

MINISTRY OF PUBLIC HEALTH OF UKRAINE
THE NATIONAL UNIVERSITY OF PHARMACY

**ACTUAL QUESTIONS
OF DEVELOPMENT
OF NEW DRUGS**

April 22-23, 2014
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A43

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Укладачі: *Горяча О.В., Андріяненко М. В.*

A43 Актуальні питання створення нових лікарських засобів: тези доповідей всеукраїнської науково-практичної конференції молодих вчених та студентів (22-23 квітня 2014 р.). – Х.: Вид-во, 2014. – 413 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; інформаційних 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: *corresponding member of NAS of Ukraine Chernykh V.P., prof. Kovalenko S.N., Andriyanenkov O.V., Rosolovska O.A.*

Compilers: *Goryacha O.V., Andriyanenkov N. V.*

A43 Actual Questions Of Development of New Drugs: Abstracts of XX International Scientific And Practical Conference Of Young Scientists And Student (April 22-23, 2014). – Kh.: Publishing Office, 2014. – 413 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 grouped according to the main directions of scientific, research and educational work of the National University of Pharmacy. Theoretical 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 pharmacoconomics during the development, implementation and use of drugs, quality management in development, production and trafficking 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 pharmaceutical and medicinal employees.

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Dear students and young scientists!
I greet you at the National University of Pharmacy – Center of Science and Education!

Traditionally in spring we hold Youth Scientific Forum. In this audience those are gathered who love to create, explore and comprehend the new. We are colleagues. We have one mission – science.

Making your way in the science is easy and difficult. Easy – because there are no restrictions in the University and all conditions to carry on scientific research are developed. Difficult – because science is made by strong personalities.

A perseverance and great work are required.

When we began our scientific path, there were no information resources: no Internet, no wide access to scientific literature, opportunities to travel abroad.

Today we live in a global world where a lot of information is available. Many conferences are carried out, a huge number of scientific journals is published, scientometrical databases function.

State supports youth. There are many scholarships, government programs, internships.

The only needed are a desire, skills and knowledge of foreign languages for free communication.

Soul must work both day and night. This is a continuous work.

To become a personality in science you must become an expert in your field. Today the number of publications, patents, followers of scientific school are important criteria for a scientist. You must be well-known in the world, you must be cited as a reputable researcher.

The highest recognition of the scientist is the introduction of his results into the practice. In Pharmacy it is the development of a drug. And today pharmacists of country are faced a task to develop effective domestic drugs.

For this purpose synthetic chemists, pharmacologists, analysts, technologists, clinicians are needed. And for the further introduction – organizers, managers, logisticians and economists.

Be ambitious in science, set big goals. And achieve them. You are the future of scientific elite. At least for 50 years you will work and develop science, intellectual potential and country's image in the world.

Such conferences help express yourself as a scientist, represent your scientific work.

I wish you to become Academicians, Honored Workers, State Prize Winners and the Nobel laureate in future.

And today I wish you a successful fruitful work, interesting meetings, inspiration, new discoveries and, of course, love.

SECTION № 1

SYNTHESIS OF PHYSIOLOGICALLY ACTIVE SUBSTANCES

PREPARATION OF 6-(1,3-BENZOXAZOL-2-YL)-5-METHYLTHIENO[2,3-D]PYRIMIDIN-4(3H)-ONE

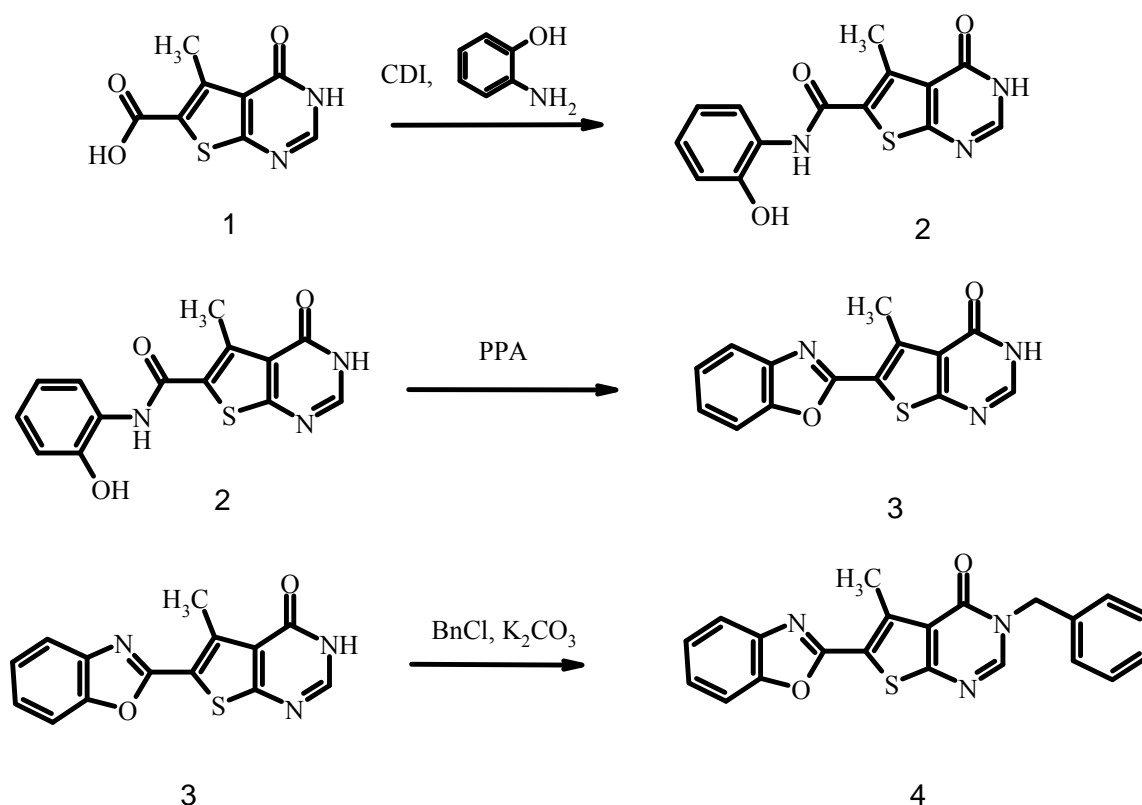
Galimskiy I.O., Vlasov S.V., Kovalenko S.M., Chernykh V.P.

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Many of compounds containing benzoxazole fragment were reported as biologically active ones. They are inhibitors of reverse transcriptase, anti-inflammatory and antimicrobial agents. Some of them were mentioned as the agents that may potentially be useful for early detection and monitoring the progression of Alzheimer's disease; they have effects on COX-2 mediatory responses and on DNA topoisomerases. Interaction of carboxylic acids with 2-aminophenols is a good and well-known way for benzoxazole ring closure. Therefore we focused our attention on the interaction of 5-methyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidine-6-carboxylic acid **1** with 2-aminothiophenol. At the first step just simple acylation has been observed. The cyclization has been performed by heating of the amide **2** in polyphosphoric acid (scheme).

