the market there are preparations of active dry wine and cider yeast, which are interested for exploring the possibility of obtaining on their basis of drinking honey. Therefore, at the Department of Biotechnology of NUPh the influence of inoculum on the qualitative characteristics of drinking honey is conducted.

ANALYSIS AND RISK ASSESSMENT OF THE CURD DESSERT'S PRODUCTION

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Milk and milk products are provided to implement must have high quality and meet the requirements. At the moment, the requirements for the quality of the food product and the control of all stages of its production are regulated by the HACCP standard and ISO 22000 in Ukraine.

The subject of the research is a curd dessert, cream "Mashenka" 5.0% TM "Smachnenka". The purpose of the research is to study the quality indicators of the product and make sure that it meets the requirements presented above. A curd dessert, cream "Mashenka" 5.0% TM "Smachnenka" is a product of the yogurt-dessert group. It is produced in accordance with TU U 15.5-00447451-013-2003 "Virobi Sirkovi. Tehnichnyi umovi". It consists of low-fat cottage cheese, cream from cow's milk, sugar and flavor "Vanillin". This curd dessert is made by mixing low-fat cottage cheese with a creamy mixture (cream, sugar, flavor). After that, the product ripens during cooling to storage temperature. The product should be stored at a temperature of + 2° C to + 6° C in clean, dry, well-ventilated storage areas. Shelf life - no more than 12 days if the storage conditions are observed. After opening the consumer packaging product is not subject to storage. End-product is subjected to production control according to the following parameters: organoleptic, physicochemical and microbiological. The safety of the end-product is characterized by the absence of microbiological and physicochemical risks.

Microbiological risks: coliforms (not allowed in 0.01 g of product), *Enterobacteriaceae* (not more than $1 \cdot 10^2$ colony forming units in 1.0 g), *E. coli* (not more than 10 colony forming units in 1.0 g), pathogenic microorganisms, including bacteria of the genus *Salmonella* (not allowed in 25 g of product), *Staph. aureus* (not allowed in 1.0 g of product), *Listeria species* (not allowed in 25 g of product), *Listeria monocytogenes* (not allowed in 25 g of product), *B. species* (not more than 20 colony forming units in 1.0 g), *Ps. species* (not more than $1*10^2$ colony forming units in 1.0 g).

Chemical risks: toxic elements content, mycotoxins, radionuclides, hormonal drugs, antibiotics, genetically modified organisms.

According to the research and the results obtained, it can be concluded that the curd dessert, cream "Mashenka" 5.0% corresponds to the standards shown for its quality and safety, and therefore, is suitable for sale and eating.

GENETIC ENGINEERING METHODS OF ONCOLOGICAL DISEASES CURE

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Introduction. Oncological diseases is one of the biggest problem of modern medicine. This disease develops because of influence of strong ultra-violet and radioactive radiation, violations at the genetic level, complications of infectious diseases, effect of some chemical reagents, etc. Statistically in the world about 8200000 people annually die from this disease. It is about 13% of all death in the world. Annually in Ukraine about 90000 people die and 35% of them are people of working-age which die from cancer.

Aim. To study modern genetically engineered methods of fight against oncological diseases.

Results and discussion. Biotechnological medicines and methods against oncological diseases creation is very advanced for medicine. One of these methods is the IF therapy. Its biomechanisms of action are connected with simultaneous antiviral effect (activation of cellular genes), and immunomodulatory effect (ability to strengthen the HLA antigenes expression on cellular membranes and to increase the cytotoxic T- and NK-cells activity). IF therapy is useful against skin melanoma, prostate cancer, bladder, stomach, glial tumors. Such medicines as Realdiron, Viferon-Feron, Bioferon, Introferobion, Alviron, Alfarekin, Pegferon, Eberon Alpha R containing recombinant interferon are presented at the market of Ukraine. One more perspective method of cancer therapy is gene therapy. By means of gene therapy it is possible to exclude the tumor blood supply by introduction to blood cells the specific protein synthesis controlling therapeutic gene; by the p-53 gene modification in cells (the tumor suppression gene); the "self-liquidation genes" insertion to the patient cancer cells; the *ras* oncogene suppression (the known carcinogens mutation gene). Unfortunately, there are no the gene therapy medicines which were created by genetic engineering method in Ukraine. But in the world there are such recombinant oncolytic viruses containing drugs as Gendicine, OncoVex and Oncorine (produced at China).

Conclusion. Gene therapy and IF therapy are the examples how it is possible to force human immunity struggle against tumors by the biotechnological scientific achievements. Biotechnological and genetic engineering methods have broad opportunities for oncological diseases cure.

RESEARCH OF FERMENTED MILK ECOPRODUCTS

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Ecological products or organic food is food and agricultural industry, made without the use of synthetic pesticides, fertilizers, growth regulators, artificial food additives and without the use of genetically modified foods. To date, the market for organic products is rapidly growing worldwide, the use of is relevant and is gaining greater acceptance among different segments of the population. The advantages of organic food – is organic production, which ensures the traceability of every product at all stages of its production, from the field to the store shelf, healthy, the best flavor, no harmful substances. Considering consumer preferences, existing about organic products, are several of the most popular groups of products. According to the largest marketing agencies The Hartman Group about 65% of adult consumers of organic food give preference to organic fruits and vegetables, dairy products, baked goods and meat products.

The production of any organic product certification begins land (pasture). Land, pastures should be free of pesticides and chemicals. Such organic certification confirms that it has at least three years from the date of last use of agrochemicals and GMOs, and the land is no more harmful substances. After receiving the certificate of land a farm has the right to receive a certificate for the livestock. Then may initiate the preparation of dairy products. The technology of producing fermented milk products, traditional and organic food is no different. Dairy products – these are products obtained by fermenting milk, cream, buttermilk, whey, passed the compulsory heat treatment. The main feature of dairy products in the technology of fermentation. Used two ways: thermostat and reservoir. In the first case, the fermentation of milk and maturation of beverages are produced in bottles that are in the incubation chambers. In the second – fermentation, fermentation, ripening of the product occurs in a single container. The choice of method and parameters depends on the type of the resulting finished product.

The aim of this work is the comparative analysis of fermented milk, traditional and ecological products, namely yogurt 1% TM "Buttermilk" and ecoyougurt 1% Organic TM Organic Milk.

At the Department of biotechnology conducted a study on the organoleptic, microbiological and physico-chemical properties of these groups of dairy products and their comparative analysis with the aim of obtaining reliable data on the advantage of ecology organic food.

DETERMINATION OF THE PATHOGENICITY FACTORS OF STAPHYLOCOCCUS ISOLATED FROM SKIN

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Introduction. The urgency of the staphylococcus infections problem worldwide has been steadily increasing. Staphylococcus are members of the normal microflora, but their detection in the clinical material is not always objective evidence of their etiological role, because of the pathogenicity degree, wide variability under the antibiotics influence and the clinical forms of these infections extraordinary variety. Staphylococcus are the human skin microbiome important components. Staphylococcus aureus is the causative agent of skin infections and chronic dermatitis, from atopic dermatitis to acne.

Aim. To study the factors of pathogenicity of Staphylococcus and the features of their identification in clinical material.

Results and discussion. According to the Bergey's manual the genus Staphylococcus includes 48 species and subspecies. Staphylococcus are gram-positive microorganisms of spherical shape, 0.5-2.5 microns in diameter, immotile, form regular or irregular clusters in smears. Staphylococcus are facultative anaerobes, have enzymatic and respiratory metabolism, they are catalase-positive and oxidase-negative. Staphylococcus are permanent inhabitants of the skin and mucous membranes, therefore the diseases caused by them have the character of autoinfection or exogenous infection, with airborne, airborne, contact-household or alimentary mode of infection. There are a number of staphylococcus pathogenicity factors that change the microenvironment and create favorable conditions for the microorganisms growth and reproduction. They are: plasmacoagulase, fibrinolysin, DNAaza, hyaluronidase, lecithinase, β-lactamase. Anti-complementary activity is the ability to destroy complement, a natural factor of resistance. Antilysozyme activity is one of the factors that increase the bacteria tolerance to the serum lysozyme action in humans and animals. Anti-interferon activity is an autonomous property of microorganisms intended for targeted, specific inactivation of the human leukocyte interferon bactericidal fraction.

Conclusion. The importance of the problem of staphylococcal colonization of the skin and secondary infections in dermatology remains high.

The bacterial pathogenicity factors detection will help in-depth study the colonization resistance mechanisms in oder to increase the antimicrobial therapy effectiveness.

DEVELOPMENT OF TECHNOLOGY AND STUDY OF THE PROPERTIES OF SOLID CHEES ON THE BASIS OF THE "MEITO" FERMENT AND PROBIOTIC CULTURES

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Cheese is a nutritious food product that is derived from milk by enzymatic protein folding, the extraction of cheese mass followed by processing and maturing. Useful cheese properties are largely explained by its nutritional value. The composition of cheese includes vitally important and valuable for human proteins, milk fat, minerals, vitamins and extracts. The protein that is found in cheese is much better absorbed than the protein of fresh milk, and is also an integral part of biological fluids in the human body (blood, lymph), the most important component of immune bodies, hormones, enzymes. Vitamins of group B, have a beneficial effect on the hematopoiesis-B_{12}, B_1- increases efficiency, and B_2 promotes energy production and is a catalyst in the processes of tissue respiration. Extractive substances of cheese have a beneficial effect on the digestive glands, increasing appetite.

The purpose of this study is to obtain a solid cheese with probiotic cultures in the laboratory and study of its properties. To obtain a hard cheese an enzyme of plant origin "Meito" and leaven is used. "Meito" is a milk-coagulating enzyme, represents a specific protease, which in its amino acid composition is identical to a veal rennet enzyme. The given plant-derived enzyme is produced from a food fungus, then fermented on barley and dried by extrusion. Leavens are bacterial combinations, used for manufacture of dairy products. The composition of leavens includes lactic acid bacteria and rods, kefir fungi and many other microorganisms that promote fermentation and lead to milk fermentation. To produce cheese, two main types of leavens are used: mesophilic - prefer low temperatures - 25-30 ° C. This is the most common leaven for many cheeses, such as Cheddar, Manchego, Parmesan. The strains of mesophilic bacteria include bacteria such as, *Lactococcus lactis ssp lactis* and *Lactococcus lactis ssp.cremoris*. Thermophilic bacteria are bacteria that work best at temperatures of 30-40 ° C, but also survive at a temperature of 65 ° C. These starter cultures are most often used to produce cheeses with a high second heating temperature, for example Swiss cheeses. The thermophilic bacteria include strains of bacteria-*Streptococcus thermophilus*, *Lactobacillus delbrueckii ssp. bulgaricus* and *Lactobacillus helveticus*. As of today, the Department of Biotechnology studies the production of hard cheeses based on the enzyme "Meito" and probiotic cultures, and the study of their microbiological and organoleptic properties.

INFLUENCE OF CULTIVATION CONDITIONS ON ANTIMICROBIAL PROPERTIES OF MICROBIAL SURFACTANTS

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Introduction. The last decades saw an increase in pathogenic microorganisms' resistance towards established biocides, which stimulated on the search for new alternatives in antimicrobial preparations. According to, microbial surfactants are among such preparations. Due to their overall environmental safety, their applications can span medicine, agriculture and food production.

Microbial surfactants belong to secondary metabolites and are, as a rule, synthesized as complexes of similar substances (amino-,glyco-, phospho- and neutral lipids). Under different conditions of the producers' cultivation, the components ratios in the secondary metabolite complexes can change, which is followed by changes in their biological properties.

In our previous work we researched the influence of surfactants synthesized by *Rhodococcus erythropolis* IMV As-5017, *Acinetobacter calcoaceticus* IMV B-7241 and *Nocardia vaccinii* K-8 on phytopathogenic bacteria. It was shown that the survival of cells (105–107 in ml) of the *Pseudomonas* and *Xanthomonas* phytopathogenic bacteria was found to be 0–33% after treatment with surfactants of the IMV Ac-5017 and IMV B-7241 strains for 2 h (0.15–0.4 mg/ml). In the presence of *N. vaccinii* IMV B-7405 surfactants (0.085–0.85 mg/ml), the number of cells of the majority of the studied phytopathogenic bacteria decreased by 95–100%/

However, in the these work we had not studied the influence of producers' cultivation conditions on the biological properties of produced surfactants. Also, the literature contains fragmentary reports that some microorganisms under certain cultivation conditions can produce not only the surfactants, but other metabolites as well (enzymes, bacteriocins, polysaccharides, etc.). It is rather likely that the properties of such complexes of surfactants and other metabolites can differ from the properties of pure surfactants.

With this in mind, the aim of our current work was to research the antimicrobial against phytopathogenic bacteria properties surfactants synthesized under different cultivation conditions of *N. vaccinii* IMV B-7405.

Materials and methods. The main study object was the strain *Nocardia vaccinii* K-8, registered in the Depository of microorganisms of the Zabolotny Institute of Microbiology and Virology of NAS of Ukraine under the number IMV B-7405.

By the chemical nature, the extracellular surfactants of IMV B-7405 strain are a

complex of neutral, glyco- and aminolipids. We used phytopathogenic bacteria from the Ukrainian Collection of Microorganisms (UCM): *Pectobacterium carotovorum* UCM B-1095, *Pseudomonas syringae* pv. *atrofaciens* UCM B-1015, *P. syringae* pv. *coronafaciens* UCM B-1154, *Xanthomonas campestris* pv. *campestris* UCM B-1049. *N.vaccinii* IMB B-7404 was grown in liquid mineral medium, as a source of carbon and energy we added refined sunflower oil "Oleyna" (Dnipropetrovsk oil extraction plant), waste oil after frying potatoes and meat (the McDonald's network of fast food restaurants, Kyiv). The content of oil-containing substrates in the medium was 2% (v/v). The cultivation duration was 5 and 7 days. The following preparations were used for researches: preparation 1 – supernatant of culture fluid; preparation 2 – solution of surfactant, dedicated by Folch mixture extraction (chloroform and methanol, 2:1) from the supernatant of culture fluid (preparation 1). The water phase remained after the surfactants extraction was termed as preparation 3. The antimicrobial properties of surfactants were determined in suspension culture by Koch method and also by index of the minimum inhibitory concentration.

Results and discussion. It has been established that antimicrobial properties of surfactants depend on the nature of the carbon source in the medium (refined sunflower oil, as well as waste oil after frying potatoes and meat), the duration of the cultivation (5 and 7 days), the degree of surfactants purification (the supernatant of cultural liquid, purified surfactants solution) and the test culture type.

The highest antimicrobial activity was exhibited preparations 2 (solutions of surfactants synthesized on all studied growth substrates) than the corresponding preparations 1 (the cultural liquid supernatant). Thus, after treating test cultures of the phytopathogenic bacteria belonging to the genera *Pseudomonas, Xanthomonas* and *Pectobacterium* with preparation 2, their survival was 20–75, 38–71 and 44–85%, respectively. Be noted, regardless of the nature of the oil-containing substance and the degree of surfactant purification, increasing the duration of *N. vaccinii* IMV B–7405 cultivation to seven days was accompanied by production of the surfactants with more prominent antimicrobial properties against the phytopathogenic bacteria compared to the surfactants obtained if the producer was cultivated for only five days. The results are evidence that the most efficient antimicrobial agents are surfactants, synthesized when the strain IMV B–7405 was cultivated in the medium with waste oil after potatoes frying, for seven days: the MIC for the phytopathogenic bacteria under study, was 7–20 μg/ml.

Conclusions. We determined the dependency of antimicrobial properties of the surfactants not only on the degree of purification and type of the test cultures, but also on the nature of the carbon source and duration of the cultivation. The results confirm the necessity of studying the influence of the cultivation conditions of the producers of microbial surfactants on the biological properties of the compound.

A COMPARATIVE STUDY OF THE ANTIBACTERIAL ACTIVITY OF OINTMENT BASED ON DIPEROXYAZELAIC AND BENZALKONIUM CHLORIDE AND «PEROXYGEL 3%» PREPARATION

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Introduction. It is known that inflammation of the skin are accompanied by inflammation bacterial contamination and therefore require the use of antimicrobial prolonged action. This effect can be achieved by using external antimicrobial agents in the form of ointments, creams and gels. Azelaic Acid – natural saturated dicarboxylic acid, has a wide range of biological properties, is used in skin care products, mainly for the treatment of acne, reducing hyperfunction of the sebaceous glands, eliminating hyperpigmentation.

Hydrogen peroxide has almost universal antimicrobial action, which is related to its oxidative high resolution. Released as a result of microbial decomposition of H_2O_2 tissue proteases and reactive oxygen species (ROS) oxidize sulfhydryl and hydroxyl groups of proteins and lipids, causing the death of germs. Deadline specified time reducing background bacteria sensitivity to hydrogen peroxide and the emergence of drug-resistant variants of the bacteria. Further scientific research in the chemistry of hydrogen peroxide, improving its stability, combined processing facilities give hope to address the shortcomings of this valuable. Benzalkonium chloride (BzAlk) has bacteriostatic and microbial effect on gram in relatively large doses - in Gram-negative bacteria and candida. Used as an antiseptic to treat acne, folliculitis, seborrhea a concentration of 0.025-0.1%. So interesting was a development of new combined dosage forms for external application, which would combine the advantages of relatively stable organic peroxide and QAC.

Aim. The aim of the study was a comparative study of antimicrobial activity of the ointment based of our proposed new substance - diperoxyazelaic acid (nonanebis (peroxoic acid), hereinafter both **DPAA**) (HO_3C-$(CH_2)_7$-CO_3H) in the combination with benzalkonium chloride and European branded drug – «Peroxygel 3%» («GEMI» (Karchev, Poland).

Materials and methods. DPAA cyntecize the known method Sverna, mp. + 90-90,5ºS (with decomposition), active oxygen content (AOC) was 14.2%. Benzalkonium chloride, pharmacopeia purity is containing basic substance $C_9H_{13}ClNR$ 99. 0% (China). We studied ointment composition: 1.0 wt. % DPAA,

benzalkonium chloride 0.05% sodium edetate (0.01 wt.%), The rest - polyethylene oxide basis: PEO-400 (80 wt.%), PEO-1500 (20 wt.%). The product comparison «Peroxygel 3%» produced by Pharmaceutical Production Enterprise «GEMI» (Karchev, Poland), 15 g tubes (Series 011014). Composition of drug: 100 g product containing hydrogen peroxide 30% 10 g; Excipients: dynatriyedetat, poloxamers 407, 96% ethanol, concentrated phosphoric acid, peeled water. According to WHO to evaluate antibacterial and antifungal activity of drugs as a test culture museum used strains and clinical isolates (*Candida tropicalis*, *Candida krusei*, *Candida glabrata*). Microbial load was $1 \cdot 10^6$ colony-forming units to 1 ml of the nutrient medium.

Results and discussion. Comparative antimicrobial activity of the samples studied drugs given in a Table 1.

Table 1

Test culture	**Zones of growth inhibition test cultures mm (*n* = 3)**	
	Ointment with DPAA 1%, BzAlk 0,05%	**«Peroxygel 3%»**
St. Aureus ATCC 25923		55,5±2,6
E.coli ATCC 25922	28,4±1,2	59,0±1,1
Ps.Aeruginosa ATCC 27853	27,6±2,0	43,5±1,5
ATCC 6633	28,1±1,5	26,2±0,8
	36,2±0,8	36,6±1,4
	37,0±1,1	34,7±2,8
	36,1±1,2	35,5±2,5
Candida glabrata	33,2±2,2	24,6±2,2

Conclusion. New combination of ointments with DPAA 1% of benzalkonium chloride 0.05% based on PEO sufficiently high inherent antifungal activity and spore activity which almost not inferior to branded drug "Peroxygel 3%." Due to much lower levels in the API new processed ointment, it can be considered promising for further in-depth research.

MICROBIOLOGICAL METHODS FOR THE QUALITY OF DRINKING WATER MONITORING

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Introduction. Drinking water is water that is meant for daily unlimited and safe consumption by humans and other living beings. Its main source is natural water, which is subjected to purification and disinfection, passes the required stages of water treatment and water purification, which are necessary to obtain technical first, and then tap water. The main factors of drinking water pollution are microbiological, heavy metals and toxic substances, nitrates and pesticides. The problems of drinking water pollution can be solved by using modern biotechnological methods of purification. These include: bio-cleaning, the use of ion-exchange resins, modern biofilters. The drinking water biotechnological purification is the newest approach to protecting and human health promotion, as well as maintenance of environment.

Aim.To study the basic standards and methods for the drinking water microbiological quality monitoring, which are used in Ukraine.