Scheme



The alkylation of 6-(1,3-benzoxazol-2-yl)-5-methylthieno[2,3-d]pyrimidin-4(3H)-one **3** has been carried out in dimethylformamide and promoted with addition of potassium carbonate. The structure of the compounds obtained was confirmed by ¹H NMR, LC/MS and NOESY-spectra.

SYNTHESIS OF SPIRO[PYRROLIDINE-3,2'-OXINDOLE]

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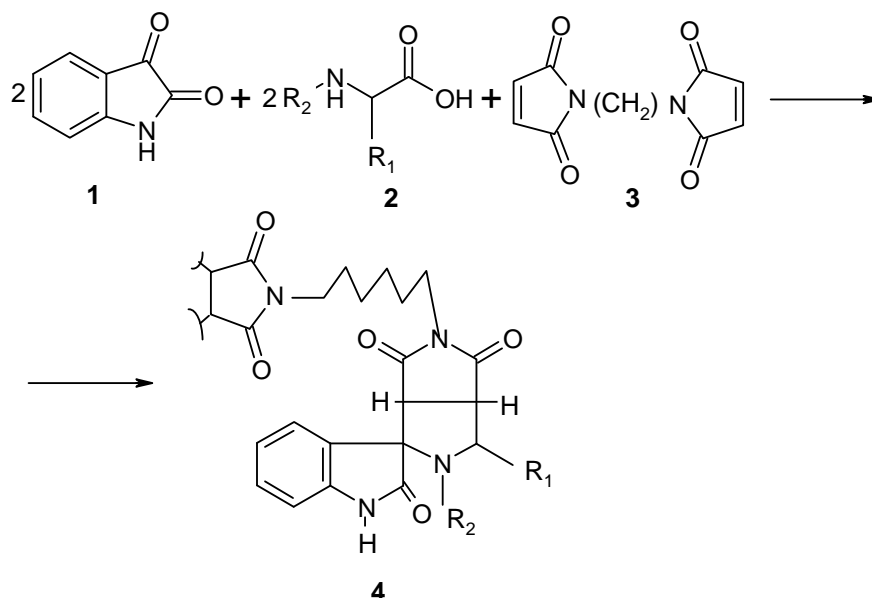
Spirooxindoles have been found as a core structure of many alkaloids with different pharmacological activities, such as antitumor, analgesic, antihypoxic and some other types.

Particularly, spiro[pyrrolidine-3,2'-oxindoles] reveal cerebroprotective properties and ability to reduce the high stressor-induced level of corticosteroid hormones in the blood in models of ischemic and hemorrhagic strokes.

Among the different synthetic strategies, multicomponent reactions (MCRs), which include stage of 1,3-dipolar cycloaddition, play a key role in the spirooxindoles' constructions.

To synthesize spiro[pyrrolidine-3,2'-oxindoles] domino reactions (Strecker reaction / [3+2] cycloaddition) involving isatins (1), α -amino acids (2) and 1,3-dipolarophile (heksametylendimaleynimid) (3) were used. The molar ratio was 2:2:1. As a solvent was used a mixture of isopropanol with water (3:1). The reaction proceeded under reflux for 2 hours. We obtained two types of products – amorphous precipitates, or oils. Recrystallization was performed from isopropanol. As a result we obtained products (4) with yields 35 – 95%.

Condensation reaction of isatins with α -amino acids and appropriate



dipolyarophiles has great synthetic possibilities and the variation of each component allows to achieve a high degree of chemical diversity of the target connection pool.

SYNTHESIS OF ETHYL 9-METHYL-3-[3-(R-AMINO)-3-OXOPROPYL]THIENO[3,2-*e*][1,2,4]TRIAZOLO[4,3-*c*]PYRIMIDINE-8-CARBOXYLATES

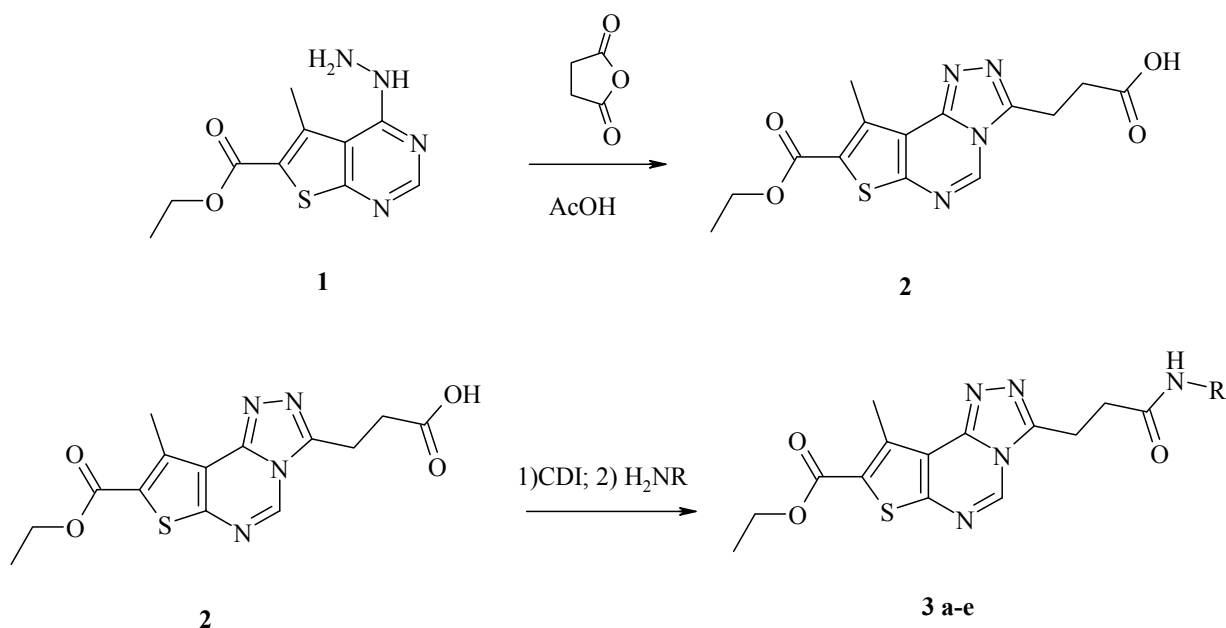
Derecha Yu.O., Vlasov S.V., Kovalenko S.M., Chernykh V.P.

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Some derivatives of thieno[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidines are known as the compounds with wide range of biological activity. Many of them were reported as antifungal and antimicrobial agents. Therefore the development of highly effective methods for obtaining of such potently biologically active heterocyclic compounds is of the great importance. The possible approach to these compounds is interaction of 4-hydrazinothieno[2,3-*d*]pyrimidines with carboxylic acids anhydrides; but the interaction of ethyl 4-hydrazino-5-methylthieno[2,3-*d*]pyrimidine-6-carboxylate with succinic anhydride has not been studied yet. We have performed this reaction in acetic acid media at boiling for 5-6 hours. The product isolated has been identified as the product of triazole ring closure. The reaction has been performed according to the scheme.

Scheme



Reaction of the compound **2** with amines has been performed via coupling procedure promoted by 1,1'-carbonyldiimidazole.

The structures of all of the compounds obtained were confirmed by ¹H NMR spectral data. The screening of the amides **3** for their antimicrobial activity has been performed.

SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF 3-AMINO-5-METHYL-2-(ALKYTHIO)-4-OXO-3,4-DIHYDROTHIENO[2,3-d]PYRIMIDINE-6-CARBOXYLIC ACID DERIVATIVES

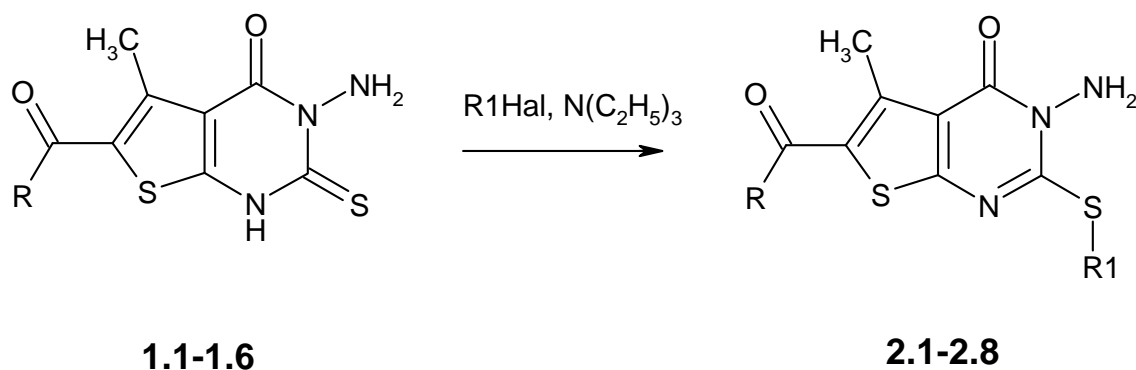
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Synthesis and study of antimicrobial activity of 3-amino-5-methyl-2-(alkythio)-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidine-6-carboxylic acid derivatives is an important task, because many of the compounds with the similar structure were reported as antimicrobials.

Synthesis of the target compounds **2** has been performed by alkylation of the compounds **1** with benzyl chlorides and chloroacetic acid. The reaction was carried out in dimethylformamide media using triethylamine as a basic catalyst.



- 2.1** R = OEt, R1 = CH₂COOH; **2.2** R = NH(p-CH₃Ph), R1 = CH₂COOH;
2.3 R = NH(p-CH₃Ph), R1 = CH₂Ph; **2.4** R = NH(o-CH₃Ph), R1 = CH₂Ph;
2.5 R = NH(p-CH₃Ph), R1 = CH₂(p-CH₃Ph); **2.6** R = NH(2-Pyridyl), R1 = CH₂(p-CH₃Ph);
2.7 R = NH(p-FPh), R1 = CH₂(p-CH₃Ph); **2.8** R = NH(p-OCH₃Ph)

The structures of all of the compounds were confirmed by ¹H NMR spectroscopic data and in some cases chromatographic analyses.

The antimicrobial activity of the compounds **2** has been studied by agar well-diffusion method. In general the larger zone of growth inhibition was considered as indicator of higher antimicrobial activity for the exact tested compound. The highest activity has been determined for **2.3** and **2.5**, which are modified with *p*-methylphenyl substituent in amide fragment of the molecule. Though the activity of all of the compounds **2** tested may be classified as moderate.

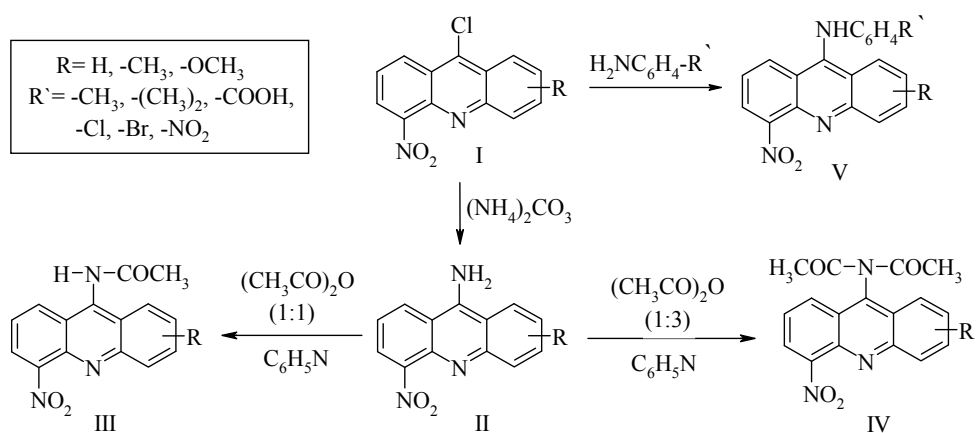
**SYNTHESIS, PHYSICAL-CHEMICAL PROPERTIES,
BIOLOGICAL ACTIVITY OF 9-ACETYL- AND 9-N-ARYLAMINO-
DERIVATIVES OF 5-NITROACRIDINES**

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Derivatives of acridine are well-known for their antimicrobial properties. Their action is conditioned by ability to contact with nucleic acids that predetermines their influence on genetic elements of bacteria. These circumstances defined the necessity of further expansion of chemical and pharmacological study of the 9-acetyl- and 9-N-arylamino derivatives of 5-nitroacridine not investigated earlier (scheme):



In the interaction of 9-chloroacridines (I) and ammonium carbonate the corresponding 9-aminoacridines (II) were synthesized. Acetylation of 9-aminoacridines (II) was carried out by heating them with acetic anhydride in pyridine medium in the ratio 1:1 or 1:3. Respectively 9-monoacetyl aminoacridines (III) and 9-diacetyl aminoacridines (IV) were obtained as a result. In the interaction of 9-chloroacridines (I) and aromatic amines 5-nitro-9-N-arylaminoacridines (V) were obtained. The synthesis of 5-nitro-9-N-arylaminoacridines (V) was established experimentally to be more expedient to be conducted in the dioxane medium in the presence of hydrochloric acid. The advantages of the developed method are: exception of toxic phenol from the synthesis, reduction of the experiment time, a high yield of the desired product.

The structure of compounds (II-V) synthesized was confirmed by elemental, IR-, NMR-, UV-spectral analysis and their individuality has been proven by thin-layer chromatography.