Results and discussion. According to regulatory requirements, the main drinking water quality indicators include mechanical pollution, organoleptic objectives (including chemicals that affect the water or anoleptic properties),toxicological and epidemiological indicators (bacteriological, virological, parasitic contamination).Currently in Ukraine, the quality of water in centralized drinking water supply is regulated by the Laws and documents: "On ensuring sanitary and epidemiological welfare", "On Drinking Water and Water Supply", GSanPiN 2.2.4-171-10 "Hygienic requirements for drinking water, intended for human consumption".

Microbiological contamination of water arises from the unusually large number of microorganisms appearance in the environment. They can enter to the water supply system with wastewater the poor-quality filters usage. The microbial and viral drinking water contamination is very dangerous for human health, so bacterial and viral strains can cause salmonellosis, cholera, typhoid fever, dysentery, poliomyelitis, gastroenteritis, hepatitis A, etc.

According to normative documents, in Ukraine the drinking water epidemiological safety main microbiological indicators are: the total microbial count, the presenceof E. coli group bacteria, pathogenic Salmonella, Shigella, Enterococcus, somatic coliphages, enteroviruses, adenoviruses, rotavirus, reoviruses, Hepatitis A

virus antigens. According to epidemiological indications, tap water is tested for the Vibrio cholera presence.

Of the total microbial count determination is carried out by the method of deep inoculation into nutrient agar and all microorganisms visible colony calculation at a 2-5 fold increase that grew in the agar thickness and surface at (36 ± 1)°C for(24 ± 2) h or at (22 ± 1)°C for (48 ± 2) h.

Detection of the E. coli group bacteria is carried out by a membrane filtration method when a certain volume of water is passed through a 0.45 micrometers filter, which is incubated at (36 ± 1)°C for 24 h on Endo medium. Then the number of bacteria is count. A titration method (the most probable number) can also be used, in which the volume of tested water is inoculated into a storage medium (glucose-peptone, lactose-peptone), incubated at (36 ± 1)^{0}C, inoculated Endo medium and identified the grown bacteria.

The Salmonella detecting method consists in drinking water samples concentrating, two different nutrient media (selenite broth and magnesium medium) using preliminary and elective enrichment, inoculation on differential diagnostic media (Endo and Ploskirev) and microorganisms identification according to biochemical, serological properties and Salmonella O-bacteriophage sensitivity.

To Shigella testing the bacteria concentrating or accumulation in enrichment media (selective and bile broth), inoculation on differential-selective media (Endo, EMC-agar, Ploskireva, McConkey medium), followed by microorganisms identification by biochemical and serological characteristics is used.

The determination of coliphages, depending on the drinking water purity degree, occurs in a titration method (the coliphage accumulation in liquid nutrient media and the *E.coli* test culture lysis zones on nutrient agar detection) or by a more rapid direct method (direct inoculation by a single-layer agar method and the lysis zones on the test culture lawn counting).

Conclusions. Today the one of the main problems is the drinking water contamination, because it is necessary for human life, because the human body consists of 70% of water and is a source of various minerals and macroelements.

Biotechnological approaches for improving the drinking water quality are the use of new ion exchange and silt filters, new methods of coagulation and sedimentation, the quality monitoring methods employment.

At the Department of Biotechnology in cooperation with bacteriologists from the SI «Kharkiv regional laboratory center of Ministry of health of Ukraine» the centralized water supply sources drinking water quality in the city of Kharkov is investigated using microbiological control methods. The obtained results can be used in the formulation of recommendations on biotechnological treatment of drinking water from contamination.

SUMMARY OF THE MOBILE TECHNOLOGIES DEVELOPMENT FOR HUMAN HEALTH

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On average, people use phone for five hours a day. Moreover, users themselves are sure that they address device twice less. Besides, smartphone is already not just a phone: for example, a quarter of British users do not even ones a week exploit it in a traditional mode, i.e. for calls. Such intensive usage of phone has made it perspective and convenient device for constant monitoring of user's body state.

Applications serving not only to simplify communication or for entertainment, but also for education, health monitoring and even for diagnostics were created.

The purpose of the paper is the review of the perspective methods and ways of the mobile technologies application to the person everyday life and during the sport by the data from the literature.

First of all, we should mention that different mobile devices software benefit human health, and raise the level of its knowledge. Some applications allow to give important information to a certain group of people in an accessible form. In the modern world, such work is particularly necessary, since the gap between real scientific knowledge and the level of awareness of ordinary people is great.

In addition to informing about scientific achievements mobile devices are able to collect and process data about the user himself. One of the most famous classes of devices that may be connected to the smartphone are fitness trackers, such as Jawbone UP and Fit-Bit. The pedometer is already part of some smartphones. In the steps, exactly, many health organizations set the minimum level of necessary physical activity today. Such devices and applications allow to control the amount of physical activity of the user.

Special place in new technologies is assigned to professional athletes and just to fans of physical activity. Nowadays, the technique can register the individual endurance, and achievements of individual athletes and the teams in the whole. In addition, devices help physicians to control physical exercise and activity to improve athletic performance. Traditionally, these are already mentioned pedometers, accelerometers and gyroscopes, devices with built-in GPS-

receiver for recording motion, as well as various sensors for recording physiological characteristics, such as heart rate, temperature, etc. Today, new devices are added here, such as a sensor that determines the loss of fluid during training.

However, in addition to improving the physical form and effectiveness of training, scientists have another purpose, the minimization of trauma. For example we mention here sneakers with microdevice from the Spanish Institute of Biomechanics of Valencia (Instituto de Biomecánica de València) and the shoe production company KELMĖ.

The equipment can "teach" the user the correct technique of running and thus prevent potential trauma. The integrated microelectronic measuring system collects the biomechanical parameters that characterize the runner's technique during the passing of the distance, and wirelessly transfers it to a mobile phone. The mobile application itself processes the data in real-time, sends alerts about changing the running style, if necessary, and even requires to stop the run if the probability of trauma is very high. Combining obtained characteristics with the readings of the pulsometer, one can track the level of the athlete fatigue. Finally, the program is also able to operate as a social network. Fans of physical activity will be able to exchange experiences and useful information.

So, in this paper the mobile technologies used in everyday life of a person and in sports are studied. Part of the technologies is informational, i.e. they are called to inform people about scientific achievements. Part of the technologies collects and processes information about the user, thereby allowing the users, for example, monitor their health in a better way. And part of the technologies is designed to preserve health and even life by minimizing the risk of traumas.

In order to be successful, applications and devices must satisfy a number of requirements: be small in size, inexpensive and consume little energy. In addition, it is necessary to properly motivate the person to use it. It can be concluded that nowadays mobile technologies are ones of the most actively developing and promising.

PERSPECTIVE OF USING BACTERIOPHAGES

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In connection with the growing resistance of microorganisms to antibiotics and the problems of selecting antibacterial drugs that arise against this background, bacteriophages have prospects as antimicrobial therapy. The use of antibiotics is accompanied by a violation of the composition of normal microflora, allergization and adaptation of microorganisms to the environment. A distinctive feature of bacteriophages as therapeutic agents is the almost complete absence of side effects, which allows them to be prescribed to patients of different age groups, pregnant without any restrictions. Depending on the bacteriophage species, various processes with contractile proteins, spines , Basal plates. The shape of the bacteriophage-icosahedral, spherical, lemon-shaped, pleomorphic depends on the capsid. The phages are exclusively intracellular parasites, since they do not have mechanisms for producing energy and ribosomes for protein biosynthesis. Phages have strict specificity, i.e. Are capable of parasitizing only in a certain form of microorganisms: streptococci, staphylococci and others. Phages with more stringent specificity, which are parasitized only by certain representatives of this species, are called typical phages. The phages that lyse organisms closely related species, such as species belonging to the genus agents of dysentery (Shigella), called polyvalent. Underlying their actions are natural physiological mechanisms of interaction between phages and bacteria can be predictive of both the infinite variety of bacteriophages and their possible applications. Due to their merits, bacteriophages have found wide application in medicine and agriculture. Preparation containing bacteriophages effectively struggling with lung and urogenital infections with pyogenic diabetic foot ulcers, pathogenic bacteria of the gastrointestinal tract, without violating the person's own microflora. Also phages successfully cope with drug-resistant microbial films, which are formed in chronic otitis and using prostheses. Bacteriophages may make a worthy substitute antibiotics as able to fight even with antibiotic-resistant microorganisms. At the moment, the development and production of phage-containing products are carried out by Biopharm (Georgia), Pharmaceuticals AmpliPhi Biosciences (USA and UK), GangaGen Biotechnologies (USA and India), Intalytix (USA), Micreos (Netherlands), Phage Biotech (Israel), FSUE "NGO Microgen "(Russia), Prio" Biopharma "(Ukraine). At the Department of Biotechnology, work began with checking the antimicrobial properties of the drug with a bacteriophage.

MODERN ASPECTS OF USING BACTERIOPHAGES

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Nowadays the increase in distribution of an antibiotic steady activators which received the name of epidemic of resistance is noted. According to WHO data already more than 60% of activators are steady against the basic antibiotics, and in 10-20 years most of them will gain resistance to germicides. Use of antibiotics and other germicides can be a little effective and is often followed by disturbances of normal microflora what can lead to formation of immunodeficiency and allergization. The basic causes of antibiotic resistance at microorganisms can be considered: absence of structure which the antibiotic affects; impermeability for antibiotic (the majority of Gram-negative bacteria are unreceptive to Penicillinum as the cellular wall is protected by an additional membrane); ability of microorganism "to extort" antibiotic from a cell; ability of a microorganism to transfer antibiotic to inactive form. At this conditions one of effective components of fight the formed antibiotic resistance is development of alternative antibiotic drugs. Bacteriophages can act as such drugs. Bacteriophage – is a virus which is selectively affects bacteria. Specificity of phages is the cornerstone of their name on patrimonial or specific accessory of bacteria, sensitive to them. There is a bacteriophage staphylococcal, streptococcal, salmonellae, pyocyanic and others. In order the bacteriophage could be recommended for use in clinical practice, it is necessary, its compliance to the following parameters: the high virulence causing a full lysis of bacteria; — conservation of activity in cell owner; the possibility of long storage with conservation of lytic activity; lack of activity concerning representatives of a resident microbiota. Bacteriophages are issued as in form of monomedications and in the form of the combined medications. Medications of bacteriophages possess a series of advantages: highly effective biological medications of antibacterial action for prophylaxis and treatment of infectious diseases; during use don't break normal biocenoses of the person; are irreplaceable in case of fastness of originators of infections; can be applied in complex therapy with other medicines; can be applied at treatment of dysbacterioses in a complex with medications normalizing an intestine microbiota; are safe in pediatric practice; are highly stable and can be stored during rather long period of time. Efficiency in use of bacteriophages consists in lack of contraindications and complications, compatibility with other medications, active impact on antibiotic-resistant microbes. Thanks to these properties, bacteriophages are estimated as future medications for successful fight against infections.

THE CHAMPIGNON CULTIVATION AT HOME

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Introduction. Mushrooms have become very popular in medicine, cosmetology and cooking. Currently difficult to imagine our life without this extraordinary product. Humanity has found usage of all, the selection of mushrooms is very diverse, but the most available to the public are champignons. It is possible to buy champignons or to them without any problems.

Why these fungi have gained such fame? They are often used in slimming diet, because fungi contain proteins, vitamins and minerals.

Aim. To study the conditions of growing mycelium in compost and get a harvest of edible champignons at home.

Materials and methods. We used the commercially prepared planting mycelium strain A-15. Mushrooms grown in the private cellar, which was previously subjected to disinfection. We created the necessary parameters of temperature, humidity and air circulation. Crop capacity determined by fruit bodies weighing.

Results and discussion. According to the information that manufacturers provide us the purchased champignon mycelium strain A-15 has a high yield. This strain requires a large amount of fresh air during fruiting, also the quality of the substrate plays an important role. In the beginning the mushrooms growing correct conditions were created. The optimum temperature for the fruiting bodies development is (14-16)ºC.

In our experiment the cellar was equipped with thermometer and hygrometer to measure temperature and humidity. The temperature during the cultivation ranged within (15-19)ºC. Aeration was carried out through ventilation. Humidity was 80%, the level ensured by periodic spray of clean water. The mycelium began to form fruiting bodies.

The first fruiting bodies appeared about 7 days after coating the substrate by rich black soil. Since the scale of cultivation was minimal, during the 30 days three harvest waves were collected, with each wave of 300-400 g of mushrooms. Fruit bodies were correct shape, density and color corresponding to the strain A-15 characteristics.

Conclusions. The champignon cultivation at home is not only interesting, but profitable work. Creating the correct mode of temperature, humidity, ventilation, light and enrichment substrate providing will expand the scope of work to the maximum and will result in a substantial yield of fruiting bodies of fungi, useful for consumption.

BIOTECHNOLOGICAL METHODS OF BIODEGRADATION OF PETROLEUM

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Introduction. Before mankind the largest problem of destruction of natural ecosystems under the influence of the biosphere contamination with crude petroleum and products of its processing emerged. The reasons for this are: a large number of accidents involving trucks carrying oil and oil products; reset enterprises uncleared waters containing petroleum products. Currently, the biotechnology that has made a big step in the biodestruction drugs development can help to alleviate problems with spills.

Aim. To study the range of hydrocarbons biodestructors products available on the market of Ukraine. To examine microbial structure and transforming potential of the biosorbent "Ekolan - M".

Results and discussion. The range of biologics destructors in Ukraine at the moment is quite large. It includes biological preparations "Ekolan - M"; "Econadin"; "Ultracet"; "Hydrocarbon treat granular"; "Desna"; "Lestan".

We chose the biosorbent – "Ekolan - M", developed by the D.K. Zabolotny Institute of Microbiology and Virology of the NASU. Its sorption capacity is 6-8 kg of hydrocarbons/kg, the ability to retain oil is around 99%. State sanitary - epidemiological examination showed that the preparation meets all the requirements of the current sanitary legislation of Ukraine, has medical and hygienic, toxicological and ecological contraindications. This does not require recycling from the application site after use. The sorbent is able to detoxify a fairly wide range of hydrocarbons: crude petroleum, fuel oil, mineral oil, diesel and aviation fuel, gasoline, kerosene and other petroleum products. The final products of disintegration are environmentally neutral compounds. The selected biosorbent is the most effective and safest of all available biological preparations in Ukraine. The ability to degrade petroleum products bacteria of the species Acinetobacter calcoaceticus, Rhodococcus erythropolis, Nocardia vaccinii have. They are cultured on mineral nutrient media with hydrocarbons.

Conclusions. At the Department of biotechnology in The National University of Pharmacy we conduct research in biotechnology of microbial composition, the optimal methods for biological preparation microorganisms growing. The sorbent "Ekolan - M" effectiveness against various types of hydrocarbon pollutants is being studied. It is possible to apply the results obtained in order to improve the technology of hydrocarbon xenobiotics biodegradation.

THE ROLE OF *ACINETOBACTER CALCOACETICUS* IMV B-7241 SURFACTANTS IN BIOFILMS DESTRUCTION

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Introduction. The surfaces colonization by bacteria and further formation of the biofilms in food industry and medicine can cause not only the products damage, but also the spreading of infectious diseases that endanger the consumers' health. The most synthetic disinfectants do not penetrate deep into the biofilm; hence, disinfection is only partial.

It is well known from the literature that microbial surface-active substances (surfactants) can not only prevent adhesion of microorganisms on biotic and abiotic surfaces, but also destroy already formed biofilms on them.

Aim. Before it was found out that *Acinetobacter calcoaceticus* IMV B-7241 surfactants had possessed antimicrobial activity and antiadhesive properties. The purpose of this paper is an investigation ability of *Acinetobacter calcoaceticus* IMV B-7241 surfactants to destroy bacterial biofilms.

Materials and methods. *A. calcoaceticus* IMV B-7241 was grown in a liquid mineral medium containing ethanol, *n*-hexadecane (2%, v/v) and glycerol (1%, v/v). Such preparations of surfactants were used in studies: preparation 1 – supernatant of culture liquid; the surfactant-containing supernatant was subjected to extraction with the 2:1 chloroform/methanol (Folch) mixture to isolate the surfactant (preparation 2). The destruction degree of test-cultures (*Bacillus subtilis* БТ-2, *Escherichia coli* IEM-1, *Staphylococcus aureus* БМС-1) biofilms, pre-formed on holes of polystyrene immunological plate, was determined by spectrophotometric method.

Results and discussion. The experiments have shown that all synthesized surfactants at the concentration of 0.04–1.28 mg/ml can destroy the bacterial biofilms, regardless of the carbon sources nature (ethanol, glycerol, *n*-hexadecane) in the cultivation medium of *A. calcoaceticus* IMV B-7241 and the degree of purification (supernatant, surfactant solution). Thus, *A. calcoaceticus* IMV B-7241 surfactants destroyed the biofilm of *S. aureus* БМС-1 by 21–88%, and the destruction increased with the increase in surfactant concentration (Table 1). The highest degree of biofilm destruction of the *S. aureus* БМС-1 (88%) was obtained with 1.28 mg/ml solution of surfactant synthesized on *n*-hexadecane. At the concentration of 0.04 mg/ml we already observed destruction of the biofilm of the test culture by 54 and 58%, respectively.

Table 1

Effect of *A. calcoaceticus* IMV B-7241 surfactants synthesized on various substrates on the destruction of *S. aureus* БМС-1 biofilm

Carbon source in medium	Preparations	Test culture biofilm destruction (%) after treatment with surfactant of certain concentration, mg/ml					
		0.04	0.08	0.16	0.32	0.64	1.28
Ethanol	Supernatant	21	25	27	31	38	42
	Surfactant solution	31	35	46	50	54	54
Glycerol	Supernatant	31	42	54	58	62	65
	Surfactant solution	42	50	54	56	58	62
n-Hexadecane	Supernatant	54	58	61	62	69	73
	Surfactant solution	58	65	67	69	73	88

Further research showed that unlike of *S. aureus* БМС-1, biofilm of *B. subtilis* БТ-2 and *E. coli* IEM-1 were more efficiently destroyed by surfactants (0.04–1.28 mg/ml) synthesized on ethanol. Thus, the maximal degree of biofilm destruction of test cultures after treatment with surfactant solution (1.28 mg/ml) was 86 and 53%, respectively.

Should be noted, that surfactants synthesized by strain IMV B-7241 were more efficient destructors of bacterial biofilms compared to rhamnolipids of *P. aeruginosa* LBI and surfactin of *B. subtilis* RT7, which supports the possibility of using them as novel disinfectants to eliminate bacterial biofilms. Thus, using of *P. aeruginosa* LBI rhamnolipids and *B. subtilis* RT7 surfactin accompanied by bacterial biofilms destruction not more than 63 and 58% respectively.

Conclusions. The capacity of *A. calcoaceticus* IMV B-7241 surfactants to destroy already formed bacterial biofilms has been determined. The degree of biofilm destruction practically did not depend on the purifying degree (supernatant, surfactant solution) but depended on carbon sources nature. The obtained data certify the possibility to use microbial surfactants in creation of new effective disinfectants.

STUDY OF THE LICHENS ANTIMICROBIAL ACTIVITY

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Introduction. In recent years the interest in herbal medicines significantly increased. Medicinal plants do not have a harm, have a softer effect, less toxic, non-addictive and allergenic, with no side effects, which are their advantages over synthetic crude drugs. At the present time to enhance medicinal plant raw material resources very little-studied objects, include lichens, which variety is more than 26000 species worldwide, has been used. Lichens produce secondary metabolites with strong antimicrobial effects – lichen acids, the most important among which are usnic, barbatinique and squamatic.

Aim. The aim of our study was to determine the antimicrobial properties of extracts obtained from lichens, growing in Kharkiv region.

Results and discussion. Among lichens growing in Ukraine, the genera Cladonia, Usnea, Lecanora, Ramalina, Evernia, Parmelia, Alectoria are well-known by their medicinal properties. The genera Evernia and Parmelia (family Parmeliaceae) are most often found in Kharkiv region. Evernia has a bushy thallus and grows primarily on the oak trunk and branches. Parmelia has foliose thallus, grows on the deciduous and coniferous trees trunks and branches. We studied Parmelia sulcata and Evernia prunastri, which were collected in the autumn in the National nature Park "Gomolshanskie Lesa"recreational area. For species identification we investigated the thallus, fruit bodies, organs for substrate attachment morphology and anatomy and biochemical properties.

The lichens antimicrobial activity is determined by gram-positive and gram-negative microorganisms test cultures growth inhibition identifying. It is a result of secondary metabolites action. Research are carried out by the agar diffusion method. Quantitative parameters are tested by the serial dilution method. For the antimicrobial properties studying the water and alcohol extracts of lichen materials are used. Maceration is carried out with 40% and 70% ethanol, the ratio of dry lichen and extractant is 1:7, temperature is (27±2)0C, infusion period is 24 h. The aqueous extraction conditions are: the dry crushed raw materials and water ratio 1:5, boiling water bath for 15 minutes, water digestion at (22±2) ^{0}C during 45 minutes, percolation.

Conclusion. At the present time the problem of bacterial infections development is still relevant in medical science. The national medicine and pharmacy are in great need in drugs having the antimicrobial activity. The lichens antimicrobial activity study enables the new effective and safe drugs creation.

IMPORTANCE OF USING DAIRY PRODUCTS AND INCREASE THEIR RANGE BY PRODUCTION OF NEW – KUMYS, TAN, MATZOON

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Dairy productions are enough used in the population, because it contains beneficial lactic acid bacteria. Recently, these products are becoming more popular because they have diabetic and treatment-preventive properties; they well assimilate by the organism and have a pleasant taste and aroma.

Subject of dairy products is now urgent and widespread, because they can normalize intestinal microflora and metabolism, can strengthen immunity, improve digestion, and be able to remove toxic substances from the organism. In addition, lactic acid bacteria can produce vitamins such as B1, B2, C, and antibiotics which inhibit growth and development of pathogenic bacteria. Dairy products are recommended to use for dysbiosis, constipation, heavy metal poisoning and are used for treatment with antibiotics.

In Ukraine, dairy products are widely used; it’s used as by children as by adults, so study the expansion of the range and development alternative methods of production are an important step. As the products are demanded in the consumer market not only in Ukraine but also in the whole world, manufacturers constantly expand the range of dairy products. For example, for producing is used not only natural cow's milk also sheep’s and mare’s milk.

Therefore kumys, tan and matzoon are very popular today. These milk drinks are similar. It has such useful properties: to improve and increase the appetite, to normalize the intestine work, to accelerate digestion, to tone the body, to reduce the level of cholesterol and sugar, to protect from possible formations of kidney stones, to lower weight, to protect from cardio-vascular diseases. For making these productions are used leaven with combined or bioactive natural microorganisms of different seasonings and various spices. Kumys, tan, matzoon are used in diabetic nutrition and to support normal life activity. These dairy products can purify and rejuvenate the organism.

So, fermented milk products have a lot of useful properties which have positive influence on the body and life activity; available to the public; not need specific condition for cultivation and production; are common on food markets in Ukraine and in the world.

Therefore, the Department of Biotechnology develops new varieties of fermented milk products with treatment and preventive properties.

GENETIC ANALYSIS OF OLEATE CONTENT IN CORN OIL

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Introduction.Vegetable oils with high content of glycerides of oleic acid provide the normalization of blood pressure, reduce the intensity of peroxidation and thrombus formation, the aging of cells and the development of oncological diseases, precipitate the healing of the damaged tissues and prevent the bile duct dysfunction. So, high oleic oils are widely used in pharmaceutical practice and the demand for them is constantly increasing.

Olives are the traditional source of oil of the above type, the content of oleate in the neutral lipids of olives is about 80%. However, olives can be grown only in certain geographical areas but Ukraine does not belong to such areas. It causes the necessity to develop own import-substituting sources of high oleic oils.At present the forms of sunflower that contain up to 90% oleate in the oil, rape with the content of oleate up to 70%, soya and mustard with the content of oleate up to 40 % that is 1,5 -3,5 times higher than in the traditional forms of the above plants have been identified in the Ukrainian genetic collections. However, special attention should be paid to the forms of corn – carriers of endosperm mutations as the potential sources of high oleic oils. It has been found out that mutant genes of endosperm structure arespatially coupled with oleate-coding locuses and the carriers of su1 and sh 2 mutations have the highest content of oleate in the oil (up to 40%).Another advantage of the use of the above endosperm mutants is that they allow to combine high quality of oil, protein and carbohydrates.

Aim of the investigation. The aim of the investigation was to conduct the genetic analysis of the effect of endosperm mutations su1 and sh 2 to develop raw sources of high oleic corn oil for pharmaceutical use.

Materials and methods. A series of unrelated by origin lines of maize–carriers of monogenic mutationssu1 and sh 2 (10 lines of each type) with trustworthy registered useful effect on the content of oleate in oil has been taken for the investigation. The genetic analysis of oleate content has been conducted on a series of hybrids produced from diallele crossings of Griffing's second method between the lines with identical allele condition of mutant genes su1 and sh 2 (6 lines in each system of crossings). The effects of nonallelic interactions of su1 and sh 2 genes with other genes of endosperm structure have been analyzed on a series of the carriers of paired combinations of these genes with mutant genes o2, sh1, su2, aeand wx.

Fat and acid composition of oil has been analyzed by the Peysker's modified gas and chromatographic method. The obtained results have been subjected to the statistical treatment by the methods of disperse, multidimensional and diallelic analysis for 95% probability level with the use of the packet of applied statistical programs "OSGE". Heyman'salgorhyme has been used to interpret the results of the diallelic analysis.

Results and discussion. It has been found out that the effect of the increase in the content of oleate in the corn oil by mutant genessu1 and sh 2 significantly modify polygenic complexes and the content of oleate in the carriers of these mutations has quantitative nature. It ranged from 23,9 to 27,2% in the lines of common maize, in the lines – carriers of mutation su1 - 37,6 – 42,8% and in the lines – carriers of mutation sh 2 - 34,8 -40,55%. When making genetic analysis of the sign it has been revealed that the system of regulation of high content of oleate approaches to Heyman's additive and dominant model. The incomplete dominance with thesignificant contribution to the dispersion of additive effects was the predominant type of the study of high content of oleate. The inbred lines of maize on the basis of one endosperm mutation differed from each other by the effects of the combined ability as for oleate content and the level of oleate content in the best hybrids exceeded 44%.

In some cases synergic increase in the content of oleate has been revealed at nonallelic interactions of genessu1 and sh 2 with other endosperm mutations as compared to monogenic mutants and the best combinations of endosperm mutant genes provided the content of oleateat the level of more than 46%.

Conclusions. The content of oleate in the oilof the carriersof corn mutationssu1 and sh 2 has qualitative nature and the effect of these mutations on the content of oleate is greatly modified by polygenic complexes. The incomplete dominance with the significant contribution to the dispersion of additive effects was the predominant type of the study of high content of oleate. The significant increase in oleate content in corn mutations can be achieved by the use of the effects of gene : genotype interaction as well as by nonallelic interaction of mutant genes su1 and sh 2 with other mutant genes of endosperm structure.

THE PERSPECTIVE OF DEVELOPMENT OF TECHNOLOGY OF NEW FUNCTIONAL FOOD

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In the last decades biotechnologists conformities to law of forming and functioning of microbal associations attract attention all anymore. The study of conformities to law of forming of structure and functioning of associative microbal cultures has a general biological value, as idea about the mechanisms of organization of the natural stable biological systems is extended, and also is basis for development of technology of creation and practical management by valuable microbal associations, for providing of their stability and high activity. One of such morphological executed stably functioning associative cultures of microorganisms is kefir fungus. Kefir fungus is complex symbiosis of a few types of the microorganisms, presented by different bacteria and fungi, appearing as a result of the cooperative existence. They have a certain structure and behave biologically as large as life organism, which grows, divides and passes the properties and structure to the following generations. By appearance kefir fungus looks like getting soaked rice or grainy curd. It has white color with a small mother-of-pearl ebb. Living kefir fungus has a wrong form strongly plicate or scabrous surface; kefir granes are resilient, softly-gritly; the sizes of them can hesitate from a 1-2 mm a to 3-6 cm and more. Kefir fungus is the object of active researches, firstly, as producer of the widely used sour-milk products, possessing a high biological value, and also as a model of the folded, stably functioning associative structured evolutional culture, that is produces polysaccharides. Kefir fungus executes a structure-forming role, possessing a immunomodulatory, antitumoral, antiinflammatory, wound healing and antimicrobial action and can be used in medicine, in cosmetic and food industry. A basic microflora consist lactic acid bacteria, yeasts, acetic acid bacteria and aromatherapie microorganisms. Despite numerous studies of microflora and properties, nature of kefir fungus still remains unknown. Thus kefir fungus is a prime example of biological symbiosis at once a few types of microorganisms, that is a necessary component for the receipt of high-quality sucklings drinks for a functional feed. To date a few types of drinks on the basis of kefir fungi, containing vitamins, organic acids and other bioactive substances, are known. However, the assortment of them limits, therefore on the department of biotechnology work is conducted on development of composition and technology of medical and preventive food stuff on the basis of kefir fungus.

METHODS OF INVESTIGATION OF SYNOVIAL FLUID FROM PATIENTS WITH REPLACEMENT ARTHROPLASTY COMPLICATIONS

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Introduction. At present, the number of patients with surgical pathology of limb joints is steadily increasing, and the frequency of this pathology varies from 30 to 55% among all orthopedic diseases. However, often infectious complications after surgery on joints with implants lead to severe orthopedic defects. Most often these postoperative complications have a microbial etiology.

Aim. The aim of the work was to study the methods for pathogens under replacement arthroplasty complications identification and for the latent intraarticular infection diagnosis quality improvement.

Results and discussion. Synovial fluid is a thick, elastic mass that fills the joint cavity. Investigation of synovial fluid is of great importance in the diagnosis of joint diseases, the degree of local inflammatory activity elimination, the nature of the inflammatory process identification, the dynamics of the pathological process in the joints monitoring, the effectiveness of intraarticular therapy evaluation. In the investigation of synovial fluid from patients with replacement arthroplasty complications microbiological methods play a leading role.

The technology of synovial fluid research consists of such procedures:

1. Synovial fluid collecting (puncture of the joint, sampling of biomaterial in sterile test tubes with observance of asepsis rules).
2. Synovial fluid transportation to the laboratory (immediate transfer to the clinical diagnostic and microbiological laboratory).
3. Synovial fluid testing:

3.1. Biochemical studies (color, amount, transparency, viscosity, presence of sediment, density of mucinous clot detection).

3.2. Microscopic studies (cells counting in Goryaev's chamber for the cytosis detection, study of native and stained preparations, synoviocytogram calculation).

3.3. Microbiological studies (microscopy of stained preparations, identification of microbial cultures).

Conclusion: The synovial fluid study remains one of the most important diagnostic methods for inflammatory joint diseases and replacement arthroplasty complications. The conducted researches will help to reveal etiological agents and improve their identification.

THE STUDY OF ANTIMICROBIAL ACTIVITY OF ALOE COMBINED PREPARATIONS

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Aloe vera has an incredibly rich and various chemical composition. This plant consists of a huge list of amino acids, minerals, enzymes, vitamins and other biologically active substances.

Aloe has a number of useful properties, it is an antiseptic, an adaptogen, a cell growth stimulator, a source of nutrients, an antitoxic component, an analgesic and an immunomodulator at the same time.

Aloe vera has high antimicrobial activity. These properties were accepted in 1949 due to R.Y. Gottshalla`s experiments and researches. Aloe extract in high concentrations has bactericidal activity against a number of bacteria. So it was found effective against Streptococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Streptococcus pyogenes, Streptococcus agalactiae, Enterobacter cloacae.Aloe preparations are also known for use in the complex treatment of numerous fungal and even viral infections.

Aloe has powerful healing properties, including anti-inflammatory and reparative effects. Aloe juice can quickly heal the skin, clearing it of small chaps and wounds. Aloe juice is added to cosmetic products, which makes them intensively moisturizing for skin and contributing to the constant stimulation of its own collagen formation. It is also expedient to create and use medicinal preparations and cosmetic products based on aloe, combined with other active components to enhance its antimicrobial, regenerating and other properties.

The addition of calendula tincture to aloe juice is important for the treatment of oily and problematic skin. Calendula is a powerful anti-inflammatory, disinfectant and antimicrobial agent, it also promotes skin regeneration. Therefore the complex of aloe and calendula is able to show a strong disinfecting and wound healing effect.

Vitamin B5 (Dexpanthenol) stimulates the skin regeneration and mucus membranes, increases the strength of collagen fibers and so is used to moisturize and treat various skin lesions in pharmaceutical and cosmetic products. Using a combination of aloe and vitamin B5 will make it possible to obtain more effective remedy for treating and regenerating skin than well-known monotherapies.

As many people of all ages face with skin problems, the topic of studying the antimicrobial, anti-inflammatory, wound-healing and reparative properties of aloe and complex preparations based on it is an actual problem.

DETERMINATION OF FAVORABLE CONDITIONS AND ENVIRONMENTS FOR GROWING A CEFIR FUN

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Dairy products have always been an important part of the diet of consumers. Clinical trials of sour-milk drinks showed their high therapeutic and prophylactic effect for various gastrointestinal diseases. Regular use of sour-milk products in food contributes to the strengthening of the nervous system due to the accumulation in them of vitally important vitamins, synthesized by lactic acid bacteria. A special place among fermented milk products is kefir, in the production of which a natural multicomponent symbiotic starter is used, the organism-zoogloea is a kefir fungus. The microflora of kefir fungi is represented by homo- and heterofermentative lactococci, thermophilic and mesophilic lactobacilli, yeast and acetic acid bacteria. These main groups of microorganisms are found both in fungal kefir leaven and in kefir, although the number of some genera of bacteria differs. In kefir fungi, lactic acid microorganisms of the species *Lactococcus lactis subsp*. *lactis biovar. diacetylactis* (up to 30%), *L. lactis subsp. lactis* (up to 20%) and lactobacilli *Lactobacillus sp*. (up to 20%). Among the mesophilic lactobacilli, *L. lactis subsp. cremoris* (~ 7%) and *Leuconostoc sp.* (~ 7%). Obligatory microflora of the kefir fungus are acetic acid bacteria *Acetobacter aceti* - they constitute up to 3% of the total amount of the microflora of the kefir fungus, as well as the yeast *Saccharomyces* and *Kluyveromyces marxianus* - 10%. The balanced growth of yeast, lactic acid and acetic acid bacteria is due to the symbiotic nature of the relationship of these groups of microorganisms. In form, kefir fungi are similar to inflorescence of cauliflower, 0.3-3.5 cm in diameter, from white to light yellow. The approximate chemical composition is 89-90% water, 0.3% fat, 3.2% protein, 6.0% carbohydrate and 0.7% mineral components. The purpose of this work is to determine the favorable conditions and environment for the cultivation of kefir fungus. Important factors that affect the growth of the kefir fungus biomass are temperature, nutrition, air. To date, the department of biotechnology is conducting research to determine the favorable conditions and environment for the cultivation of kefir fungus. At the first stage kefir fungi were placed in different conditions: warm milk, room temperature; warm milk, room temperature +10 g of sugar; temperature of the refrigerator; water; water +10 g of sugar; dried kefir mushrooms; frozen mushrooms, etc. After determining the most favorable environment and the conditions for cultivation of the kefir fungus, further studies should be conducted to assess its viability under the given conditions.

METHOD OF PRODUCING A SUSPENSION OF RABIES VIRUS STRAIN L. PASTEUR FOR THE PRODUCTION OF THE RABIES VACCINE

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Rabies is the anthropozoonoses infectious viral disease that is almost always fatal after clinical signs. According to WHO 55 thousand people in the world die from rabies annually.

The only method of controlling the disease are pre- and post-exposure prophylaxis, in which rabies immunoglobulin and rabies vaccine are used.

One of the rabies vaccine production stages is obtaining of the rabies virus suspension. Are used as the substrate for the biological tissue (brain suspension); chicken embryos; cell culture (primary and constant cell culture) propagation of the virus biomass.

With the biotechnological methods development all over the world, the virus suspension propagation of in biological tissues and chicken embryos is almost never used, since that such vaccines can contain a large number of unnecessary agents. The most economically profitable and safe method is the obtaining rabies vaccine using permanent cell cultures.

PJSC "PHARMSTANDART-BIOLEK" (Kharkov, Ukraine) develops a rabies vaccine for humans use based on rabies virus a fixed strain L. Pasteur and a permanent cell line Vero (kidney cells of the green monkey).

The permanent cell line Vero is widely used as a substrate for production of the cultural rabies vaccine against rage. This cell culture meets the requirements of the World Health Organization, State Pharmacopoeia of Ukraine and European Pharmacopeia to substrates for human vaccines production because it is not tumorigenic.

The aim of the study was to master a technique of the rabies virus propagation of the fixed strain L. Pasteur in the Vero cell culture.

The object of the study was a fixed rabies virus strain L. Pasteur the was obtained from the Novi Sad Pasteur Institute (Novi Sad, Serbia) and deposited with the Depository of the State Scientific Control Institute of Biotechnology and strains

(SSCIBS) from 05.01.2017 years (registration number 678), adapted to the permanent cell line BHK-21 clone 13 (kidney cells of a newborn Syrian hamster).

The cells were cultured in vials sterile for the cell cultures in a parietal monolayer 1 day after passaging in DMEM medium with 10% content of blood serum of cattle under conditions of CO_2 incubator at 37 °C and 5% CO_2. To infect a permanent cell line, a sterile rabies virus suspension strain L. Pasteur was used.

The cell culture was infected in the presence of 80% monolayer on the second day after reseeding. Virus suspension was cultivated within 3 days from the moment of infection in the supporting environment (99% of DMEM, 1% of blood serum of cattle) at 33 °C and 5% CO_2. The received virus suspension was merged in sterile centrifugal test tubes and centrifuged in the refrigerator centrifuge at 4 °C for removal of a cellular detritus. The supernatant was poured into sterile containers and frozen at -80°C.

For definition of infectious activity of the accumulated biomass of the virus used a titration method in the culture of BHK-21 clone 13 cells. The viral suspension was titrated with 5-fold dilution in 96-well plates in 5 replicates. The cells were cultured for 48 hours at 37 °C and 5 % CO_2.

The cell monolayer was then washed with phosphate buffer, fixed and stained with monoclonal anti-rabies antibodies labeled with fluorescein isothiocyanate. The results were recorded using a laboratory microscope equipped with a luminescent nozzle, with an increase in the objective of 10×, the eyepiece of 10×. At microscopy, a bright green specific glow was taken into account in each well of the plate. The viral titer was calculated using the Spearman-Carber formula and expressed in a decimal logarithm of a 50% infection dose for cell cultures (lg $CCID_{50}$).

During the conducted researches the technique of accumulation of suspension of a virus of a rabies of the fixed strain of L. Pasteur in a Vero cell culture. A method for controlling the infectious activity of a fixed rabies virus by titration in the culture of BHK-21 clone 13 cells using labeled monoclonal anti-rabies antibodies has also been developed.

The infectious activity of the obtained virus suspension was 5.82±0.08 lg $CCID_{50}$, which indicates that this method of accumulating a suspension of rabies virus can be used in the technological scheme for producing a rabies vaccine. This will create a drug that will meet the requirements of World Health Organization, State Pharmacopoeia of Ukraine and European Pharmacopoeia.

STUDYING OF THE MARKET OF THE COMMERCIAL STARTERS FOR NUTRITIONAL FERMENTED MILK PRODUCTS

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Today there are widely spread so-called functional products, which contain biologically active components and which being used regularly provide wholesome effect on human organism or on its certain functions. They include products of fermented milk derivation: kefir, yoghurt, clabber, fermented baked milk, cheese, sour cream, curds. The domiciliary production of mentioned products using ferments is becoming more popular.

Ferment – is a microbiological (more often bacterial) consistency causing fermentation. It is used for milk souring with the aim of getting fermented products and also for preparing dough and beverages (kvass, beer). There are also liquid and dry live ferments. Dry live ferments are more preferred then liquid ones, since the product made with the help of such leavens, as a matter of fact, becomes a medicine. Besides, liquid leavens have short shelf life and gotten products differ from regular ones in taste. Dry leavens represent lyophilized microorganisms which remain alive for the whole year in fridge and for 18 months in freezer.

The most popular leavens which are being sold at Ukrainian market belong to such trademarks as VIVO, Іпровіт, Good Food, Genesis, MIO. These enterprises develop and produce wide range of ferments. The main components of which are such bacteria: Lactobacillus bulgaricus, Lactococcus lactis, Lactobacillus acidophilus, Streptococcus thermophiles, Bifidobacterium bifidum, Bifidobacterium breve, Bifidobacterium lactis.