According to classification by K.K. Sydorov the derivatives of 5-nitroacridine belong to the compounds with low toxicity, their DL₅₀ is higher than 2500 mg/kg at intragastric introduction. Synthesized compounds (III-V) possess antimicrobial, antifungal, anti-inflammatory, cholagogue activities.

SYNTHESIS AND PHARMACOLOGICAL PROPERTIES OF 1-FURFURYL-2-OXO-4-HYDROXY-1,2,5,6,7,8-HEXA- HYDROQUINOLINE-3-CARBOXYLIC ACID'S ANILIDES

Zaviazun M. A., Bereznyakova N. L.

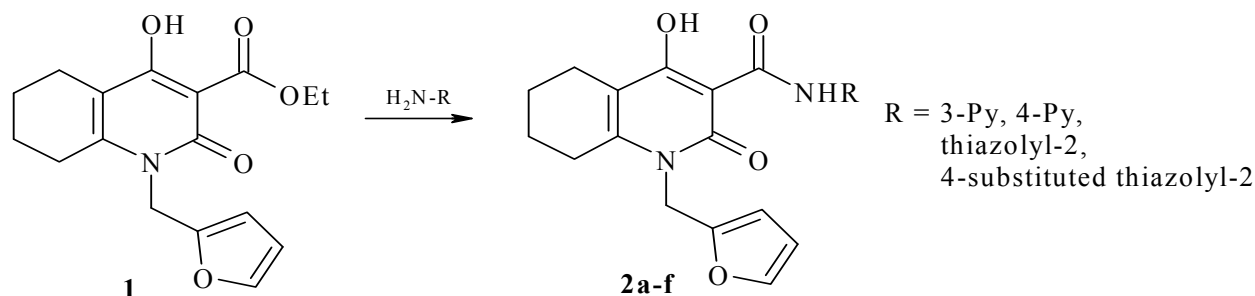
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The great attention of researchers involved into search for biological active substances and new drugs' creation on their basis, has recently directed to the 1-furfuryl-2-oxo-4-hydroxy-1,2,5,6,7,8-hexahydroquinoline-3-carboxylic acid's anilides. This can be explained by not only the increased interest in a wide range of pharmacological properties of furan's derivatives and their natural abundance, but also the easiness of the parent structure chemical modification.

With the purpose of regularities determination of the “structure – antituberculosis action” relationship, the synthesis of range of 1-furfuryl-4-hydroxy-2-oxo-1,2,5,6,7,8-hexahydroquinoline-3-carboxylic acid's anilides has been carried out.

By means of amidation of ethylic ester **1** of 1-furfuryl-2-oxo-4-hydroxy-1,2,5,6,7,8-hexahydroquinoline-3-carboxylic acid the relevant anilides **2a-f** have been got.



To confirm the chemical structure of all synthesized compounds the elemental analysis and NMR¹H spectroscopy were applied, and moreover, for unambiguous interpretation of the methylene groups' signals the special NMR techniques were used that is homonuclear Overhauser effect.

Study of antituberculosis activity of the synthesized compounds was conducted at the National Institute of Allergy and Infectious Diseases (USA) by the radiometric method in relation to Mycobacterium tuberculosis H37Rv ATCC 27294.

The conducted microbiological research of the synthesized compounds have allowed to identify a number of general regularities of relationship between chemical structure and antimycobacterial activity.

MICROWAVE SYNTHESIS AND QUANTITATIVE DETERMINATION OF PHARMACOLOGICALLY ACTIVE OF 6-NITRO, 4,5-DIMETHOXY- AND 3,5-DINITRO-N-PHENYLANTHRANILIC ACIDS BY TWO-PHASE TITRATION

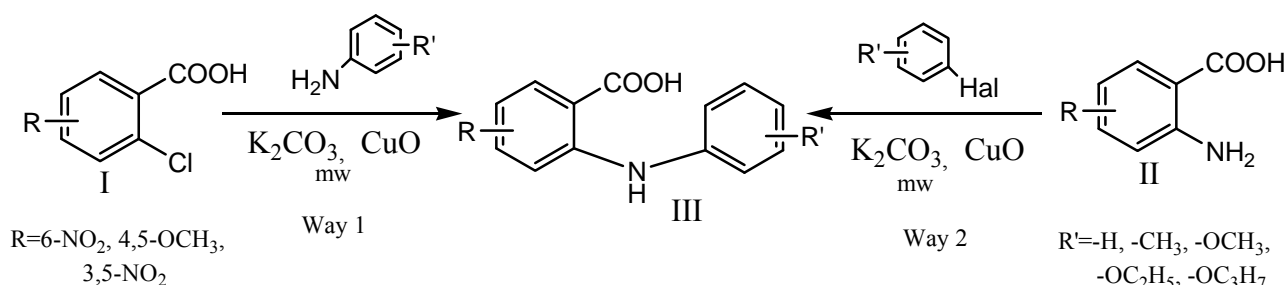
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The aim of our work was to develop a method for the synthesis of N-phenylanthranilic acids with using microwave irradiation and also to develop an express method of their quantitative determination.

The synthesis of N-phenylanthranilic acids (III) was carried out by the interaction of o-chlorobenzoic acid (I) with arylamines (way 1) and arylation of anthranilic acid (II) by substituted of halogen benzene (way 2) among the n-amyl alcohol, in the presence of copper oxide, and potassium carbonate, in the microwave reactor at 180⁰C:



For the quantitative determination of synthesizing acids was developed the method by the two-phase titration. The method consists in the direct titration with 0.1M solution of NaOH of the two-phase system, consisting of the organic phase, which contains the analyzed substance (not soluble in water) and the aqueous phase, where the indicator – phenolphthalein. This extraction equilibrium is disturbed and the sodium salt of N-phenylanthranilic acid passes into the aqueous phase. The experimentally selected n-octanol, as organic phase, which had the highest solubility of the test compounds.

These data of quantify of the new compounds by two-phase titration, characterized by a high accuracy and representativeness. The relative error of this method is less than 0.5%. Given technique an express, reliable, and favorably differs from the method of potentiometric titration.

**THE LAB METHOD OF SYNTHESIS OF NEW ACTIVE
PHARMACEUTICAL INGREDIENT, 6-NITRO-N-(2'-CARBOXY-5'-
BROMOPHENYL)ANTHRANILIC ACID AND DEVELOPMENT
OF ITS QUALITY CONTROL METHODS**

Ivanova K.S., Yeromina H.O., Isaev S.G., Yeromina Z.G.