Fermented milk cultures included in leaven have a beneficial effect on all organism systems, and they also regulate Metabolism. They normalize the work of alimentary system, protect organism from putrefactive bacteria, and also purify an organism from harmful slags and toxins. Fermented milk products contain a lot of substances, which are active natural antibiotics. These substances struggle rather successfully against a great deal of causative agents of disease, which are in human intestines. They are essential components of a healthy diet for children and adults. As a result fermented milk production has a great supply among a lot of countries of the world including Ukraine. Our country produces a lot of fermented milk leavens every year, and these leavens are used for getting different foodstuffs. Therefore, the development of the new composition of starter cultures and formulations of the products prepared on their basis is relevant today.

THE IMPROVEMENT OF PROBIOTICS WITH ESSENTIAL AMINO ACIDS

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Today a huge number of people committed to an active lifestyle. During physical activity, as well as after serious illnesses, traumas spent all the body needs trace elements, amino acids, vitamins that can degrade the proper functioning of the body. Interest is the opportunity to support the recovery of the body through dietary supplements (or dietary supplements) that contains probiotics and essential amino acids.

The aim of this work was to study the possibility to combine in a single dietary Supplement, two kinds of active substances, namely probiotics and essential amino acids. This combination can prevent a decrease in immune defenses, a violation of the General metabolism, breaking down muscle tissue, lowering resistance to infections, deterioration of the skin (hair, nails), emaciation, retardation of growth and development, as well as anemia and fatty degeneration of the liver.

We studied the properties of essential amino acids, which are products of hydrolysis of the protein, namely valine, leucine and isoleucine. This is a group of proteinogenic amino acids, characterized by a branched structure of the aliphatic side chain, they are known as BCAAs (from the English. the branched chain amino acids).

In addition to the obvious role in the construction of molecules of proteins, BCAAs have many other functions. During muscular work, they can be used for the synthesis of intermediate compounds of the Krebs cycle and of gluconeogenesis, that is, act as sources of energy. In addition, these amino acids have regulatory functions: they regulate the processes of synthesis and degradation of proteins, cellular metabolism and growth, as well as insulin secretion.

The objective of this research is to obtain high efficiency of the combined product containing a probiotic and a complex of three essential amino acids BCAA's. The action of this drug due to the properties of its components and is aimed at building or rebuilding muscle tissue, to strengthen the production of interferon, and therefore to increase the immunity, increase the rate of metabolism, the production of enzymes involved in the breakdown of proteins, fats and carbohydrates and promotes the assimilation of macro - and micronutrients, weight management, rapid recovery after the severe conditions of stress, after taking antibiotics.

Thus, the creation of such a product based on probiotics, adding essential amino acids and is a relevant work in this direction is carried out at the Department of biotechnology of NUPh.

DIAGNOSTIC ASSESSMENT OF INTESTINAL MICROFLORA IN ADOLESCENTS

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Introduction. Currently dysbiosis is a clinical and laboratory syndrome that occurs in multiple diseases and clinical situations, characterized by a change in the qualitative and quantitative composition of the microflora, the movement of its various representatives into unusual habitats, metabolic disorders that are accompanied by clinical manifestations in some patients. According to statistical data, intestinal dysbiosis occurs in 70-90% of the population of different age groups. The normoflora biological balance is easily disturbed in the presence of exogenous and endogenous factors, in adolescents it is frequent acute respiratory-viral infections, allergic diseases, drug addiction.

Aim. The purpose of this work is to study the diagnostic method and examine the dysbacteriosis statistical data of the SE «Institute of Child and Adolescent Health of the NAMS of Ukraine» clinic patients.

Results and discussion. Depending on the microecological disorders in the intestine severity, different combinations of individual microbiocenosis representatives are possible, that characterize the dysbiotic changes. In practice, the number of 15-20 microorganisms species contained in feces are studied for the intestinal dysbiosis diagnostic (bifidobacteria, lactobacilli, enterobacteria, Enterococcus, Staphylococcus, Pseudomonas and Candida). The quantitative E. coli content is determined on Endo's medium. Normal composition is E. coli content 10^1-10^5 CFU/g faeces. To the hemolyzing coliform identification the blood agar is used. The norm it is up to 10^5 CFU/g. To determine the Staphylococcus amount the egg-salt agar is used (norm is up to10^3 CFU/g). The lactobacilli amount is determined on MRS medium, their normal content is 10^6-10^7 CFU/g. To determine the anaerobic bifidobacteria, a culture is made on the modified Blaurococcus medium, their norm content is 10^7-10^9 CFU/g. Quantitation of Enterococcus is determined on Enterococcagar. Normally their quantity in the intestine for patients is from 10^5 to 10^8 CFU/g.

Conclusion. The use of the method of diagnostic examination for dysbacteriosis is necessary in clinical and scientific practice. Bacteriological studies are crucial in this process. The statistical data show the importance and urgency of improving the diagnostic methods, as well as drawing up a program for the correction of qualitative and quantitative disorders in children and adolescents.

THE ROLE OF THE NUTRIENT ENVIRONMENT IN THE PRODUCTION OF PROBIOTIC PREPARATIONS BASED ON LACTOBACTERIA

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Nowadays, the world has seen an increase in infectious diseases of the skin and gastrointestinal tract. One of the reasons is the decrease in the quantity and quality of representatives of normal microflora lactic acid bacteria. These include representatives of the genus Bifidobacterium and Lactobacterium. Therefore, for the pharmaceutical and perfumery-cosmetic industry, the development of drugs containing living probiotic bacteria is urgent. The general scheme for obtaining the preparation of human normoflora includes first of all the isolation from the environment of the strane-producer, the scaling of the seed, the accumulation of biomass, the standardization and the creation of a dosage form. The critical stage of the technological process is the accumulation of bacteria, which depends on the selection of optimal conditions and composition of the nutrient medium. Traditionally, for the study of lactic acid bacteria uses expensive nutrient media that ensure their growth and the selection. In the world practice, for cultivation of lactobacilli there are several tens of nutrient media. The most recognized were the environment of Maine, Rogoza, Sharp (MRS). The culture medium of MRS-4 differs by the presence of additional hepatic water, fermented peptone casein hydrolyzate, which in turn makes it possible to reduce the amount of the added baker's yeast extract. The introduction of additional components, along with improving efficiency, also affects the cost of the medium. Bacteria of the genus Lactobacillus have specific nutritional needs (nucleic acids, polysaccharides, amino acids, etc.), that is, organic forms of nitrogen not synthesized by them, as well as vitamins, macro- and micro elements. Therefore, today nutrient media contains various extracts of plant raw materials are known. So developed nutrient medium based on the enzymatic hydrolyzate of cabbage and the enzymatic hydrolyzate from the colonies of Tibetan Milk mushroom that allows you to get lactobacilli with high growth rates. It should be noted that, to date, there are no strict recommendations for selection medium, therefore, in the pharmaceutical development it is necessary to make a reasonable choice of the nutrient medium for a particular producer, which will provide the microorganism with all the necessary components to achieve the maximum specific rate of biomass growth. At the Department of Biotechnology of the National University of Pharmacy, a nutrient medium for the accumulation of lactobacilli as an active pharmaceutical ingredient of a soft dosage form will be selected.

Section 6.

PHYSIOLOGICAL AND BIOCHEMICAL BASIS OF ACTION OF BIOLOGICALLY ACTIVE COMPOUNDS

THE GRAPE POLYPHENOL CONCENTRATE EFFECT ON LIPID METABOLISM IN RAT AORTA UNDER EXPERIMENTAL INSULIN RESISTANCE

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Introduction. Many studies have documented an association between insulin resistance and accelerated cardiovascular disease (CVD) in patients with type 2 diabetes. Insulin resistance and lipotoxicity represent the missing links that help to explain the accelerated rate of CVD. Accumulation of toxic lipid metabolites in muscle, liver, adipocytes and beta cells contributes to insulin resistance, beta cell dysfunction and accelerated atherosclerosis. Treatment with diet, exercise and drugs mobilizes fat out of tissues, leading to enhanced insulin sensitivity, improved beta cell function and decreased atherogenesis.

Grape are the source of polyphenols, compounds characterized by their antioxidant properties, which may protect against atherosclerosis. Grape polyphenols affect several metabolic processes that lead to reductions in atherosclerosis including decreases in LDL oxidation and platelet aggregation, increases in flow-mediated vasodilation, reduction in inflammatory cytokines.

Aim. The aim of this work was to study the effect of grape polyphenols complex on lipid metabolism in the rat aorta wall under experimental insulin resistance.

Materials and Methods. The experimental study was conducted on 3 months male rats and weight that were procured from vivarium NUPh. Animals were kept on a high-fat and high-fructose diet during 5 weeks to induce experimental insulin resistance. Grape polyphenols were administered two weeks in dose 9 mg polyphenols/kg/day. Thoracic aorta was isolated and homogenized in potassium phosphate buffer, pH 7.6. Lipids were extracted by chloroform/methanol solution and separated by TLC. The lipid content was determined according to the March method.

Results and discussion. We observed an increase of triacylglycerol (TAG), free fatty acids (FFA) and cholesterol levels in the rat aorta wall under experimental insulin resistance. The observed changes indicate that the insulin resistance state is accompanied by the development of pro-atherogenic changes in the aortic wall. The grapes polyphenol administration led to a decrease in the TAG, FFA and cholesterol content by 1.97, 2.34 and 2.23 times, respectively.

Conclusions. The data obtained indicate that the investigated grape polyphenol complex prevents the development of proatherogenic changes in the aortic wall of rats under experimental insulin resistance.

INVESTIGATION OF THE PRUNUS DOMESTICA EXTRACTS LAXATIVE ACTION

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Introduction. Plum home (lat. Prunus domestica), the family Rosaceae is widespread in Ukraine, has many regional and local varieties of plants and the number second only to apple, pear and cherry. According to published data plum fruits contain 6-17% sugar, up to 8% of pectin, organic acids of up to 1.6%, flavonoids, tannins and vitamins. Kernels of plum bones contain oils up to 42%, which are used in medicine as "peach oil" (Oleum Persicorum).

Aim. The aim of our study was to investigate the laxative effect of dry and aqueous extracts of plum fruit with the fiber-free skin and extracts of plum fruit with the polysaccharide complex-free skin.

Materials and methods. Objects of the research were extracts obtained from Prunus domestica variety "Donetsk Vengerka". A study of the laxative effect of dry and aqueous extracts of plum with a skin without fibers and extracts of plum fruit with the skin without polysaccharide complex was carried out according to the ability of test samples to influence the intestinal motility. The ability to increase intestinal contractions was assessed by the rate of passage of contrast mass through the intestine in mice by the Sticknay J. S. method.

Results and discussion. Analysis of the experimental data showed that, in general, the greatest laxative activity was found in dry extracts of plum fruit with the fiber-free skin. In the range of doses studied, the extracts increased intestinal contractions by 16-25%. As a result of the laxative effect, dry draining extracts with a fiber-free skin at doses of 50 and 75 mg/kg (23% and 25.7%, respectively) and drains of skin without polysaccharide complex at a dose of 50 mg/kg (22%) statistically significantly exceeded the reference preparation Picolax (17,6%). A relatively less laxative effect was exhibited by an aqueous plum extract with a skin without polysaccharide complex at a dose of 0.5 ml/kg, the activity of which was 15%. The effectiveness of the water extract of plum with a skin without polysaccharide complex is not inferior to the comparison drug Picolax.

Conclusions. Thus, the mild laxative effect of the extracts studied is established. The effectiveness of the laxative effect of dry extract in these doses was predominant, and the aqueous extract was not inferior to the activity of the Picolax comparison preparation. The obtained experimental data justify the expediency of further pharmacological studies to create an effective agent with a mild laxative effect.

BIOCHEMICAL MECHANISMS OF HIGH-PROTEIN DIET (DUKAN DIET) MAIN AND SIDE EFFECTS

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Introduction. It is well known that the prevalence of obesity worldwide is very large, and the search for new methods of correction of such conditions today is a topical issue. It is also very important that the conduct of any pharmacotherapy for obesity is common accompanied by the development of complications of various severity degrees, which is why many doctors recommend non-pharmacological treatment – diet therapy, in particular the Dukan diet. However, it should be noted that fundamental changes in human diet can also lead to the formation of side effects that today are little studied.

Aim. The aim is to study the biochemical mechanisms of the high-protein diet therapy main and side effects.

Results. According to the literature data, the main effects of protein diet (Dukan diet) occur through a deep shortage of the carbohydrate food components that is accompanied by the development of energy starvation of cells and requires the involvement of other sources of energy – primarily peripheral liver fat oxidation energy with ketone bodies formation. It is known that spontaneous decarboxylation of acetoacetate with the formation of highly toxic acetone can lead to the development of severe complications of blood ketosis. This is the case of excessive synthesis of ketones in the liver due to the lack of NADH (H+) in the conditions of glucose deficiency. Also, excessive oxidation of fats can cause the release of free acetoacetate in the blood with the formation of ketoacidosis. However, it should be noted that this diet in the early stages involves the use of a large number of proteins without cellulose-containing products that are necessary for the active intestine peristalsis. Therefore, excess consumption of protein products and sluggish peristalsis may be accompanied by the chyme stagnation formation and sharp increase of putrefaction in the large intestine with the formation of the excess amount of over-toxic compounds (indole, cresol, putrescine, cadaverine), which can lead to poisoning of the body.

Conclusions. Thus, the Dukan high-protein diet contributes to the peripheral fat oxidation in the liver, however on the other hand it leads to complications such as blood ketosis and ketoacidosis, and increases the risk of protein poisoning through increased formation of products of putrefaction in the large intestine.

PARACETAMOL EFFECTS ON LIVER FUNCTIONAL INDICES UNDER EXPERIMENTAL INSULIN RESISTANCE

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Introduction. Insulin resistance (IR) is the metabolic disorder that is caused by inefficient glucose uptake and utilization in peripheral tissues as a respond to insulin stimulation. This condition is characterized by hyperglycemia, dyslipidemia, peripheral tissues glucose tolerance, oxidative stress and the development of proatherogenic state. IR is the main risk factor for cardiovascular disease, diabetes mellitus type 2 (DM2) and non-alcoholic fatty liver disease (NAFLD). Nowadays acetaminophen (APAP) is one from ten most popular medical preparations in Ukraine, so it is used a lot as an antipyretic and analgesic drugs.

Aim. The aim of this study was to investigate the APAP effects on liver functional indices under experimental IR in rats.

Materials and methods. 24 male rats weighting 160-180 g, who were kept in standard vivarium conditions, were randomly divided into 4 groups. Experimental IR was induced by feeding experimental animals high-fat diet enriched with fructose during 5 weeks. APAP was injected intraperitoneally once (in dose 600 mg/kg body weight) 24 hours before the end of the experiment. In blood serum were measured alanine aminotransferase activity (ALT) and in liver reduced glutathione (GSH) and TBA-reactive substances (TBARS) content.

Results and discussion. IR development was accompanied by increased activity of serum ALT in 2.3 times compared with intact animals and proved hepatocytes injury, however, APAP injection for IR rats enhance ALT activity in 1.2 times compared with experimental pathology. So, the APAP injection enhanced the hepatocyte destruction under IR.

It was also shown that the APAP single injection in healthy animals significantly increased the content of TBARS in 1.7 times and decreased GSH in 1.5 times liver tissue. As for GSH and TBARS content under IR the same tendency was observed. However, in rats with IR APAP administration led to the significant decrease in GSH content and elevated TBARS in the liver, indicating the lipid peroxidation activation and antioxidant system attenuation.

Conclusions. Thus, we have found that APAP administration under experimental IR significantly deepened antioxidant system attenuation and deteriorate liver cells injury. The additional investigations of APAP effects can help to prevent the complications development under treatment of patients with IR.

SUBSTANCES FROM COMMON GRAE EXTRACT WEAKEN LIPOGENESIS CHANGES IN PATIENTS WITH METABOLIC SYNDROME

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Introduction. The metabolic syndrome is a special symptom-complex which includes insulin resistance development, the disturbance of glucose tolerance, augmentation of body weight or a gross obesity, atherogenous changes in the blood lipoprotein profile, predilection towards thrombogenesis and other pathological changes. There are many factors that contribute to metabolic syndrome development. Major factors are low physical activity and a high-caloric diet. The correlation of central obesity with an insulin resistance in muscles can be explained by high rate of triglyceride exchange and free fatty acids metabolism. It is widely known that under the metabolic syndrome there is a high level of glucose-6-phosphate accumulation. Pentose phosphate pathway is one of the ways of glucose-6-phosphate utilization. This results in the high NADP(H+) levels in cells, wich upregulates the fatty acid synthase activity. Therefore activity changes in NADP-producing dehydrogenases can be considered as an indicator of intensity of lipogenesis.

The **aim** of the present work was to investigate changes in lypogenesis indices in animals with experimental metabolic syndrome.

Materials and methods. Activities of key enzymes of lipogenesis were measured in liver homogenates on male Syrian hamsters fed with high-caloric diet with fructose.

Results and discussion. It was found that metabolic syndrome was followed by a small augmentation of NADP-dependent malate dehydrogenase activity and the decrease of penthose phosphate pathway dehydrogenases activity, which proves that contribution of lipolysis activation to hyperlipidemia is insignificant. At the same time lipid levels in blood serum and liver homogenate was elevated significantly. This results corresponds with the statement that, first of all, metabolic syndrome lowers the lipid oxidation without exerting any significant effects on the intensity of steroids and fatty acids synthesis. The main reason of the high interest in antioxidant therapy was the intensification of lipoperoxidation in metabolic syndrome. In our study we used the common grape extract which can be characterized by the high content of phenolic antioxidants. We found that this type of antioxidant therapy within 2 weeks in metabolic syndrome models caused the essential changes in the registered parameters. Lipid accumulation was decreased during all of the study period, dehydrogenase activity was normalized.

Conclusions. Results indicate the high effectivness of the antioxidants use in complex therapy of a metabolic syndrome.

THE STUDY OF HEPATOPROTECTIVE EFFECT OF APPLE POLYPHENOL CONCENTRATE UNDER EXPERIMENTAL INSULIN RESISTANCE IN RATS

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Introduction. In the modern food industry, products with a high content of sugars, in particular fructose, are increasingly used. Over the past 50 years, the world consumption of sugar has tripled. Today, the manufacturer added it almost all conceivable food. Previously the food industry is added to foods mainly sucrose, but now it is increasingly replaced with fructose. Fructose is the sweetest sugars about 1.5 times sweeter than sucrose and 3 times than glucose, which allows manufacturers to achieve the same flavor substance fewer effects. Excessive consumption of fructose leads to insulin resistance, in which oxidative stress and the formation of free radicals develops. In consequence of that it violated the integrity of plasma membranes of liver cells.

Aim. The aim of the study was to study the effect of polyphenol concentrate from apples on the activity of hepatospecific enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transpeptidase (GGT) in rat serum under experimental insulin resistance.

Materials and Methods. The studies were conducted on female rats weighing 190±15 g, kept under standard conditions in the vivarium NUPh. Insulin resistance was modeled by keeping animals on the high-fat diet enriched by fructose for 5 weeks. Polyphenol concentrate was administered from the 3rd week of the experiment intragastric for 14 days. At the end of the experiment, the rats were decapitated, blood was collected for serum. ALT, AST and GGT activity was measured in rat serum. The data obtained were processed statistically.

Results and discussion. The development of insulin resistance was accompanied by an increase in the activity of hepatic enzymes in the blood: ALT from 0.433±0.021 to 0.986±0.057 mkat/l, AST from 0.978±0.064 to 1.981±0.085 mkat/l, GGT from 0.284±0.019 to 0.653±0.19 mkat/l. Increased ALT and AST activity constitutes a violation of the integrity of cell membranes. Polyphenol concentrate administration to rats with experimental pathology resulted in a significant decrease of the activity of ALT, AST, GGT in 1.58, 1.65 and 1.64 times, respectively.

Conclusions. The results indicate that the analyzed polyphenols concentrate exhibits hepatoprotective activity and can be used for the correction of disturbances in liver insulin resistance and related pathologies.

NITROGEN METABOLISM INDICES UNDER EXPERIMENTAL INSULIN RESISTANCE IN RATS

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Introduction. Obesity-associated insulin resistance (IR) is the main cause of diabetes mellitus type 2 (DM2). The modern life style, particularly consumption of the diet, more and more often leads to IR that mediated the dramatic changes in body metabolism. IR is frequently associated with liver and kidneys metabolic alterations that induce non-alcoholic fatty liver disease, chronic kidney disease, etc.

Aim. The aim of the experiment was to study some indices of nitrogen metabolism in blood serum and in liver and kidneys tissues under experimental IR in rats.

Materials and methods. In order to cause IR the male rats were fed high-fat diet enriched with fructose (HFDF) during 5 weeks. At the end of the experiment animals were decapitated, blood, liver and kidneys were sampled. Total protein (TP), urea (U) and uric acid (UA) were determined in blood serum, liver and kidney homogenates using the standard kits (OOO NPP "Phyllis-Diagnostic", Ukraine).

Results and discussion. It was observed the significant decrease in blood serum TP level by 14% in IR rats. Lowering of protein in the blood can be mediated by alterations in liver metabolism as blood serum proteins have liver origin. In general liver TP content reduced by 11% and in kidneys by 14%. This evidence is correlated with increased level of catabolic products such as U and UA in blood as well as in studded organs. Thus U level in blood increased by 24% Also, acute U increase that was found could show the contribution of muscle protein breakdown as well as could be explained by impaired protein synthesis in insulin-sensitive tissues and usage of amino acids as the substrate for gluconeogenesis.

UA is one of the end products of purine metabolism in rats. It was demonstrated an increase in UA blood concentration in 18% and at the same time substantial UA accumulation was determined in liver – by 36% and less increase in kidneys – by 15%. High blood UA concentration induced by IR can lead to cardiovascular disorders development and stimulate the aggregation of thrombocytes and as a result increased the risk of coronal thrombosis.

Conclusions. The experimental IR caused catabolic processes activation that is revealed by protein decrease in blood serum and elevated levels of catabolism products in blood serum as well as in tissues.

INVESTIGATION OF POLYPHENOL CONCENTRATE FROM GRAPE SEEDS ANTI-INFLAMMATORY EFFECT

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Introduction. Biologically active derivatives of arachidonic acid play the leading role in the exudation development. There are two alternative ways of transformation of arachidonic acid from the phospholipids of cell membranes for bioactive compounds: cyclooxigenase way the formation of prostaglandins (PG) and lipooxygenase way of formation of leukotrienes (LT) with the participation LOG. Drugs that are composed of phenolic compounds inhibited the LOG.

Aim. The aim was to establish the ability the polyphenol concentrate from Grape seeds to suppress the activity of key enzymes of transformation of arachidonic acid.

Materials and methods. We used a zymosan edema model, the mechanism of development of which is the formation of LT (0.5 hour) and PG (3 hours). As the comparison drugs were selected diclofenac sodium, which is a nonspecific inhibitor of COG, and quercetin – drug polyphenol of nature.

Results and their discussion. Administration of zymosan leds to the edema development in the control group of animals after 0.5 hours and 3 hours. Preliminary administration to animals concentrate from Grape seeds inhibited the growth of zymosan edema in all studied periods. So, after 0.5 hours in rats that were treated with a concentrate of Grape seed swelling was significantly lower in 2 times than the control group pathology. After 3 hours, concentrate from Grape seeds significantly reduced the swelling in 1,4 times in comparison with the control group. High anti exudative activity of the investigated extract in these terms suggests that in the early stages of development of the inflammatory reaction it actively suppresses the formation of LT, 3 hours - moderates PG. The reference drug diclofenac sodium showed in the experiment characteristic anti-inflammatory effect. The highest activity was observed 3 hours after the administration of zymosan, which is probably related to its ability to suppress the synthesis of PG.

Conclusions. Thus, the data indicate a high antiexudative activity of the concentrate from Grape seeds. The ability of extract to inhibit effectively the development zymosan swelling in the early stages, perhaps due to the action of phenolic compounds, which are part of it. The effect of concentrate from Grape to reduce edema 3 hours after administration of inflammation allows to make the conclusion about the presence of his moderate anti cyclogenase activity.

METABOLIC DISORDERS UNDER HIGH FRUCTOSE DIET AND DEXAMETHASONE MODELS OF INSULIN RESISTANCE

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Introduction. Type 2 diabetes is a serious public health problem due to its wide spread, a significant number of macro- and microvascular complications that lead to increased disability and mortality. It is known that the basis of type 2 diabetes is the disturbance of insulin homeostasis: insulin resistance of peripheral tissues and dysfunction of beta cells of the pancreas. To develop antidiabetic drugs, knowledge of the mechanisms of insulin resistance development is necessary. Therefore, the modeling of insulin resistance is important.

Aim. The aim of this work was to investigate some indicators of glucose-insulin homeostasis and prooxidant-antioxidant status in rats blood serum under two models of insulin resistance.

Materials and methods. Insulin resistance was modeled by keeping animals on high fructose diet (HFD) for 6 weeks or intraperitoneal administration of dexamethasone (Dex) for 5 weeks. Glucose and immunoreactive insulin (IRI) content were determined by glucose oxidase and radioimmunoassay using standard kits. Insulin resistance index was calculated using the algorithm HOMA. Determination of 2-thiobarbituric acid-reactive products (TBA-RP) and reduced glutathione (GSH) contents were carried out by spectrophotometric methods. Statistical analysis of the data was performed using STATISTICA software package (StatSoft Inc., USA, version 6.0). The significance of differences between groups was assessed by non-parametric Mann-Whitney test. Significance was assigned at $p<0.05$.

Results and discussion. Both researched models were accompanied by disturbances of glucose-insulin homeostasis and prooxidant-antioxidant balance. It was shown that under HFD the increase in glucose level was 160% compared with the intact group, insulin level − 140%, HOMA index − 170%. Under Dex model glucose content increased 1.9 times in comparison with the intact group, insulin level − 1.5 times, HOMA index – 1.8 times. Regarding the disturbances of prooxidant-antioxidant balance the decline of GSH was the same in both models but the growth of TBA-RP was stronger in dexamethasone model (almost 2 times higher than under HFD).

Conclusions. Thus HFD and Dex model caused approximately the same glucose-insulin homeostasis disturbances, but different changes in prooxidant-antioxidant status due to different mechanisms of fructose excess and dexamethasone action.

STUDY OF ANTITHROMBOTIC ACTIVITY OF "VARIKOZNET" PREPARATION

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Introduction. On the basis of local raw materials antitrombogen gel form of the drug "Varikoznet" had been used in the Tashkent Pharmaceutical Institute. This article is about its specific impact on the results of the research.

Aim.. The study of the antithrombotic activity of the drug was carried out on the model of generalized adrenaline-collagen thrombosis in mice.

Material and methods. As the agent causing thrombosis, a mixture of solutions of two solutions was used: collagen in a dose of 0.5 mg / kg and epinephrine at a dose of 0.06 mg / kg. The experiments were performed on white mongrel mice (both sexes) weighing 18-22 g, 6x10 animals in each group, 180 animals were used in total. As a reference (standard) drug was chosen "Heparin" ointment. To do this, once and daily animals were injected onto pre-cut skin of the entire back and sides of mice, an area equal to 21 cm2 (3x7 cm), were applied to the preparations for five days 1. Control group (control) - animals without prevention: 2. The test group - the animals received the preparation "Varikoznet" gel, in the form of 7% of the gel, in a dose of 1050 mg / kg, in a volume of 0.3 g / 20 g; 3. Comparison group - the animals received the preparation "Heparin" ointment, in the form of 100 IU / g ointment, in a dose of 300 IU / kg (in heparin), in the volume of 0.3 g / 20 g. Then, on the fifth day, two hours after the last administration of the test preparations, a mixture of two solutions was injected once intravenously , In the form of 0.0056% solution for injection, at a dose of 0.56 mg / kg, in a volume of 0.2 ml / 20 g. A mixture of solutions was prepared in physiological saline. The next day after the introduction of a mixture of solutions of two solutions, counted the surviving and dead animals.

Results and discussion.. According to the results of the study, it was found that the test subject statistically significantly increases the survival rate of animals under conditions of generalized adrenaline-collagen thrombosis. Also, if we compare the results of survival of animals in the conditions of generalized adrenaline-collagen thrombosis, the test preparation with the reference preparation, then the test drug will appear, that there is no statistically significant difference between them: Control-0,67 (0,12÷1,21), «Varikoznet» gel-6,50 (5,40÷7,60), Heparin" ointment-5,50 (4,40÷6,60).

Conclusion. Antithrombotic activity of the preparation "Varikoznet" gel was studied. As a result, it was found that the study drug has a reliable antithrombotic activity, not inferior to the reference drug.

INVESTIGATION OF ACUTE TOXICITY OF THE EXTRACT FROM THE LEAVES OF CORYLUS AVELLANA

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Introduction. When researching a new drug, an important characteristic along with a study of pharmacological properties is a study of toxic properties, which makes it possible to assess the degree of its safety. Given that the extract from the leaves of Corylus avellana is a promising remedy for internal use, the **aim** of our research was to study the acute toxicity with intragastric administration.

Materials and methods. Acute toxicity of the extract from the leaves of Corylus avellana was studied using the express method of T.V. Pastushenko. The degree of toxicity was determined according to the classification of K.K. Sidorov. The extract was administered intragastrically once to rats at doses of 500 mg/kg, 5000 mg/kg 10000 mg /kg, 15000 mg/kg and mice at a dose of 100 mg/kg, 1000 mg/kg, 3000 mg/kg and 5000 mg/kg. Observation of the general condition and behavior of animals was carried out for two weeks.

Results and discussion. Based on the results of the study of acute toxicity, it has been established that the administration of an extract from the leaves of Corylus avellana at doses of 500 mg/kg to 15000 mg/kg to rats does not lead to intestinal death. When monitoring animals for two weeks, there was no evidence of intoxication. Skin covers and reflex excitability, as well as appetite and behavior in all animals after the administration of the extract remained unchanged. The obtained data indicate the absence of a significant toxic effect of the extract within these doses and characterizes it as relatively harmless (VI^{th} class of toxicity, LD_{50}>15000 mg/kg).

The administration of the extract in the dose range of 100 mg/kg to 5000 mg/kg in mice does not lead to animal deaths and does not cause any manifestations of intoxication, which indicates the absence of a significant toxic effect of the extract from the leaves of Corylus avellana in the range of these doses and characterizes it as practically non-toxic (V^{th} class of toxicity, LD_{50}>5000 mg/kg).

Conclusion. Thus, on the basis of the conducted studies in accordance with the generally accepted toxicological classification of K.K. Sidorov extract from the leaves of Corylus avellana after single intragastric administration is a relatively harmless remedy (LD_{50}>15000 mg/kg).

THERAPY OF DEPRESSION WITHOUT AFFECTING WEIGHT, ISN`T IT POSSIBLE?

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Introduction. For a long time, the dominant theory of the mechanisms of depressive disorders was the monoamine theory, according to which one of the leading factors in the depression development is a deficiency of biogenic monoamines in the synaptic cleft. But the monoamine theory does not explain the limitations in the effectiveness of antidepressants and the slow development of their therapeutic effect, which made one think about the lack of breadth of this theory. In recent years, the neurotrophic theory of the development of depression has been actively studied. This theory fills the missing links of the monoamine theory, explaining the morphological changes in the brain. Thus, neurotrophic factors occupy one of the leading roles in the etiology of depression, affecting the ratio of the processes of death of nerve cells and reparative processes.

In the context of the foregoing, it is very important to start treatment of depression in a timely manner, which will facilitate its therapy.

Aim. The aim of present work was to investigate the possibilities of improving the therapy of neurotic disorders, in order to eliminate the side effects that play the role of constraints in the timely initiation of treatment.

Discussion. One of important factors is the influence of modern psychotropic drugs on body weight. Motivational activities, food behavior and emotional reactions were closely linked during evolution. Serotonin, dopamine and norepinephrine contribute to the regulation of each of these processes. What makes it difficult is the isolated regulation of one of the components of this system. Also, taking into account that although weight gain is indicated by a possible side effect, in most cases, the mechanisms of this effect have not been studied enough to correct them without affecting the main therapeutic effect. Overweight significantly increases the risk of diabetes type II and cardiovascular diseases, due to the usually associated dyslipidemia. Therefore, a more detailed study of biochemical mechanisms of the influence of psychotropic drugs on body weight is a very urgent problem of modern pharmacy.

Conclusions. It is necessary to investigate in more detail the mechanisms of the influence of psychotropic drugs on protein, lipid and carbohydrate metabolism.

HYPOGLYCEMIC EFFECT OF APPLES POLYPHENOLS UNDER EXPERIMENTAL INSULIN RESISTANCE

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Introduction. The syndrome of insulin resistance – one of the leading reasons for the diabetes mellitus development and increased risk of cardiovascular diseases and their complications. Diabetes mellitus is characterized by a chronic course and disturbance of all types of metabolism: carbohydrate, fat, protein, mineral and water-salt. Diabetes covers 7% of the adult population in the world and about 2.9% of the population in Ukraine. The prevalence of diabetes is growing every year. Consequently, the search and development of medicines for the prevention and treatment of diabetes mellitus are relevant for today. Polyphenols are promising diabetes mellitus treatment agents because of a wide variety of pharmacological effects: anti-microbial, anti-inflammatory, diuretic, hypotensive and others. One of the best known and most accessible sources of polyphenols is Malus domestica.

Aim. The aim of this work was to investigate the hypoglycemic effect of apple polyphenols extract administration on glucose and insulin content in rats blood serum under insulin resistance.

Materials and methods. Insulin resistance was modeled by keeping animals on high- fructose diet for 6 weeks. The suspension of polyphenols were administered intragastrically the last 2 weeks of the experiment. Glucose and immunoreactive insulin content were determined by glucose oxidase and radioimmunoassay using standard kits. Insulin resistance index was calculated using the algorithm Homeostasis Model Assessment. Statistical analysis of the data was performed using STATISTICA software package (StatSoft Inc., USA, version 6.0). The significance of differences between groups was assessed by non-parametric Mann-Whitney test. Significance was assigned at $p<0.05$.

Results and discussion. The development of insulin resistance was revealed in animals with high fructose diet: accumulation of glucose (1.6 times higher compared with intact animals), insulin level enhance (1.44 times higher compared with Intact animals) and insulin resistance index enhance (3.02 versus 1.78 in the intact animals). The use of apple polyphenols normalized all indexes studied, obviously, due to a diverse composition (quercetin, procyanidins, catechins, phenolic acids) and, accordingly, to mechanisms of insulin resistance and hyperglycemia correction.

Conclusions. Investigated apple polyphenols complex is a prospective raw materials for new medications development to improve the glycemic and insulin homeostasis.

THE BIOGENIC ROLE OF PHOSPHORUS

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Introduction. Phosphorus has an important role in building tissues and ensuring the functioning of the body. The element is part of the protein, NA, nucleotides, ATP and other. In biological environments element is composed of phosphate ion, in the form of inorganic and organic in composition of biological active substances: nucleic acids, nucleotides, phospholipids, nucleoproteins, phosphoproteyidi, ethers of carbohydrates and other.

Aim. Review the biological properties of phosphorus.

Biological role of Phosphorus. Phosphorus is a unique role in the implementation of phosphorylation of carbohydrates and fatty acids, which leads to the formation of the universal energy of body cells. Due to the collapse of carbohydrate energy accumulated in the organic phosphoric acid compounds such as adenosine monophosphate, adenosine diphosphate, adenosine triphosphate, creating phosphate. Triprotic phosphoric acid is multifunctional reagent that provides versatility biochemical function of ATP. ADP and ATP - derivatives diphosphate $H_4P_2O_7$ and triphosphate $H_5P_3O_{10}$ acids. At physiological pH = 7.4 ATP and ADP completely ionized to anions ATP^{4-} and ADF^{3-} that hydrolyzed: $ATP^{4-} + HOH \leftrightarrow ADF^{3-} + HPO_4^{2-}$. In intracellular fluid ATP and ADP are in the form of complexes with magnesium: $MgATP^{2-}$ and $MgADP^{-}$. In enzymatic reactions, where ATP is a donor of phosphate group, the active form is complex $MgATP^{2-}$. For this reason, Magnesium is a vital element for the body. Phosphorus is in the middle of the periodic system, has a middle energy of density electron affinity (as opposed to very electronegative F, O, Cl, N), and therefore the phosphorus and phosphoric acid inherent role of deposit and biocatalytic using of energy. Carbon and nitrogen are not able to participate in these processes because they do not have d-orbitals. Arsine is toxic and silicon insoluble acid was formed. From this perspective, Phosphorus is a unique example of individual chemicals. Exchange of phosphorus in the body is closely linked to calcium. The required ratio of the body Ca : P = 2 : 1. Phosphate ion takes part in the buffer system of blood. Phosphorus stimulates mental, heart, muscle activity involved in the metabolism of proteins, fats and carbohydrates. Nuclides phosphorus used in biomedical research mechanisms of metabolism and energy.

Conclusions. Thus, feature of the electronic structure of phosphorus atoms provides unique functions of its compounds: the ability to store and bio catalytic using of energy.

MODERN ORAL DRUGS TREATMENT OF DIABETES MELLITUS TYPE 2

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Introduction. Diabetes mellitus (DM) is a group of endocrine diseases, developing as a result of absolute or relative deficiency of insulin, resulting in a persistent increase in the level of blood glucose — hyperglycemia. It complicates with numerous pathologies such as atherosclerosis, nephropathy, neuropathy, retinopathy etc.

Aim. To perform from a biochemical point of view the most effective drug in the treatment of diabetes mellitus type 2.

Materials and methods. Scientific literature and statistics practitioner endocrinologists.

Results and discussion. Classification of drugs of diabetes II type: sulfonylureas (1st generation - carbutamide, tolbutamide, generation 2 – glycidone, gliclazide, glibenclamide, glipizide, glimepiride); biguanides (Metformin, bufan) thiazolidinediones (rosiglitazone, pioglitazone); inhibitors of α-glucosidase (acarbose); glucose-lowering herbal remedies. Among of them glimepiride (Amaryl) has a dual mechanism of action: to insulin secretion and to insulin resistance. It acts by blocking cytoplasmic ATP-dependent potassium channel of the beta cells of the pancreas. This is accompanied by opening of calcium channels in the membranes of beta cells and enhancing the penetration of calcium (depolarization). Glimepiride inhibits platelet aggregation in vivo and in vitro due to inhibition of growth of intracellular calcium in platelets and selective inhibition of the cyclooxygenase, which suggests the possibility of its use for prevention of late vascular complications in diabetic patients.

Conclusions. Metformin decreases hyperglycemia, does not provoke hypoglycemia. In contrast to derivatives of sulfonylurea, stimulates insulin secretion and does not show hypoglycemic effect in healthy people. Sulfanilamides increase the sensitivity of peripheral receptors to insulin and glucose utilization by cells, inhibits gluconeogenesis in the liver, delaying induction carbohydrates in the gut. Glimepiride (Amaryl) has a number of advantages, in particular the appointment of lower doses, fast onset and longer duration of action, much more rare hypoglycemic reactions, positive effect on lipid metabolism, which, no doubt, opens up new horizons in the treatment of patients with non-insulin dependent diabetes.

STATE AND PERSPECTIVES FOR THE AROMATASE INHIBITORS USE IN THE METABOLIC SYNDROME THERAPY

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Introduction. Metabolic syndrome (MS) is a set of metabolic-modifying factors that include obesity and increase the risk of type 2 diabetes and cardiovascular pathology development. The risk of cardiovascular disease increases more than two-fold with MS. According to the WHO data, mortal rates from cardiovascular diseases in Ukraine reach 68%. The insulin resistance and obesity development are also observed in MS. In accordance with WHO data for 2014, about 11% of adult men and 15% of adult women were afflicted by MS and abdominal obesity.

Aim. One of the secondary components of MS is an imbalance of sex hormones and their transporter protein, that take part in regulation of glucose and lipids metabolism, control body weight and lipogenesis. Also there is substantial data on the role of abnormal mesenteric aromatase activity in MS and obesity. Consequently, the testing of aromatase inhibitors as a new medicines for the therapy of metabolic syndrome became a focal point of our research.

Materials and methods. The study was carried out on 60 Syrian hamsters at the age of 8 weeks, which were divided in 3 groups by 10 animals of each sex (n=20). MS in animals was recreated using classic for hamsters model based on fructose-enriched (≥60%) diet for 2 weeks. The treatment of animals was carried out by oral administration of anastrozole (Anastrozole-Sandoz, pills, 1 mg) in the dose 0.13 mg/kg for 14 days. Assessment methods: physiological, biochemical, immuno-enzymatic, mathematical statistics.

Results and discussion. Anastrozole administration reduced obese hamster`s total body weight by 7%, visceral fat mass – by 17% in male and female animals. It decreased serum estradiol level by 15% in males, and by 10% in females; increased serum total testosterone level by 18% in males, and by 7% in females. In kinetic studies of mesenteric fat tissue *in vitro* anastrozole decreased aromatase activity in fat homogenate by 26% in animals of both sexes.

Conclusions. The results of our study confirme the advisability of using aromatase inhibitors, particularly Anastrozole, in the therapy of metabolic syndrome. Further study of this therapeutic group drugs and search for relevant doses for efficacy and safety will expand the list of the aromatase inhibitors indication with the treatment of metabolic syndrome and obesity.