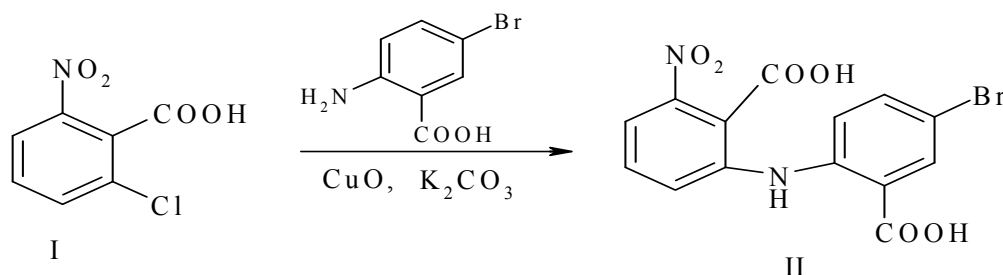
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The synthesis, research and development of new active pharmaceutical drugs are the major challenges in pharmacy and medicine.

Design of the new derivatives of N-phenylanthranilic acids and development of its quality control methods have been the aim of this research.

The new active pharmaceutical ingredient API (II) has been synthesized by the reaction of 6-nitro-2-chlorbenzene carboxylic acid (I) with 5-bromanthranilic acid in the presence of the CuO and K₂CO₃ as catalysts and at temperature 180-200°C for two hours.



This method has remarkable advantages such as simple experimental procedure, mild reaction conditions, low reaction time, and high product yields (92% of the theoretical), avoiding hazardous organic solvents. The proposed method lets to obtain the API II by the efficient, step-economical, and scalable way.

The structures of the synthesized compound 6-nitro-N-(2'-carboxy-5'-bromophenyl)anthranilic acid has been confirmed by FT-IR, UV, ¹H NMR-spectroscopy and elemental analysis.

Fundamental to all aspects of drug development and manufacturing are the analytical methods. The methods of identification based upon tests for functional groups such as carboxylic-, nitro-, covalent bonded bromine were developed. The method of acid-base titration (alkalimetry) for assay of the compound was proposed.

The synthesized compound API II was screened for wide range of biological activity and it has shown anti-inflammatory, analgesic, diuretic and antifungal activity. In the same time the substance exhibits low toxicity (LD₅₀ in mice > 6500 mg/kg).

In summary, the conducted researches indicate the prospects of finding new biologically active compounds based on derivatives of anthranilic acid.

SYNTHESIS OF SPIROHYDANTOIN DERIVATIVES BASED ON ALIPHATIC KETONES AND THEIR CHEMICAL PROPERTIES INVESTIGATION

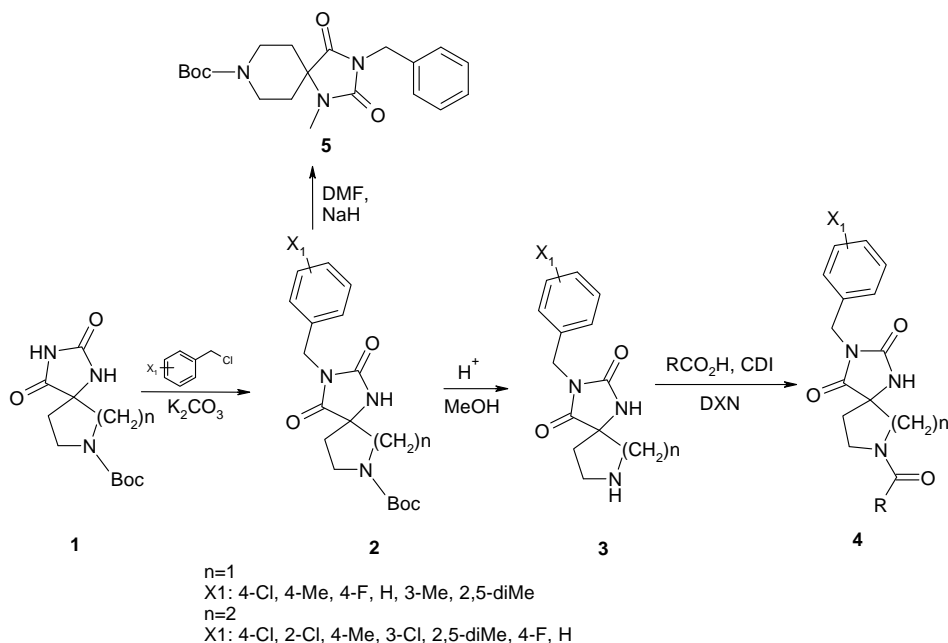
Krolenko K.Yu., Vlasov S.V., Zaremba O.V.,
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In the two last decades it was found, that hydantoins have great range of therapeutic effects. They can be used as anticonvulsants, antagonists of 5-HT receptors, inhibitors of platelet aggregation, antiarrhythmic, antiviral, antihypertensive agents etc. There are many works, devoted to application of spirohydantoins as stabilizers for production of macromolecular compounds. Considering a wide range of practical use we have synthesized the starting spirohydantoins based on 3-N-Boc-pyrrolidone and 4-N-Boc-piperidone (on a scheme $n=1$ and $n=2$ respectively) and their nitrogen atoms reactivity in alkylation and acylation reactions has been investigated.

^1H NMR spectra of all pyrrolidine ranges compounds contain the signals near 1.37 and 1.95 ppm, produced by protons of methylene-group in position 9. Such non-equivalence may be explained by the different spatial arrangement of these protons. Probably the signal of that proton which is close to carbonyl-group is shifted downfield.



As the result of this work the ranges of new compounds were obtained. Most of them were not reported before. The structures of all of these compounds were confirmed by LCMS, ^1H NMR- and ^{13}C NMR spectroscopic methods.

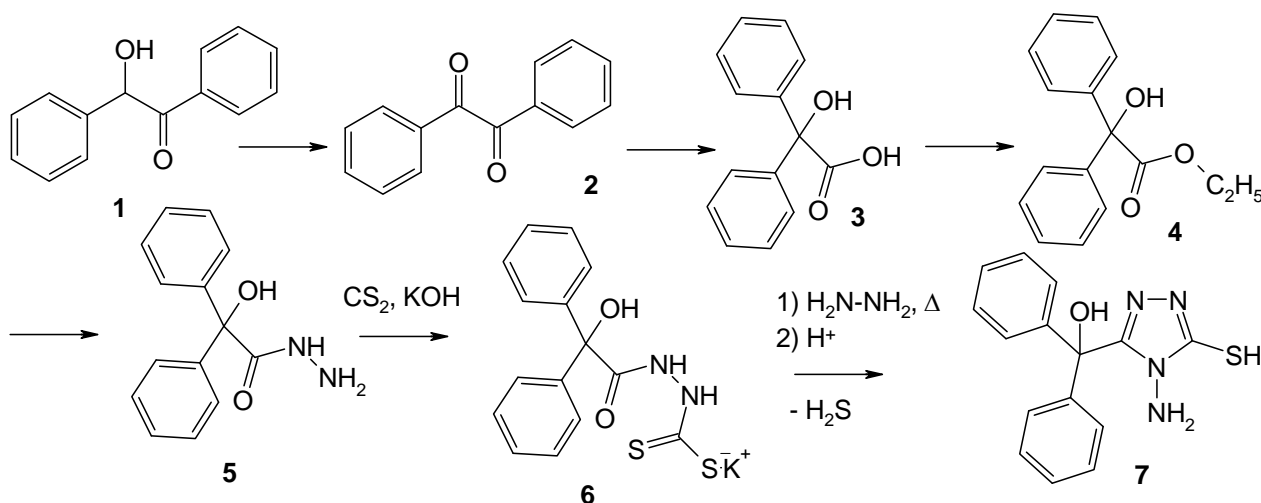
**(4-AMINO-5-MERCAPTO-4H-[1,2,4]TRIAZOL-3-YL)-
DIPHENYLMETHANOL AS BUILDING BLOCK IN THE SYNTHESIS
BIOLOGICALLY ACTIVE SUBSTANCES**

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It is well known that diphenylcarbinol fragment is a pharmacophore, which is present in the structure of many medicinal substances. The aim of this work was to obtain compounds combining this pharmacophore with the other functional groups, which may undergo further chemical transformations. This plan of our experimental work was realized using benzoic acid derivatives. Benzoin **1** has been used as the starting compound for this synthesis. Oxidation of benzoin with concentrated nitric acid resulted in diketone **2**. Dibenzoyl **2** was converted to benzoic acid **3** by benzilic rearrangement. Further ethyl ester of benzoic acid **4** was prepared by esterification of **2** with ethyl alcohol; compound **4** has been used to prepare corresponding hydrazide **5**. Target (4-amino-5-mercapto-4H-[1,2,4]triazol-3-yl)-diphenylmethanol **7** was obtained in good yield in two steps after the treatment of **5** with carbon disulfide followed by further cyclization of addition product **6** with hydrazine.



It is important to mention that the derivative of mercaptoaminotriazole modified with diphenylcarbinol fragment has not been reported before. To our opinion this compound may be used as a building-block for synthesis of variety of biologically active compounds with diphenylcarbinol fragment. The structure of all of the compounds was confirmed by modern instrumental methods of organic analysis.

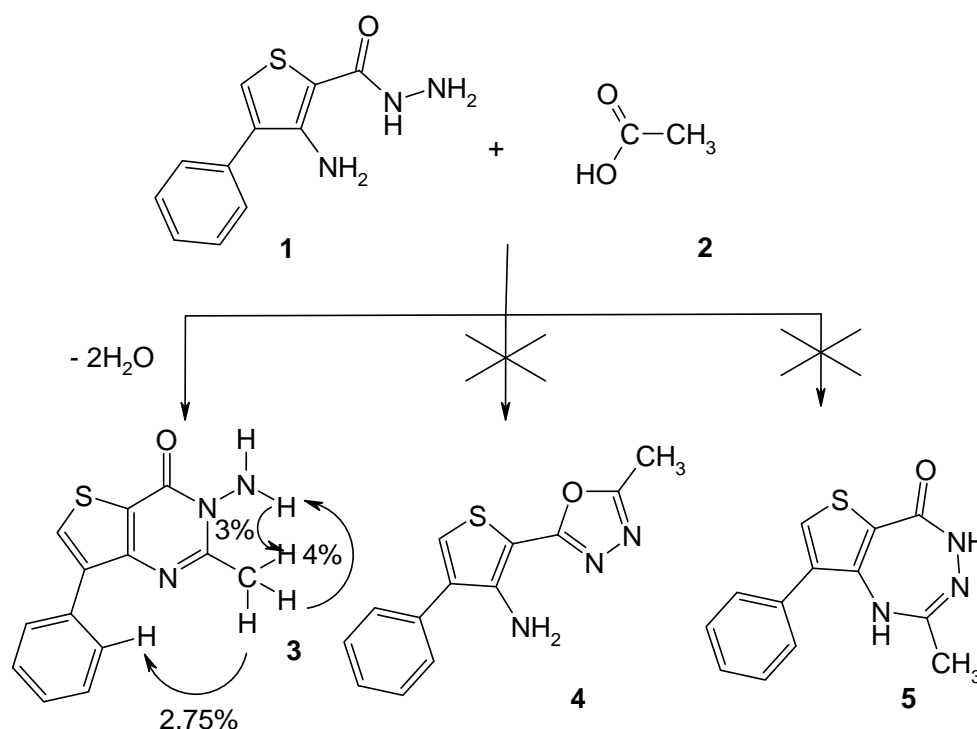
CONFIRMATION OF 3-AMINO-2-METHYL-7-PHENYL-3H-THIENO[3,2-d]PYRIMIDIN-4-ONE STRUCTURE BY NOE-SPECTROSCOPY

Ovsjanykova Yu.O., Sytnik K.M., Shemchuk L.A., Chernykh V.P.

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It was found that heating of hydrazide **1** in glacial acetic acid is accomplished by interaction of these components. The aim of our work was to confirm the structure of this reaction product. Initially some possible reaction routes, which may result the products with the structures **3**, **4** or **5**, were proposed.



To confirm the structure of the product isolated we used NMR spectroscopy. The possible structure **5** has been excluded, because the spectrum of the compound contained the signal of NH₂-group of double intensity. For the final confirmation of the product structure NOE-spectroscopy appeared to be effective. The most important structural information has been obtained by observation of CH₃ group NOE-effect with its neighbor protons. The experiment showed that saturation of CH₃ signal at 2.60 ppm, increases the intensity of the signal at 5.9 ppm (NH₂-group protons) by 4 % and the signal of o-protons of phenyl radical at 7.97 ppm by 2.75%. Such fact clearly confirms the formation of the structure **3**.

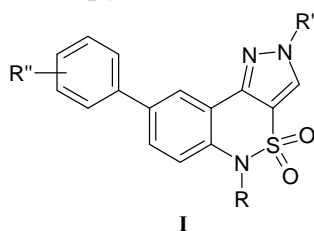
THE SYNTHESIS OF NEW SPIROCYCLIC COMPOUNDS DERIVATIVES OF N-ETHYL-1*H*-BENZO[*c*][2,1]THIAZIN-4-ON-2,2-DIOXIDE

Prokopets S.V., Lega D.A., Levashov D.V.