THE EFFECT OF CARNITINE ADMINISTRATION ON THE STATIN-ASSOCIATED MYOPATHY DEVELOPMENT UNDER NUTRITIONAL DISLIPOPROTEINEMIA WITH HYPERLIPIDEMIA IN GUINEA PIGS

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Introduction. Today cardiovascular diseases are the important problem, which ranks leading positions of mortality in the world. Among the reasons of this diseases group is atherosclerosis development. Statins are the most commonly prescribed drugs for the atherosclerosis treatment, that shows myotoxicity accompanied by the development of myopathy, and in serious cases, rhabdomyolysis. One of the causes of myopathy could be a carnitine deficiency. Carnitine is a vitamin-like compound that activates the fatty acids oxidation and normalizes the energy supply of muscle tissue and prevents myocyte apoptosis.

The **aim** of our work was to study the applicability of L-carnitine using for the prevention of the statin-associated myopathy formation in guinea pigs.

Materials and methods. Studies were carried on male guinea pigs, which was modeled nutritional diislipoproteinemia with hyperlipidemia. Animals were administered fluvastatin (Lescol Xl, Novartis, Switzerland) or a combination of fluvastatin with L-carnitine (L-carnitine, "Farmakom", Ukraine). Content of α-cholesterol, β-cholesterol concentration of myoglobin, lactate, the enzyme activity of lactatedehydrogenase (LDG) and creatinephosphokinase (CPK) was determined; the atherogenic coefficient (AC) was calculated.

Results and discussion. In animals with control pathology, the content of β-cholesterol grew in 3.61 times, and α-cholesterol content was reduced by 75%, AC was significantly increased in 20.25 times. In animals treated with fluvastatin β-cholesterol ltvel was significantly decreased by 45.7%, and α-cholesterol were not significantly different from intact animals, the AC returned to normal value. However, the myoglobin and lactate content were significantly increased (in 2.8 and 2.3 times respectively), the activity of LDG increased by 18.97%, and CPK – in 1.34 times, that indicate the statin-associated myopathy formation. The combination of fluvastatin and L-carnitine were accompanied by a more correction effect of dyslipidemia and offset by negative changes in the indices of muscle damage, due to normalization of myocyte energy maintaining and inhibition of apoptosis.

Conclusions. The researches carried out testify to expediency of L-carnitine using to the prevention of statin-associated myopathy development associated with long term use of these lipid-lowering drugs.

EFFECT OF YOHIMBINE HYDROCHLORIDE ON THE LEVEL OF SOMATOTROPIN IN RATS

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Introduction. Yohimbine is a common compound of medicines and dietary supplements misused by athletes to improve results and fitness. These dietary supplements used by sportspersons irrespective of age and gender, and theirs therapeutic regimen is rather long-term. In this mode, the use of this drug can cause not only common side effects (tachycardia, increased blood pressure, tremor, headache etc.) by the exposure to sympathoadrenal system, but also have a negative impact on other regulatory systems of the body, particularly on hypothalamic-pituitary axis (*somatotropin* secretion).

Aim. The aim of this research was evaluation of the effect of yohimbine hydrochloride on serum growth hormone content in rats of different sex and age as a spicific aspect of drug safety, which displays processes of growth and enlargement.

Materials and methods. The experiment was carried out on 80 Wistar line rats of different sex and age, divided by 8 experimental groups of 10 animals each. We used animals aged 1 month and 3 months, to assess the impact of yohimbine hydrochloride on rats before and after puberty. To simulate the therapeutic intake of yohimbine hydrochloride in animals, rats ware intragastrically administered per 0.34 mg/kg for 21 days. For an unbiased assessment of the influence of the drug on the growth and enlargement processes, the dynamics of animal`s body weight and serum somatotropin content were studied.

Results and discussion. Result of our study showed that after a therapeutic course of yohimbine hydrochloride content of growth hormone in young male rats serum was significantly lower than the intact control values by 37.2%. Young female rats somatotropin levels in blood decreased dramatically by 51.7% compared to the physiological normal values, due to females α-adrenal system occupies a very important role in the regulation of the hypothalamic-pituitary system. The obtained data positively correlated with the dynamics of the body weight of animals during the growth period: yohimbine hydrochloride reduced body weight from 15 to 22 g depending on the sex of the animals. In animals that have passed puberty, yohimbine hydrochloride caused less measurable changes of the content of growth hormone in the blood serum. This partly deals with the fact that with aging in mammals common physiological secretion of somatotropin decreases.

Conclusions. This research results indicates that yohimbine hydrochloride can reduce the dynamics of weight gain and serum somatotropin level in rats. Especially, it observed in animals of prepuberty age. These data predict the potential harm to young athletes who take yohimbine and justify the restrictions on the use of medicines and dietary supplements with yohimbine within certain age groups of consumers.

THE INVESTIGATION OF BIOLOGICALLY ACTIVE ADDITIVES IN THE PHARMACEUICAL MARKET OF UKRAINE

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Introduction. In modern ecological, economical and social situation the questions of people's health diseases prevention, their cure and treatment and right (proper) balanced nutrition have great importance. Based on these, the main criteria to biologically active additives (BAA) must be: the effectiveness and safety. They must standardize the physiological processes, which are the basis of human's vitality. They must also prevent and remove the xenophobiks action and malnutrition, which suppress protective mechanisms.

Aim. Research the investigation of biologically active additives in the pharmaceutical market of Ukraine.

Materials and methods. The figures in Ukraine, the acting legal texts, the experience of toxicologist have been chosen as the object of investigations. Such methods of investigation have been used us: analytical, statistical, system review, grouping and online information.

Results and discussion. Nowadays there are nearly 3000 BBA. About 600 names are presented in the Ukraine market, which have different biological action and have diverse dosage forms. It has been known that vegetable raw material may contain from 10 to several hundreds of chemical compounds and admixtures of relative structural components. The standardization of which is difficult because of many reasons. As to experts estimations there are about 90% of counterfeiting BAA in market. This figure in Ukraine constitutes 40-45%. Quite often personnel of investigating agencies and citizens resort to Ukraine Department of Justice for solving questions about quantitative and qualitative BAA composition. They also ask to refer BAA to strong – effective medicines, which may be injurious to people's health after intake; (for example, deterioration and loss of sight, deterioration of the work of gastrointestinal tract, pain in liver and kidneys). Unfortunately such investigations can't be performed in juridical – and – expert of Ukrainian Department of Justice, because of absence of combined scientifically – developed methods of investigation and lack of legal against to BBA. According to toxicologist's opinion, the most cases of therapeutic effects absence, intoxications and poisoning unknown, because there isn't proper statistics and victims quite often don't consult a physician.

Conclusions. The Associations of BBA manufactures suggest such precautions as protection marks, line – codes and others. However to our mind it can't change the situation, because of previously described reasons. Resolute actions of (from) the state are necessary for this problem solving.

LIPOTROPIC EFFECT OF APPLE POLYPHENOL CONCENTRATE UNDER EXPERIMENTAL STEATOHEPATITIS

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Introduction. Presently, steatohepatitis is one of the most common liver diseases that lead to deterioration in quality of life, disability and death. The steatohepatitis pathogenesis is closely related to insulin resistance (IR). IR causes inflammatory-destructive changes in the liver resulting in steatohepatitis. Along with usage of medicinal preparations, nutritional factors also play an important role in the correction of this disease because patients need complex treatment of this disease.

Aim. The aim of this experiment was to study the lipotropic effect of apple polyphenol concentrate (APC) under the experimental steatohepatitis in rats.

Materials and methods. The experiment was performed on rats weighing 190 ± 15 g kept in the standard vivarium conditions. Experimental liver damage was caused by feeding rat's high-fat diet enriched with fructose during 5 weeks. 24 hours before the end of the experiment, animals were given acetaminophen (APAP) at a dose of 600 mg/kg of body weight. The APC was administered intragastrically daily during the last 2 weeks of the experiment. The animals were decapitated under chloralose-urethane anesthesia, serum total lipids (TL), TAGs, FFA, LDL cholesterol (LDL-Ch), and HDL cholesterol (HDL-Ch) were determined using standard reagent kits. The data were processed statistically.

Results and discussion. In rats with experimental steatohepatitis it was observed an increase in serum TL content in 1.97 times, apparently due to an elevated TAGs and FFA levels in 1.75 and 2.01 times respectively. At the same time, the LDL-Ch content increased in 1.43, however, the HDL-Ch content was decreased in 2.47 times. This is followed by an increase in the atherogenic index, which indicates a high probability of atherosclerosis. APC administration to animals resulted in a significant decrease in blood TAGs and FFA that led to TL content normalization. Also, under apple polyphenols effect was observed lowered LDL-Ch level in 1.3 times and rise in the HDL-Ch in 1.98 times and as a result – positive changes in the atherogenic index.

Conclusions. The steatohepatitis development is accompanied by dyslipidemic disorders in blood serum of experimental animals that are the evidence of a pro-atherogenic state formation. The APC administration reduced the neutral lipids content and the atherogenicity index that indicates the possibility of its further usage for correction of steatohepatitis and proatherogenic state.

INFLUENCE OF EXTRACT FROM THE STEVIA LEAVES ON INDICES OF LIPID PEROXYDATION UNDER EXPERIMENTAL DIABETES MELLITUS TYPE II IN RATS

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Introduction. It is proved that diabetes mellitus is a heterogeneous multifactor disease. The concept of diabetes mellitus type II development is based on the presence of two fundamental defects - insulin resistance and dysfunction of β-cells of pancreas, at that both factors aggravating each other. An important role in pathogenesis of diabetes mellitus also belongs to activation of processes of free radical oxidation (FRO), in particular pro-oxidant and antioxidant imbalance that leads to an excess of free radicals and accumulation of highly toxic products. FRO is an integral part of many vital processes occurring in the body at all the levels. Excessive amounts of oxygen free radicals is released by activated macrophages and damaged β -cells, the last are extremely sensitive to the toxic effect of free radicals. Thus, the process of lipid peroxidation is most represented in cells of Langerhans islets. Considering the important role of oxidative stress in the development of diabetes mellitus, it is reasonable to search the drugs with high antioxidant activity. The group of such compounds includes the substances of flavonoid row, which are very prospective.

Aim. Purpose of the given work was to study the impact of dry extract from the stevia leaves on metabolic disorders development in rats under experimental insulin resistance induced by high-fructose diet.

Materials and methods. Indices of lipid peroxidation was determined by the content of diene conjugates (DK) and TBK-reactive products (TBK-RAP) by the reaction with thiobarbituric acid using spectrophotometric method, antioxidant system condition was evaluated by determining the concentration of reduced glutathione (GSH) - using spectrophotometer method on the reaction with alloxan.

Results and discussion. As seen from the results, retention of rats on high-fructose diet has led to an increase in the content of TBK-AP and DK (primary products of lipid peroxidation) in the liver of animals, which correlates with the decrease of GSH content, indicating the activation of lipid peroxidation and exhaustion of antioxidant protection means.

Conclusion. Administration of dry stevia leaves extracts in our experimend conditions caused normalization of indicators of antioxidant status of organism of investigated laboratory animals that probably could be explained by antiradical properties of polyphenols of stevia leaves extracts.

INVESTIGATION OF THE PRUNUS DOMESTICA LEAVES EXTRACTS MEMBRANE STABILIZING ACTIVITY

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Introduction. One of the actual problems of modern pharmacological is the creation of new, most effective drugs for the treatment of hepatobiliary system diseases. Promising groups of substances are natural polyphenols. Since the polyphenolic compounds exhibit a wide range of pharmacological activity and are actively involved in the regulation of oxidative balance in humans and animals. Prunus domestica is widely used in folk medicine. It is important that Prunus domestica has a large number of varieties and is widely distributed in the Ukraine. At the Department of the Chemistry of Natural Compounds NUPh a extract of the Plum leaves is obtained and its chemical composition is studied.

Aim. For the first time, the membrane-stabilizing activity of the extract from the Prunus domestica leaves was experimentally studied.

Materials and methods. The object of our research was the substance of a dry extract obtained from the leaves of Prunus domestica, obtained from the Department of the Chemistry of Natural Compounds of the NUPh. The substance includes polyphenolic compounds: phenolic carboxylic acids, oxystilbene derivatives, coumarins, flavones, flavonols, flavanones, isoflavonoids and their derivatives. The membrane-stabilizing activity of the extract was studied by the F.C. Jager method. For 3 days, the extract was administrated to rats intragastrically at a dose 25 mg/kg, the most effective for antioxidant activity, and the reference preparation silibor at a dose of 25 mg/kg. Blood was collected from the tail vein and the degree of hemolysis of the erythrocytes was determined.

Results and discussion. It was found that the extract from the Prunus domestica leaves significantly reduced the degree of spontaneous hemolysis of red blood cells. Administration of the extract to the animals resulted in a decrease in this index, in comparison with the control group by 50.3%. Membrane stabilizing effect of the extract from the Prunus domestica leaves was comparable with the activity of the reference preparation Silibor, under the influence of which the degree of hemolysis of erythrocytes decreased by 55.0%.

Conclusions. The administration of the extract from the Prunus domestica leaves is accompanied by a decrease in the manifestations of the cytolytic syndrome, which probably resulted from the inhibition of the peroxide-induced destruction of hepatocyte membranes by the substance studied.

GRAPE POLYPHENOLS IMPROVE GLUTATHIONE METABOLISM IN THE RAT LIVER UNDER EXPERIMENTAL INSULIN RESISTANCE

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Introduction. Glutathione (GSH) is a tripeptide L-γ-glutamyl-L-cysteinyl-glycine. Glutathione has several additional functions in cells: it participates in the metabolism of estrogens, the reduction of ribonucleotides to deoxyribonucleotides, involved in redox signaling and the detoxification endogenous compounds and xenobiotics. It acts as an antioxidant either directly by interacting with reactive oxygen/nitrogen species and as a cofactor for various enzymes. Elevated ROS levels are a key finding in many diseases including cardiovascular diseases, insulin resistance, diabetes mellitus, etc. GSH can interact directly with ROS to reduce their levels and delay the development of pathologies. Plant polyphenols increase the GSH level by exhibiting antioxidant activity. Grape polyphenols activate signaling mechanisms in the cell and may affect the glutathione metabolism enzymes.

Aim. The aim of the work was to investigate the GSH level and glutathione reductase activity in the liver of rats under experimental insulin resistance.

Materials and Methods. The experimental study was conducted on 3 months male rats and weight that were procured from vivarium NUPh. Animals were kept on a high-fat and high-fructose diet during 5 weeks to induce experimental insulin resistance. Grape polyphenols were administered two weeks in dose 9 mg polyphenols/kg/day. The animals were decapitated under chloralose-urethane anesthesia. The liver was perfused with cold physiological solution and homogenized**.** In the liver, GSH level and glutathione reductase activity were determined. The protein level was determined by the Lowry method.

Results and discussion. It was shown that glutathione reductase activity was reduced by 1.5 times in rats under experimental insulin resistance. GSH level was also reduced by a factor of 1.69 in comparison with intact animals. GSH level decrease is due to both a decrease in the activity of glutathione reductase and the enhancement of free radical oxidation under these conditions. Grape polyphenols administration increases of glutathione reductase activity and normalizes the GSH level in the liver of rats under experimental insulin resistance.

Conclusions. Thus, grape polyphenols improve GHS content and glutathione reductase activity in rats under experimental insulin resistance. The findings suggested that the grape polyphenols could ameliorate the consequences of insulin resistance, diabetes and its complications.

THE MITOCHONDRIAL MEMBRANES – COMPOSITION, FUNCTIONS. NEW DATA.

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Introduction. The outer and the inner membranes of mitochondria are of great importance for existence and functioning of the organelles. The membranes differ as to the composition, structure and functions very much. So the outer mitochondrial membrane (OMM) is easily permeable to ions and molecules with molecular weights less than 10 kDa, but not to most proteins. The OMM is 6-7 nm in thickness, has no protrusions and invaginations. The inner mitochondrial membrane (IMM) is 6-8 nm thick, impermeable to ions and vast amount of molecules without special mechanisms, it has many convolutions (cristae) directed into the matrix. Such convolutions enlarge the IMM surface to a great extent.

Aim. For better understanding of the functions of both membranes we should have a closer look at their specific chemical composition. Almost all cholesterol is present in the OMM, stiffening the membrane. The IMM contains practically no cholesterol and has a high fluidity. In contrast, such phospholipid as cardiolipin is located only in the IMM, mostly (70-75%) in the matrix layer of the membrane. On the whole, quantity of phospholipids per unit of protein in the OMM is greater (2 or 3 times) than it is in the IMM, which may be easily explained by the difference in protein content – 50-60% in the OMM versus 70-75% in the IMM.

Discussion. The OMM is very rich in the special integral protein – porin, which β-sheets are arranged in channels to pass ions and molecules. Thus, the OMM is a barrier for large molecules only, and it possesses relatively little enzymatic activity. For instance, acyl-CoA-synthetase, phospholipase A_2, monoamine oxidase and kynurenine hydroxylase were found out on the OMM. In general, the main function of the OMM is to separate the mitochondrion from the cytoplasm. The IMM is much more complicated as to structure and functions. So phospholipids in the IMM are rich in unsaturated fatty acids facilitating its fluidity at physiological temperatures. Most proteins of the IMM are transporters, components of the 4 mitochondrial respiratory chain complexes or subunits of the ATP synthase, which resembles “tiny mushroom” on shape. The proteins of the IMM are to fulfill mainly transport and catalytic functions in the membrane.

Conclusion. A big difference between the mitochondrial membranes is obvious. If the OMM primarily delimits the mitochondrion, and large molecules do not pass it through, the IMM is freely permeable to small, uncharged molecules only. The transport and the oxidative phosphorylation are the main functions of the IMM.

THE STUDY OF APPLE POLYPHENOL CONCENTRATE ANTIOXIDANT ACTIVITY IN RATS UNDER EXPERIMENTAL INSULIN RESISTANCE.

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Introduction. According to International Diabetes Federation, the number of patients with diabetes mellitus increased from 30 to 382 billion during last 40 years. At the same time, 90% of them have diabetes mellitus type 2 (DM2). DM2 is preceded by the insulin resistance state (IR). IR is accompanied by a violation of glucose transport and utilization in cells. In these conductions hyperglycemia, dyslipidemia and insulin secretion disorders develop. Prolonged hyperglycemia and hyperlipidemia stimulate ROS production and oxidative stress development. ROS stimulate lipid peroxidation, protein glycation and plasma membrane damage, which in turn lead to the defeat of various cells and DM2 complications development. Numerous plant polyphenolic compounds exhibit variety activities, and antioxidant properties are the most important among them.

Aim. The aim of our investigation is the study of antioxidant activity of apple polyphenols complex in rat liver and serum under experimental insulin resistance.

Materials and Methods. Experiments were performed on female rats 180±15 g kept in standard conditions of vivarium NUPh. IR was induced by high-fat and high-fructose diet during 5 weeks. Apple polyphenol complex was administered intragastric during last 2 weeks. The liver was perfused with cold physiological solution and homogenized in Tris-HCl buffer, pH 7.4. TBA-reactants and diene conjugates levels were determined in liver and serum. Data were processed statistically.

Results and discussion. The development of experimental insulin resistance was accompanied by an increase in the content of TBA-reactive products in the liver and serum of rats in 2.27 and 2.43 times, respectively. Simultaneously, the diene conjugates content in the rat serum and liver with IR was lower 1.93 and 2.22-fold, respectively. These results indicate activation of the processes of peroxide oxidation and an increase in the degree of saturation of lipids in animal tissues with experimental insulin resistance. The introduction of polyphenol concentrate from apples to animals with experimental pathology leads to a decrease the TBA-reactive products level in the liver and serum in 1.65 and 1.67 times, respectively.

Conclusions. Thus, it was found that the studied polyphenolic concentrate from apple fruits demonstrates a pronounced antioxidant effect. Thus, the studied polyphenol concentrate is a promising substance for the development of new drugs for the complex treatment of IR and associated pathologies.

THE STUDY OF BIOCHEMICAL MECHANISMS DEVELOPMENT OF SOME COMPLICATIONS IN DIABETES MELLITUS TYPE 2

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Introduction. To date, the number of people with the type 2 diabetes mellitus (DM) disease is very large, and the problem is widespread and urgent. According to many literature sources type 2 DM is a metabolic disease characterized by prolonged hyperglycemia on the background of the development of insulin resistance. Most scientists agree that the formation of insulin resistance is associated with obesity and overeating that is accompanied by prolonged hyperinsulinemia. However, it is known that high levels of insulin and glucose in the blood can cause damage to the blood vessels and lead to the formation of certain complications, particularly retino- and nephropathy.