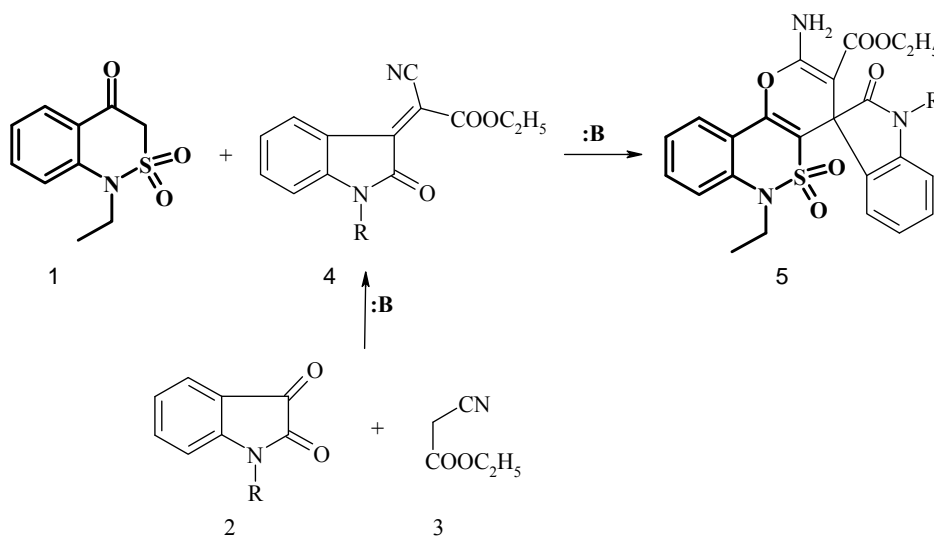
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Among heterocyclic compounds, which are perspective for screening of new drugs, derivatives of benzo[*c*][2,1]thiazin-4-one-2,2-dioxide are interesting. Such compounds, containing benzothiazinone core in their structure are showing various biological activity. For example, compound with the general formula (I) displays the high antiinflammatory, analgesic, antipyretic and antitumor activities also:



The spirocyclic derivatives of benzothiazinone were obtained as it is shown on the scheme below:



Starting benzothiazinone (1) was obtained by the method reported in literature. Except benzothiazinone (1) we used 2-(2-oxoindolin-3-ylidene)ethyl acetates (4) for synthesis of the target compounds (5) also. The compound (4) was obtained under heating of isatins (2) with ethylcyanoacetate (3) in the presence of base. As a result of interaction of benzothiazinone (1) and ylidenes (4) under the Michael reaction conditions the target spirocyclic compounds (5) were obtained.

This research allows to enhance the range of potential bioactive compounds among derivatives of benzo[*c*][2,1]thiazin-4-one-2,2-dioxide.

**SYNTHESIS, PROPERTIES AND BIOLOGICAL ACTIVITY OF THE
AMIDES OF 2-(BENZOYLAMINO)(2-OXOINDOLIN-3- YLIDENE)
ACETIC ACID**

Rayter L.M., Altuhov O.O., Kolesnyk O.V.

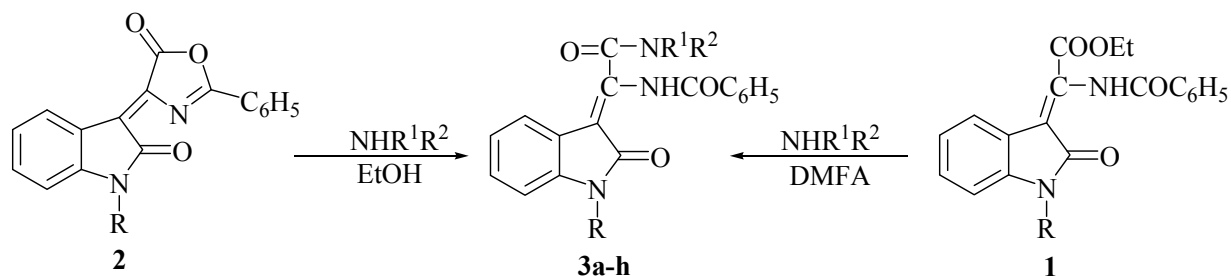
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It is well known that derivatives of the 2-(2-oxondolin-3-ylidene)acetic acid have a wide range of biological activity and low toxicity. Among them compounds with high diuretic, antiviral, antihypoxant, nootropic action etc. were found.

The aim of this work was to develop methods of synthesis of new derivatives of 2-(benzoylamino)(2-oxondolin-3-ylidene)acetic acid and to study the nootropic and antihypoxant activity of compounds produced.

In this work we propose two approaches for synthesis of amides 2-(benzoylamino)(2-oxondolin-3-ylidene)acetic acid (**3a-h**). According to the first one (Method A) the target products were prepared by interaction of ethyl ester 2-(benzoylamino)(2-oxondolin-3-ylidene)acetic acid (**1**) with amines in DMFA. The second approach (Method B) was based on acylation of amines by 2-phenyl-4-(2-oxondolin-3-ylidene)-5-oxazolone (**2**) in ethanol. The advantages of this method are the high yields (up to 80-85%) and the short reaction time.



3a. $R^1=H$, $R^2=(CH_2)_2OH$; **3b.** $R^1=R^2=(CH_2)_2OH$; **3c.** $R^1=Et$, $R^2=Et$; **3d.** $NR^1R^2=piperidin-1-yl$; **3e.** $NR^1R^2=4\text{-methylpiperazin-1-yl}$; **3f.** $NR^1R^2=4\text{-}(2\text{-hydroxyethyl})piperazin-1-yl$; **3g.** $NR^1R^2=4\text{-benzylpiperazin-1-yl}$; **3h.** $NR^1R^2=morpholyl$.

The structure of the synthesized substances has been proven by elemental analysis and NMR spectra data.

Antihypoxic and nootropic activity together with their acute toxicity were studied using standard screening models. It was found that the compounds of given series are low-toxic or non-toxic with moderate antihypoxic activity and significant anti-amnesic effect.

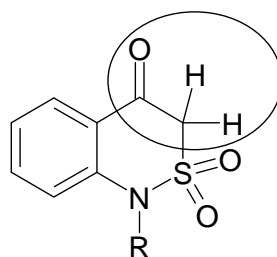
THE SYNTHESIS OF NEW HETEROCYCLIC SYSTEMS BASED ON N-ETHYL-1*H*-BENZO[*c*][2,1]THIAZIN-4-ON-2,2-DIOXIDE

Semko M.M., Lega D.A., Redkin R.G.