Aim. The aim of this work was the study of complications develoment mechanisms in type 2 diabetes.

Results. Based on literature data it can be noted that the formation of prolonged hyperglycemia and hyperinsulinemia is accompanied by increased glycosylated hemoglobin forms and the development of endothelial dysfunction. The mechanism of micro-capillary endothelium injury is associated with excessive release of arginine into the cells of vessels intima (controlled by insulin) and increased formation of specific vasodilatatore NO that is oxidized to peroxynitrite (ONOO-) under conditions of systemic inflammation. In turn ONOO- is a powerful factor of endothelial damage accompanied by inflammation, increased blood clots, vasodilation violation and, as a result, hypoxia of organs and tissues. It should be noted that retina and kidneys microcirculatory disorders with the above-mentioned mechanisms may be accompanied by deep lesions of these tissues, up to the complete cell death. However, another factor of the nephrons and retina destruction is glycosylated hemoglobin, which due to its increased molecular weight can accumulate in areas of microcapillaries inflammation and mechanically restrain the blood circulation, which in turn deepens hypoxia and nephrons lesion as well as photoreceptor cells.

Conclusions. Thus, kidney and retina damage in diabetes mellitus type 2 is primarily associated with the development of endothelial dysfunction and hypoxia of these tissues, however the search for other mechanisms of these complications requires further investigation.

INFLUENCE OLFACTORY EFFECTS OF SOME ESSENTIAL OILS ON THE FUNCTIONAL PARAMETERS OF CENTRAL NERVOUS SYSTEM IN RATS

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Today found that the human nervous system contains a myriad of different types of neurons, many of which have multiple subtypes. For olfactory epithelial neurons diversity index is particularly high, it is more than 1000 different subtypes of olfac-tory sensory neurons, each of which is defined by its own gene and has a specific odorant - receptor, which is actually involved in the recognition of odors. Confirmation of activation with olfactory cortex influences were identified according to the electroencephalogram and shown in many scientific publications.

The aim of our work was to study the effect of essential oils of lavender, lemon and rosemary on the functional parameters of the central nervous system.

Materials and methods. In order to study the effect of the essential oils of lavender, rosemary and lemon CNS performance test was carried out "open field" for male rats, with which studied the locomotor activity, exploratory behavior and vegetative support emotional reactions.

Results. For intact rats is characterized by a fairly high rate locomotor activity and research, at the same time it should be noted that the animal was in the room for him a stressful situation, as evidenced by the low rate of grooming (0,62±0,26), which animals make only peaceful state and a high level of activation of vegetative reactions (boluses: 3,75±0,53; urination: 0,87±0,23), as a reaction to stress. The five-day administration of valerian extract promoted the development of pronounced sedation. Essential oils of lavender, lemon, rosemary, and significantly reduced the locomotor activity of the animals and research, which testifies to their sedative effect. It should be noted that the most pronounced decrease in CNS excitability was observed upon exposure of rosemary essential oil. Interesting is the fact that the inhalation of rosemary essential oil was observed a significant decrease in motor activity when stored exploratory activity indicators.

Conclusions. Mounted multi-directional effects of studied essential oils. The essential oil of lavender and lemon without compromising on much expressed as valerian extract lokomotorno- motor activity, significantly reduce the level of anxiety, manifesting mild anxiolytic effect and antidepresive. Rosemary essential oil reduces locomotor activity at the level of the comparison of valerian extract preparation, it does not reduce the rate of exploratory activity of animals.

DEPENDENCE OF THE BIOLOGICAL ACTIVITY OF ELEMENTS ON THE ELECTRONIC STRUCTURE OF THEIR ATOMS

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Introdaction. Eighty-one elements out of one hundred and ten chemical elements of the periodical system are found in the human body. Classification, which is based on the biological role of elements, divides the elements that are in the body into three groups: vital (biogenic, esential); conditionally necessary and elements with an unidentified role. Famous Russian geochemist O. P. Vinogradov called biogenic elements all the chemical elements that participate in biological processes of living organisms.

Aim. It is known that the physical-chemical properties of elements and their biological role are determined in a living organism by their position in the D.I. Mendeleyev's periodic system, in particular the electronic structure of atoms. It is of interest to discover some regularities of this dependence of biological activity on the electronic structure of the atom.

Materials and methods. Depending on the average content of the element in the human body, they are divided into 3 groups:

1. Macroelements (the content in the body is more than 10^{-2}%)
2. Microelements (the content in the body is 10^{-2} -10^{-5}%)
3. Ultra-microcelements (the content in the body is less than 10^{-5}%)

The main function of macroelements is to build the tissues and skeleton of the body, to observe the constancy of osmotic pressure, ionic and acid-base composition.

The macroelements are divided into organogens (C, H, O, N, P, S - in the body 97.4%) and electrolytic background elements (Na, K, Ca, Mg, Cl), depending on the functional role.

Organogens form the basis of all living organisms. They are part of proteins, nucleic acids, carbohydrates, fats. In addition to hydrogen, organogens are p-elements of the second and third periods, which have small atomic radiuses, intermediate values of electronegativity. They are capable of forming strong but reactive covalent bonds, and carbon derivatives are able to easily form cycles.

In turn, elements of the electrolytic background K, Na, Mg, Ca are s-elements that have 1 or 2 valence electrons in the period and the lowest value of the ionization energy. They exist in the form of cations in the body, easily penetrate the cell membranes and form electrical biopotentials and biocurrents.

Except the s-elements of K, Na, Mg, Ca, six d-elements of Fe, Zn, Cu, Mn, Mo, Co are also called "metals of life ". They are vital for the existence of a living organism. These elements are in the body in the form of complexes with bioligands - amino acids, proteins, nucleic acids, hormones, vitamins.

From a biological point of view, complexing elements are the organizers of life. These are d-elements mainly. They have small atomic radiuses and atomic orbitals with free energetically, which may accept ligand's electrons.

Among the d-elements, vitally important, elements of the 4th period: Mn, Fe, Zn, Cu, Co. Recently, biological role was established and some other d-elements of this period: Ti, V,Cr. They are the lightest among the d-elements, with the lowest atomic radiuses and energy of ionization.

Such a similarity in the characteristics of these elements predetermines their interchangeability and close biological action. So the d-elements of the 4th period elements, other than Zn, provide the process of blood formation. All of them increase metabolism and affect the biosynthesis.

It is established that the ability of chemical elements to exert a catalytic effect increases millions of times if they form metal complexes.

The organism is harmed by both the shortage and the excess of the element. Elements in higher concentrations become toxic, but in small amounts are essential. There are 20 metals the list of the most toxic substances. Usually, the toxicity of an element of this group increases and their content decreases in the body, with an increase in the atomic nucleus charge.

So, an organism weighing 70 kg contains: nitrogen 2.1 kg, phosphorus 0.7 kg and antimony 0.9 g. N, P, Sb are elements VA group. Nitrogen and phosphorus are organogens, and antimony is a toxic element. The elements of period 6 are Pb, Te, Hg and the element of period 5 is Cd exert the most toxic effect.

Results. The elements of s-, p-, d-blocks with a small value of the charge of the nucleus, mainly elements of 2 and 3 periods for s- and p-elements and 4 periods for d-elements, belong to biogenic elements.

Conclusions. The biological role of the element and its toxicity is determined by the electronic structure of their atoms. With an increase in the nuclear charge, and the number of electrons correspondingly, the toxicity of the elements of this group increases, and their content decreases in the body.

STUDY OF ANTIMICROBICAL ACTIVITY OF NEW GEL FOR TREATMENT OF PERIODONTAL DISEASES

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Introduction. Oral diseases are one of the serious common health problems in life and are expensive for treatment. Dental caries, periodontal disease and gingivitis are among the most important preventable global infectious-inflammatory diseases in Ukraine and the world as a whole. More than 90% of the adult population of the Earth are prone to periodontal diseases. This leads to tooth loss, chronic oral cavity, significantly worsen health and quality of life. The activity of each component of the drug should be directed to a particular factor in the inflammatory process. Local medical treatment is carried out in order to affect the microflora of pathological gum pockets, and give preference to herbal medicines. Composition and technology of new gel based on plant extracts was developed by prof. Khokhlenkova N.V. at the Department of Drug Technology of National University of Pharmacy.

Aim. The purpose of this work is to study the antimicrobial activity of new gel containing plant extracts for the treatment of periodontal diseases.

Materials and methods. Antimicrobial activity was studied using cup diffusion method by diffusion to agar by evaluating antibiotic susceptibility on the following strains of test microorganisms: Staphylococcus aureus, Escherichia coli, Basillus subtilis, Candida albicans. The results of studies characterize the antimicrobial activity of the drug as well as the release of a substance from the base, as stunted growth of microorganisms zone formed by diffusion of substances in dense nutrient medium. Test samples of the antimicrobial activity were compared to the registered in Ukraine dental gel for gums «Metrogyl Dent» classical drug for the treatment of inflammatory periodontal diseases.

Results and discussion. The level of antimicrobial activity of the new gel exceeds the comparator, it is shown against the bacterial test strains according to the diameter of the zones. The antimicrobial effect of «Metrogyl Dent» shown by the following results: S. aureus 15.1±0.3 mm, E. coli 14.7±0.6 mm and C. albicans 22.0±0.1 mm. New gel shows more intense antimicrobial activity, as indicated by results: S. aureus 19.8±0.4 mm, E. coli 200±0.7 mm and C. albicans 29.4±0.5 mm.

Conclusions. As a result of the research it was found that new gel have a wide spectrum of antimicrobial activity and is characterized by activity against both gram-positive and gram-negative bacterial cultures of microorganisms and shows high activity against fungus Candida albicans.

Section 7.

GENETIC RESEARCH, POSSIBILITIES OF PRACTICE MEDICINE AND PHARMACY USE

CANCER AND CHEMOTHERAPY

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Cancer is one of a large number of diseases characterized by the development abnormal cells that divide uncontrollably and have the ability to infiltrate and destroy normal body tissue. Cancer has the ability to spread throughout the body.

Symptoms can include: fatigue, thickening under the skin, weight changes, skin colour changes, persistent cough, difficulty swallowing, hoarseness, discomfort after eating, muscle or joint pain, changes in bowel or bladder habits, unexplained and persistent fevers or night sweats.

Causes are like these: Chemical carcinogens e.g. smoking and alcohol, Infection, Radiation, Hormones, Genetics. All of these causes lead to gene mutation (rapid and uncontrolled cell growth and mistakes in DNA repairing during cell cycle regulation).

Problems associated with cancer chemotherapy may appear: resistance, some of cancer (neoplastic) cell are resistant to most anticancer drugs; toxicity of chemotherapeutic agents. It affects normal cells especially rapid proliferation cells e.g., buccal mucosa cell; GI mucosa; bone marrow; hair follicle.

Anti-cancer(Anti-neoplastic) drugs differ. Cytotoxic drugs: antimetabolites, folic acid analogues (methotrexate), purine analogues (6-mercaptopurine,6-thioguanine,fludarabine,cladribine and pentostatine), pyrimidine analogues (5-fluorouracil,capecitabine and floxuridine), cytidine analogues (gemcitabine and cytarabine), alkylating agents: nitrogen mustard (mechlorethamine, cyclophosphamide, ifosfamide, mephalan and chlorambucil), nitrosourea (carmustine, lomustine and streptozocine), alkyl sulfonates (busulfan), triazenes (dacarbazine and temozolomide), platinum (cisplatin, carboplatin and oxaliplatin), natural products: antibiotics: (dactinomycin, mitomycin, doxorubicin, epirubicin, idarubicin and bleomycin), plant alkaloids: vinca alkaloids (vincristine,vinblastine and vinorelbine), taxol (paclitaxel , docetaxel) – the amount isolated from 3 trees is required only for one cancer patient, enzymes (L-Asparaginase), endocrine therapy (agonist and antagonist), Monoclonal antibodies: monoclonal antibodies made by fusing cancer cells with the spleen cells from a mouse (hybridoma). The hybridomas grown in culture medium by using recombinant technology to produce humanized antibodies e.g. (Rituximab, Trastuzumab and Bevacizumab).

Eventually, people with cancer disease mostly have combination therapy to control this cursed disease, but it matters also that they don’t lose the hope of complete healing.

THIS ARTIFICIAL RETINA COULD REVOLUTIONIZE THE WAY WE TREAT SIGHT LOSS

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Introduction: Damaged retina is often something many people have to live with it for the rest of their life. it leaves them with reduced sight or even blindness.

Even those that don't suffer from an injury can suffer from an unfortunate condition where their retina's photoreceptor cells die off, and their sight slowly deteriorates over time.

Aim: to alleviate the problems associated with a damaged or defective retina. A cybernetic replacement of retina.

Materials and Method: made of sandwich of a thin layer of electrically conductive polymer, a silk based subtrate, and a semi-conductin polymer, it's able to absorb photons when light sneaks in through the eye's pupil.

The photons generate an electrical current, and make their way to the back of the device and into the retinal neurons within the optic nerve. This device inserted into rats eyes. The team tested their pupil's responses under a variety of low-light condition.

Results and discussion: under very low-light conditions resembling that ofa full moon, the rats with implants were no more responsive than rats with damaged retinas lacking the artificial retina.

However, when conditions similiar to a sky at twilight arose, the augmented rat's pupillary response were essentially no different from that of healthy rats with perfetly working retinas.

Conclusion: the implant was successful for 10 months. But this experiment was a bit of shot in the dark - at this point, it's not clear how clear an image the rats with the artificial retinas are able to process, nor is it certain how the device even works on a biological level.

Neverthless, with human trials likely to follow suit later this year, it's a remarkable step in the right direction to restoring sight to those that have lost or are losing it.

EPONYMS IN HISTOLOGY

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Introduction. An eponym in medicine is the name of an anatomical structure or disease by the name of the person who first discovered or described it (for example: Eustachian tube, Quincke's edema). Eponymic terms constitute a significant part of medical terminology. In 1974, international anatomical terms were officially approved. After this date, eponyms are very rarely used in textbooks on anatomy and histology. In clinical practice, eponyms are widely used. They reflect the history of science and the contribution of researchers to its development. A highly educated specialist in the field of medicine should know the scientists who contributed to the development of anatomy and histology, which gave their name to anatomical and histological structures.

Aim of research. Find in the literature and systematize information about scientists whose names are known histological structures, systematize eponyms in histology.

Material and methods. The methods used were: descriptive; Method of theoretical analysis of scientific data; Method of classification and systematization. A total of 176 eponyms have been studied. A total of 176 eponyms have been studied. Of these, a group of anatomical (histological) terms and a group of research methods in medicine and biology are distinguished. There were describes biographies of scientists for 47 eponyms in cytology.

Results. The most famous eponyms in histology. Golgi apparatus (intracellular plate complex) is named after the Italian histologist, Nobel Prize winner (1906) Camillo Golgi. Nislya granularity (substantia basophila) - basophilic granularity of the cytoplasm of neurons. It is a cytoplasmic network with a large number of ribosomes. Named after the German physician-neurologist Franz Nissl. Romanovsky method - the original method of coloring cells in smears and sections of tissue invented Romanovsky Dmitry Leonidovich (1861-1921) - Russian terapeuthist, hematologist, microbiologist and infectious disease specialist. He studied malaria.

Conclusions: Eponyms represent the history of medical science. They allow us to preserve for medical science and new generations the names of scientists who have contributed to science. Studying eponyms allows you to learn the forgotten names of worthy scientists. These scientists have influenced so much the development of the science of man that the trace of their activity remains to this day.

PRESENTATION AS A FORM OF ACTIVE STUDENT WORK AT THE SEMINAR SESSION ON HYSTOLOGY

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Introduction. Modern life requires of professionals the development of creative initiative, the desire to improve their theoretical training, the ability to independently receive education. Important tasks of higher education are now: the development of students' independence and ability to self-organization; readiness for cooperation, development of the capacity for creative activity; tolerance to the opinions of others, the ability to conduct a dialogue, to seek and find compromises. One of the active forms of training sessions are seminars. They are used in the teaching of all academic disciplines. At the seminars all students deliver reports on the topic of the seminar. Questions for the message each student receives in advance. After the students' speech, a discussion of their speeches, discussion, exchange of opinions is held. At the end of the seminar, the teacher summarizes the work of the students. At the seminars on histology, students' messages can be in the form of an abstract or presentation.

Aim of research. Compare different forms of conducting seminars with students in the study of the discipline "histology" - abstracts and presentations.

Material and methods. Questioning of first-year students specialty "Laboratory diagnosis". Questionnaire questions: what form of message do you like best; do you need the skills of preparing a presentation; what is the use of preparing a presentation for a student?

Results. Presentation as a form of an individual task prefer 90% of students more than preparing an abstract. The presentation allows you to more accurately perceive the material. When studying histology, visualization is very important. The design of presentation slides develops the skills of visual presentation of information. The material of the topic, which is being studied, requires repeated repetition for the development of a slide when preparing a presentation. The material is better remembered when preparing a presentation than when preparing an abstract. Preparation of the presentation is more creative and more interesting work than the preparation of the abstract. All 100% of the students surveyed consider the skills of preparing the presentation to be necessary in the future professional activity.

Conclusions: Preparing a presentation on a given topic is the most successful form of an individual assignment for a student for a seminar on the discipline "Histology."

HYPERTENSION THERAPY

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Hypertension is an abnormally high blood or a state of great psychological stress.

It is a common disorder if not effectively treated will result in stroke, retinopathy and renal failure.

Blood pressure is intimately related to the kidneys.

It is a condition in which high blood pressure is caused by the kidneys hormonal response to narrowing of arteries supplying kidneys with blood.

Hypertension is a chronic condition and is often associated with few or no symptoms.

But when symptoms do occur it's usually when the blood spikes suddenly and extremely enough to be considered a medical emergency.

There are known to be rare symptoms include dizzy spells, headaches, nose bleeds, nervousness, sweating and difficulty sleeping.

It is largely symptomless therefore branded the "silent killer" because when someone ignores his/her blood pressure thinking that a certain symptom or sign will alert him/her then that person is taking a dangerous chance with the life.

The exact causes of high blood pressure are not known but several factors and conditions may play a role in its development including smoking, obesity, lack of physical activity, excess salt in the diet, excess alcohol consumption, stress, old age and family history of high blood pressure.

Uncontrolled Hypertension can cause stroke due to blood clots that form in the arteries leading to the blocking of blood flow to the brain

ACE inhibitors also known as Angiotensin-Converting-Enzyme inhibitors is a pharmaceutical drug used primarily for the treatment of hypertension.

ACE inhibitors increase plasma levels of digoxin and lithium (dosage adjustment is necessary).

There are other drugs which are known to be very effective against hypertension.

STUDYING THE STRATEGY OF GENOTYPING IN THE UKRAINIAN POPULATION SAMPLE

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Pharmacogenetics is based on the strategy of screening for polymorphism – genotyping. With the help of this technique, the presence of a specific variant of a gene with the help of a polymerase chain reaction is determined in man. Quite often in the world, conducting preliminary genotyping, determine the status of a metabolizer for the family of cytochromes CYP-450, which are responsible for the metabolism of more than 50% of the world's produced drug. In particular, CYP1A2 and CYP2B6 are the most important liver enzymes that participate in the metabolism of a number of widely used drugs. Cytochrome CYP1A2 is involved in the metabolism of caffeine, theophylline, melatonin, clozapine, verapamil, propranolol, etc. CYP2B6 is responsible for the metabolism of such drugs as cyclophosphamide, bupropion, efavirenz, methadone, ketamine, etc. An increase in the level of IL-6 in the blood is observed in many pathological conditions, such as autoimmune diseases, severe inflammatory processes, infections, allergies.

The aim was to study the polymorphism of CYP1A2 (rs762551), CYP2B6 (rs3745274) and IL-6 (rs2069840) genes in the Ukrainian population sample.

For the analysis, a sample of 102 Ukrainians (48 male, 54 female) who were not relatives was formed. The buccal epithelium was picked up. Genotyping for the polymorphism of CYP1A2 (rs762551), CYP2B6 (rs3745274) and IL-6 (rs2069840) was performed using polymerase chain reaction. In the course of the studies, the distribution of genotypes in this group was determined for CYP2B6 (rs3745274): 57% GG, 38% GT, 7% TT; for CYP1A2 (rs762551): 37% AA, 50% AS, 15% CC and for IL-6 (rs2069840): 47% CC, 50% CG, 5% GG. Allele frequencies for CYP2B6 were determined: p_G – 0.75 and q_T – 0.25; For CYP1A2: p_A – 0.6 and q_C – 0.4; for IL-6: p_c = 0.72 and q_g = 0.28.

Conclusions: the genetic polymorphism among the Ukrainian population is shown, which is later recommended for carrying out genetic testing of the polymorphism of the genes CYP1A2 (rs762551), CYP2B6 (rs3745274) and IL-6 (rs2069840) when prescribing drug therapy regimens.

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CONGENITAL PROBLEMS

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Congenital anomalies are also known as birth defects, congenital disorders or congenital malformations congenital anomalies, can be defined as structural or functional anomalies, that occur during intrauterine life and can be identified prenatally at birth, or sometimes many only be detected later in infancy, such as hearing defects.

The aim of study of this problem can include such aspects: to save the largest number of births; developing and strengthening registration and surveillance systems; developing expertise and building capacity; strengthening research and studies on etiology, diagnosis and prevention; pronoting international cooperation.

Factors may include genetic, environnental, socioeconomic and demographic ones, infections, maternal nutritional status. Genetic factors are congenital anomalies, this might be through inherited genes that code for an anomaly, or resulting from sudden changes in genes known as mutation. Environmental factors can include medications, alcohol, tobacco and radiation during pregnancy, that may increase the risk of having a fetus or neonate affected by congenital anomalies. Low-income may be an indirect determinant of congenital anomalies, with a higher frequency among resource, constrained families and countries maternal age is also a risk factor for abnormal intrauterine fetal development, advanced maternal age increase the risk of chromosomal abnormalities, including Down syndrome. Material infections as syphilis and rubella are a significant cause of congenital anomalies in low and middle-income countries.

Maternal folate insufficiency increases the risk of having a baby with a neural tube effect while excessive vitamin A intake may affect the normal development of an embryo or fetus. Preventive public health measures work to decrease the frequency of certain congenital anomalies through the removal of risk factors or the reinforcement of protective factors, important interventions and efforts include ensuring adolescent girls and mothers have a heal they diet including a wide variety of vegetables and fruit, and maintain a healthy weight, ensuring an adequate dietary intake of vitamins and minerals and particularly folic acid in adolescent girls and mothers, ensuring mothers avoid harmful substances, particularly alcohol and tobacco, avoidance of travel by pregnant women to regions experiencing outbreaks of infections known to be associated with congenital anomalies.

DRUGS, DRUG ABUSE AND DRUG ADDICTION

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Drug abuse is found to be greatest in individuals ages 18–25, with a higher likelihood occurring in men compared to women, and urban residents compared to rural residents. On average, general medical facilities hold 20% of patients with substance-related disorders (Drug abuse And Drug addiction), possibly leads to psychiatric disorders later on. Over 50% of individuals with substance-related disorders will often have a "dual diagnosis," where they are diagnosed with Drug abuse, as well as a psychiatric diagnosis, which is the most common, and being major is depression, personality disorder, anxiety disorders, and dysthymia. Whereby this thesis sums up by expressing the number of drug addicts increasing everyday and its side effects to this world. A drug is any substance (other than food that provides nutritional support) that, when inhaled, injected, smoked, consumed, absorbed via a patch on the skin, or dissolved under the tongue, causes a physiological change in the body. In pharmacology, a pharmaceutical drug, also called a medication or medicine, is a chemical substance used to treat, cure, prevent, or diagnose a disease or to promote well-being. Pharmaceutical drugs are often classified into drug, with classes & groups of related drugs that have similar chemical structures, the same mechanism of action (binding to the same biological target), a related mode of action, and that are used to treat the same disease.

Drug abuse, is a patterned use of a drug in which the user consumes the substance in amounts or with methods which are harmful to themselves or others, and is a form of substance-related disorder. Drug addiction, is a behavior or an adaptive state associated with a withdrawal syndrome upon cessation of repeated exposure to a stimulus (e.g. drug intake). The two properties that characterize all addictive stimuli are that they are reinforcing (i.e., they increase the likelihood that a person will seek repeated exposure to them) and intrinsically rewarding (i.e., perceived as being positive or desirable).The drugs used are often associated with levels of intoxication that alter judgment, perception, attention and physical control, not related with medical or therapeutic effects. It is often thought that the main abused substances are illegal drugs and alcohol; however it is becoming more common that prescription drugs and tobacco are a prevalent problem.

QUESTIONS OF PSYCHOLOGICAL ADAPTATION OF STUDENTS OF HIGHER EDUCATIONAL INSTITUTIONS

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In modern conditions, the acquisition of education in Universities can be attributed to a specific type of activity associated with a high level of mental and physical loads, which are extremely increasing during the sessional time. Student youth may have various psychological and neuropsychic disorders. This is due to high mental and psycho-emotional stress, forced frequent violations of the regime of work, rest and nutrition, the need to adapt to new living and learning conditions. These and many other factors require students to mobilize forces to adapt to new conditions, the formation of interpersonal relationships outside the family. Specificity of university education coincides with the age of the highest risk of manifestation of mental pathology, which may be due not only to the biological nature of mental illnesses, but also to significant stress loads. Initially, there may be maladaptation in educational activities. It manifests itself in a worsening of concentration, memory loss, difficulty in expressing one's thoughts, fear of control work, before public speaking.

Given the urgency and importance of this issue, we conducted a survey among students at the National Pharmaceutical University. All courses, girls and boys aged (18-25) participated in the survey. The survey included such questions: how and what do they do in the period of stress. What causes them a stressful state. How do they get out of the stressful state. It was revealed that among students who study at the first year, signs that indicate borderline neuropsychic diseases are detected in 68.3%. According to psychotherapists, third-year students are most susceptible to various stress factors that contribute to the onset of neurotic conditions. This is due to difficulties in adapting to new professional and living conditions. To 4-5 training courses, there is a decline in such trends. The problem of violation of adaptation of students in higher education institutions exists today, and it is extremely relevant. A large number of students in the first year have those or other signs of a violation in the psycho-emotional sphere: excessive irritability, lability of mood, propensity to depressive states.

All this must be taken into account, both to the students themselves and to the teachers of higher educational institutions in the conduct of the pedagogical process. When identifying such signs need psychological help specialist.

TATTOOS AND THEIR EFFECTS ON THE CELLS OF THE HUMAN BODY

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Introduction: Tattooing has long been practised in various societies all around the world and is becoming increasingly common and widespread in the West.

In the primitive times, tattoos were used for identifying slaves and sometimes indicating their next destinations.

Today, lots of celebrities and a couple of the world's influential people have tattoos.

Aim: Assessment of the toxicity of tattoo inks has been the subject of little research and ink manufacturers are not obliged to disclose the exact composition of their products so this has encouraged me to create the awareness of the effects of tattoos through this research.

Materials and Methods: This study examines tattoo ink particles in two fundamental skin components at the nanometre level.

The use of atomic force microscopy and light microscopy to examine cross-sections of tattooed skin, exploring the collagen fibril networks in the dermis that contain ink nanoparticles. Fibroblasts in diluted tattoo ink to explore both the immediate impact of ink pigment on cell viability and also to observe the interaction between particles and the cells.

Results and Discussion: According to my findings as years pass by, skin can be itchy, red, inflamed and sensitive, with a high risk of infection and also yellow and some red pigments from tattoo ink contain cadmium sulphide, which causes an allergic reaction (dermatitis) when exposed to the sun.

Tattoo dyes causes an itchy rash at the tattoo site sometimes bumps called granulomas form around tattoo ink. Tattooing also lead to keloids and also in some countries One can contract various bloodborne diseases which includes hepatitis B and C tetanus and among others.

Conclusion: In conclusion, some tattoos are so beautiful but not all that glitters is gold thus this scientific work would create the awareness on the side effects of tattoo on the cells of the human body which would gradually eradicate tattooing.

LYMPHATIC FILARIASIS

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Lymphatic filariasis, commonly known as elephantiasis, is a neglected tropical disease. The first documentation of symptoms occurred in the 16th century, when Jan Huyghen van Linschoten wrote about the disease during the exploration of Goa.This disease is common in Africa and Asia. Infection is usually acquired in childhood causing hidden damage to the lymphatic system. The painful and profoundly disfiguring visible manifestations of the disease, lymphoedema, elephantiasis and scrotal swelling occur later in life and can lead to permanent disability. The global baseline estimate of persons affected by lymphatic filariasis was 25 million men with hydrocele and over 15 million people with lymphoedema. At least 36 million persons remain with these chronic disease manifestations. Eliminating lymphatic filariasis can prevent unnecessary suffering and contribute to the reduction of poverty. Lymphatic filariasis is caused by infection with parasites classified as nematodes (roundworms) of the family Filariodidea. There are 3 types of these thread-like filarial worms: Wuchereria bancrofti is responsible for 90% of the cases; Brugia malayi is the cause most of the remainder of the cases.

Mosquitoes are infected with microfilaria by ingesting blood when biting an infected host. Microfilaria matures into infective larvae within the mosquito. When infected mosquitoes bite people, mature parasite larvae are deposited on the skin from where they can enter the body. The larvae then migrate to the lymphatic vessels where they develop into adult worms, thus continuing a cycle of transmission. Lymphatic filariasis is transmitted by different types of mosquitoes for example by the *Culex* mosquito, widespread across urban and semi-urban areas, *Anopheles*, mainly found in rural areas, and *Aedes*, mainly in endemic islands in the Pacific. The worms can live for an average of 6–8 years and, during their life time, produce millions of microfilaria (immature larvae) that circulate in the blood. The majority of infections are asymptomatic, showing no external signs of infection. These asymptomatic infections still cause damage to the lymphatic system and the kidneys, and alter the body's immune system.

The World Health Organization recommends mass deworming-treating entire groups of people who are at risk with a single annual dose of two medicines, namely albendazole in combination with either ivermectin or diethylcarbamazine citrate. Avoiding mosquito bites, such as by using insecticide-treated mosquito bed nets, also reduces the transmission of lymphatic filariasis.

NICOTINE AND IT'S EFFECT ON THE HUMAN BODY

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Smoking has long been included in the international classification of diseases as "tobacco dependence". The need for such an action was associated with the severe social consequences of smoking. But the most interesting is that most smokers (according to statistics, about 70%) consider the nicotine as the main component that harms. While the most terrible harm of smoking causes not the nicotine, but the products of combustion of the tobacco leaf, in other words - cigarette smoke, as well as the carcinogenic substances that are contained in the cigarette.

Nicotine is a pyridine alkaloid contained in plants of the family of nightshade, mainly in leaves and stems of tobacco. Once nicotine enters the body, it quickly spreads through the bloodstream and can cross the blood-brain barrier. On average, 7 seconds after the inhalation of tobacco smoke, so that nicotine reaches the brain.

The half-life of nicotine from the body is about two hours. It acts on nicotinic acetylcholine receptors: at low concentrations, it increases the activity of these receptors, which leads to an increase in the amount of stimulating hormone adrenaline (epinephrine). The release of adrenaline leads to an acceleration of the heartbeat, an increase in blood pressure and increased respiration, as well as a higher level of glucose in the blood. Nicotine increases the level of dopamine in the pleasure centers in the brain. When used in small doses, nicotine acts as a psychostimulation.

According to statistics (Australian Statistical Bureau for 1989/90) it turned out that, in general, the health of smokers is better than those who quit smoking and non-smokers. Myocardial infarction had 11.4% quit smoking, 6.7% non-smoking, and 6% regular smokers. From the increased pressure caused by stress, former smokers are most affected - 16%, non-smokers - 13.4% and only 7.4% of smokers.

But Tobacco and tobacco smoke are sources of carcinogens and increase the risk of cancer in all anatomical structures in contact with smoke. Similarly, nicotine in large doses and regular use causes a strong psychological dependence.

Nicotine has a stimulating effect on the brain, improving memory and processing quality. In addition, smokers have a 70% less risk of developing Parkinson's disease than non-smokers. Similar data were obtained for Alzheimer's disease. Also, the harm of smoking mainly depends on the chemical compounds, the carcinogenic substances that are contained in the cigarette. But the cigarette component - nicotine has nothing to do with it. Therefore, the main task for scientists of different fields is to create the safest way of using nicotine.

POSITIVE VIBRATION – THE BODY AND MUSIC

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Happiness, health, sanity, unconventional methods of treatment, motivation even acumen, all have one common friend, music. Music over the years, through multiple examinations, researches and speculations by many reputable as well as 'layman' sources has shown its ability to affect many actions of the body and mind.

The intent of this research is to widen the minds of the readers as well as bring to their attention the numerous benefits of music in different aspects as it relates to the human body and how we can implement some of these findings into today's methods targeted at increasing the longevity of the human race.

In order to prove the findings in this research, a questionnaire was issued amongst persons within the Ukraine, Kharkov region. Also information from the work of other researchers and medical examiners was used and quoted in the discussion of this research.

In the music world, there exists the octave treble clef which means there are 8 notes per octave and in this research, these 8 notes will represent 8 benefits of music for the body: music makes you smarter, has positive medicinal effects, motivates, adjusts attitude and regulates ones mood, assists with relief of addictions, boost immune system, helps in recovery of lost memory as well as improves memory and increase spatial reasoning.

Have you ever realized that you can memorize the word of a song even when you had no intentions of it? Or found yourself singing the tune to that song you hate so much but is embedded in your mind? That's the power of music as it improves concentration and attention. Music that is easy to listen to or relaxing classics improves the duration and intensity of concentration in all age groups and ability levels. Harvard Medical School neuroscientist Gottfried Schlaug in an interview with News in Health said that through his studies, he found that when you make music, it engages many different areas of the brain, including visual, auditory and motor areas and thus the interest of music as a treatment for neurologic disorders. According to some studies, for musicians, particularly those who begin playing an instrument at an early age, music learning can encourage the development of stronger vocabularies and a better handle on nonverbal reasoning.

Music has positive medicinal effects. It has even been reported that ambient

noise, played at a moderate volume, can encourage creativity, and that listening to music can help repair brain damage. Music has also shown the ability to help in treating Parkison's disease.

Several studies have shown that music can enhance athletic performance. One 2012 study called "Effect of Music-Movement Synchrony on Exercise Oxygen Consumption" found cyclists who peddled along to music used 7% less oxygen than those who didn't couple their ride with music to match their pace.

According to research conducted at the University of Missouri, a team of scientists has confirmed that music is a mood booster. Listening to slow, quiet classical music, is proven to reduce stress. Countless studies have shown that music's relaxing effects can be seen on anyone, including newborns.

As it turns out, performing music can be relaxing and can create a distraction from withdrawal symptoms. Songwriting can help patients confront impulse control and self-deception and allows an output for negative emotions. Music directly affects chemicals called neurotransmitters which relay information in our head. Drugs work in a similar way, except they make your brain lazy and convince it to stop making its own chemicals.

Music reduces stress by reducing cortisol levels, a chemical in your brain that causes you to feel stress in the first place. Jazz, bluegrass and soft rock have been found to be especially effective at reducing stress and increasing health because of their similar musical qualities.

Listening to music engages many areas of the brain in both hemispheres, which is why it can create brain activity other methods, like conversation, do not have the ability to do. Another area it engages is the hippocampus, which is the region of the brain which handles long-term memory storage.

Spatial-temporal reasoning is the ability to create, maintain, transform, and relate complex mental images, even in the absence of external sensory input or feedback. In other words, reasoning through space and time. Math, science, physics, chess, and music all involve this type of reasoning. Mozart music, especially piano music, can raise your spatial reasoning the equivalent of nine IQ points.

From the multiple researches conducted both formally and informally, it is safe to say that music is the ultimate healer and as the late, great musician, Bob Marley, concluded "One good thing about music, when it hits you, you feel no pain".

THE INTERACTION BETWEEN GENES AND ENVIRONMENT

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Most common diseases are a result of both your genes and your environment. Your environment can include personal choices, such as what foods you eat and how much you exercise, and external factors, such as stress, clean water, and air quality.

Only a small number of diseases are a result of just a single mutation in a gene. Examples of these single-gene disorders are Huntington disease and Tay Sachs.

Most diseases, especially common diseases, are a combination of your genetic risk and your environment. It is becoming difficult to group diseases into either purely ‘genetic’ or ‘environmental’ because most diseases are a little bit of both. For example, emphysema can be the result of both smoking and a disorder called alpha-1-AT deficiency. The field of research looking at gene-environment interactions (GxE) is growing.

It is important to understand that most times your genes do not determine your health. Small differences in your genetic makeup mean that two people can respond differently to the same environmental exposure. Mutagens are pollutants in the environment that enter the body and directly change your DNA sequence. The chemicals in cigarette smoke can cause cancer.

Gene-gene interactions occur when pollutants in the environment do not change your DNA sequence, but rather cause a chain reaction that affects the functioning of one gene that then affects the functioning of another gene. Regularly drinking way too much alcohol can cause a specific gene, TACE, not to produce enough of its protein. TACE protein is supposed to help the MTHFR gene make enough of its protein. Too little MTHFR protein changes the level of folate (another protein) in our blood, and low folate levels may cause depression. Pollutants in the environment can indirectly affect the DNA sequence by altering transcription factors, which are responsible for starting the process of using genes to make proteins that are needed for different functions in the body. Stress can change the amount of proteins made by genes involved in immune system and therefore, you may get sick more easily when you’re stressed.

USAGE THE *DROSOPHILA MELANOGASTER* AS OBJECT FOR STUDYING AGING AGE: REVIEW OF RESEARCH AND TRENDS OF USE

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Introduction. The study of genetic regulation of the aging process can today be considered one of the most interesting and promising for researching the problems of medical genetics.

Since the general genetic mechanisms of the regulation of life expectancy are considered to be evolutionarily conservative, very far from human species can be used as model objects for their study.

Drosophila melanogaster is considered one of the most studied and often used model objects in genetics.

Since the discovery of the gene *methuselah* (and further many other genes affecting life expectancy), *Drosophila* has been one of the most useful model objects for studying the role of genes in the regulation of aging.

However, to date, studies on the genetics of aging using *D. melanogaster* is becoming less.

Is *Drosophila* still staying useful as a model object in this area of research?

Objectives. Analyzing the literature data, to clarify the current trends in the use of *D. melanogaster* in the genetics of aging.

The literature data analysis. Most of the recent work on the study of aging processes in which *D. melanogaster* had been used as a model object was devoted to studying not directly the mechanisms of regulation of life expectancy, but, rather, various specific cases of their action.

For example, A.M. Vayserman, E.A. Fedorenko, and others studied the effects on the viability of imago restriction components of the dietary restriction of *D. melanogaster* larvae.

In the work of N.S. Filiponenko, N.E. Volkova, L.I. Vorob'eva, the dependence of the lifespan of individuals of *D. melanogaster* lines obtained from natural populations on the radiation background in the habitats of these populations was analyzed.

In addition, in this paper, the evolutionary relationship of life expectancy with fecundity of *D. melanogaster* was considered.

Of the works dealing with the genetic aspects of aging proper, the studies of A.A. Moskalev with co-authors (A.A. Malysheva, V.G. Zainulin and others) should be mentioned first of all.

The material accumulated in the study of the influence of the illumination regime on the life expectancy of *Drosophila* served as a basis for investigating the direct effect on the life span of *D. melanogaster* genes of the transcription factor *dFOXO*, *dSir2*, and *Hsp70*.

In addition, he conducted studies of the effect of the activity of the gene of the enzyme Cu / Zn superoxide dismutase on the change in the duration of life of *Drosophila* when the illumination regime was changed.

Long enough studies of the effect on the life span of *D. melanogaster* mutational changes caused by transpositions of mobile genetic elements (MGE) have been carried out for a long time.

As old example can be considered the studies provided by L.Z. Kaidanov with co-authors in the 1990s, which have been devoted to the influence of transpositions of MGE hobo on the intensity of aging and the relationship between the level of hybrid dysgenesis induced by it in the line with the lifespan of adults.

Of more recent studies, mention can be made of the work of N. Golub and I. I. Cernik on the effect on the lifetime of *D. melanogaster* induction of transpositions of MGE by the complex action of X-rays and chemical reagents (nitrosoethylcarbamide and caffeine) to varying degrees.

The most closely related to medical genetics from all the studies examined in this paper was the study by S.A. Kopyl with co-authors (including the already mentioned A.A. Moskalev) on the *D. melanogaster* model of the role of tumor suppression genes *l(3)hem*, *Hyd*, *gd*, *ex* and *ft* in the mechanisms of aging both at the cellular and at the organism level.

Conclusions. Thus, from the examples considered in this paper, can be seen that in modern gerontology, as the general knowledge about the genetic mechanisms of aging accumulates, the importance of *D. melanogaster* as a model object is gradually decreasing.

However, *Drosophila* can still be a useful model for solving particular problems and issues in the general genetics of aging.

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