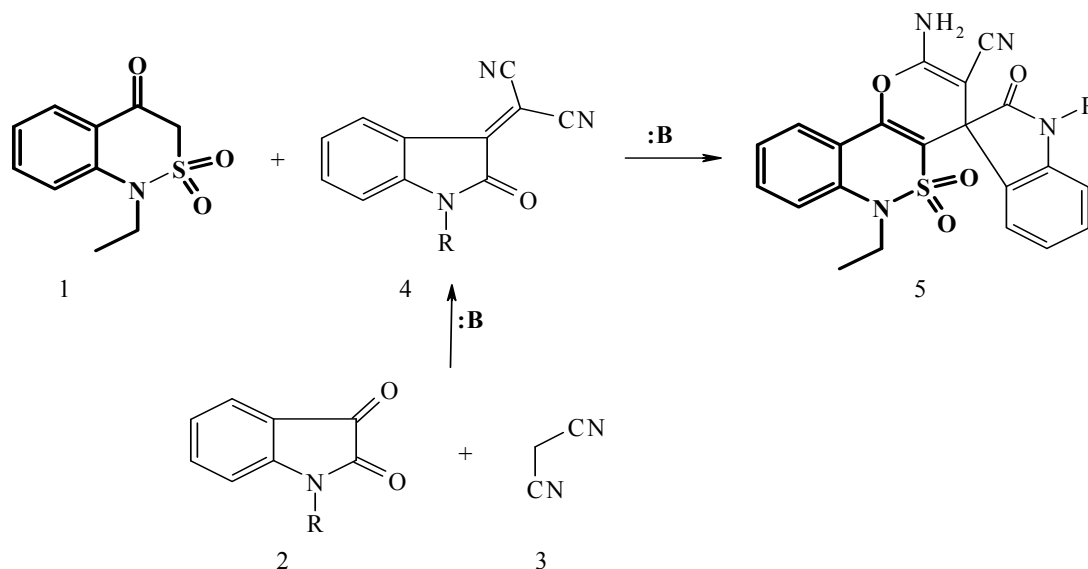
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The aim of this work is synthesis of new heterocyclic systems – derivatives of benzo[*c*][2,1]thiazine. The presence of active methylene and carbonyl groups in the molecule of benzo[*c*][2,1]thiazine-4-on-2,2-dioxide makes it very convenient and perspective synthone for new heterocyclic systems building based on it.



The starting benzothiazinone (1) was obtained as it was reported in literature. The synthesis of heterocyclic system (5) is based on reaction between benzothiazinone (1) and α -cyanoethylene derivatives of isatin (4). The latest were obtained as a result of the Knoevenagel condensation between N-substituted isatines (2) and malonodinitrile (3). After that, the products of condensation (4) and starting compound (1) were introduced into Michael reaction. As a result of their interection in the presence of base the target compounds (5) were obtained.



R = H, Me

The structures of target compounds (5) were confirmed using the instrumental methods of analysis (^1H NMR, ^{13}C NMR, X-ray).

SYNTHESIS OF Ag@Fe₃O₄ NANOCOMPOSITE BY SINGLE-PHASE SURFACE MODIFICATION METHOD

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In recent years, many research efforts aimed at obtaining nanoparticles with desired shape, size and complex physical and chemical properties. Described a lot of synthetic approaches, each with a pair of benefits is not without some drawbacks.

Putting a silver coat on the surface of magnetic nanoparticles allows such systems, along with the preservation of magnetic properties, acquire new properties, in particular due to antiseptic properties of silver. In addition to protection against aggregation, oxidation, acidic and alkaline corrosion, silver shell may act as a linker to connect pharmaceutical agents or biomolecules to magnetic media. This will allow to decrease the concentration of drug and systemic toxicity due to longer hold it in the affected area.

The aim of our research – development of a method applying a silver coating on the surface of the nanoparticles magnetite and identify factors, that influence the effectiveness of magnetic media.

The original method of single-phase synthesis of nanoparticles with a spherical core and silver shell islet type was proposed. First received systematic data on the impact and value of the components of the synthesis conditions on the structure of nanocomposite Ag@Fe₃O₄. The general algorithm to obtain core-shell nanostructures consisting of basic steps: 1) synthesis of magnetic cores specified size and shape and adsorption of Ag nanoparticles on it's surface; 2) synthesis of magnetic cores compatible Fe₃O₄ and Ag adsorption on the surface; 3) "rearing" islet Ag shell to obtain a continuous coating of a given thickness.

Phase composition and phase characteristics of the samples determined using a mix of modern physical and chemical methods (thermogravimetric and X-ray diffraction analysis, scanning electron microscopy, AAS). To determine the quantitative composition of the phases and their dispersion carried lattice parameter refinement by Rietveld method. We prove that the obtained nanocomposites containing silver particles on the surface as a monolayer point. Magnetic properties of the samples determined by the dependence of magnetization impregnation on the value of the external magnetic field.

To the resulting nanocomposite selected medicine form – magnetically suppositories urological supplies, conducted a comprehensive research of the selected drug.

SEARCH FOR POTENTIAL DIURETICS AMONG THE DERIVATIVES OF 1,3,4-OXADIAZOLE

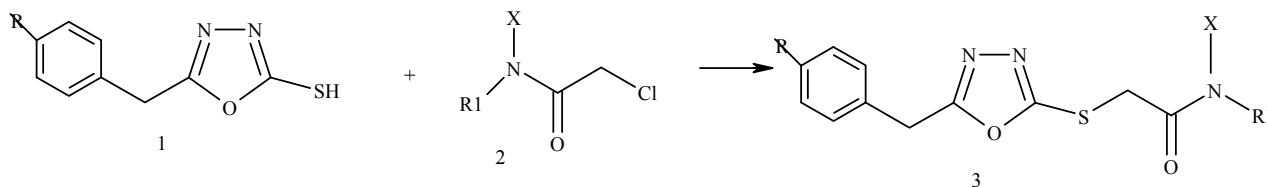
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Purpose. Purpose of the work is synthesis of potential biologically active substances the derivatives of 1,3,4-oxadiazoles and the study of their diuretic activity. Analysis of the literature shows that among the derivatives of 1,3,4-oxadiazole, there are a lot of promising compounds in terms of pharmacy, but at the same time, their biological properties have been insufficiently studied.

Materials and Methods. In order to search for new bioactive substances - potential diuretics, aryl(heteryl) amides of 5-R-benzyl-1,3,4-oxadiazol-2-yl-thioacetic acid were synthesized. The high reactivity of initial substances of 5-R-benzyl-2-mercapto-1,3,4-oxadiazoles(1) makes it possible quite easy modify their structure by alkylation, which extends the probability of finding new effective compounds in this series. To study the difference in activity depending on the presence of anilide or heteryl fragment, alkylation was performed by aryl (heteryl) amides of chloroacetic acid (2) under the conditions of basic catalysis. The structure of obtained aryl(heteryl) of 5-R-benzyl -1,3,4-oxadiazole-2-yl- thioacetic acid (3) is proved by modern physical and chemical methods of UV, IR and ¹H NMR- spectroscopy, the purity is confirmed by the method of thin-layer chromatography.



Diuretic activity of new compounds were studied by E.B. Berkhin's method on white male rats weighing of 180.0-200.0 g. Hypothiazide was used as comparator preparation. Tested compounds and hypothiazide were introduced intragastrically in a state of fine dispersed aqueous suspension stabilized by Twin-80, in a dose of 40 mg/kg.

Results and conclusions. New aryl-and heterylamides of 5-R-benzyl-1,3,4-oxadiazole-2-yl- thioacetic acid were synthesized. The structure of substances synthesized were proved by spectral methods. Received experimental data show that all 20 synthesized substances have moderate diuretic activity, and 2 compounds exceed hypothiazide activity. For promising compounds studied the toxicity *in vitro* (in a model test - system of rat bone marrow cells) and acute toxicity *in vivo*. The research results of cytotoxic activity *in vitro* and acute toxicity *in vivo* showed that the compounds synthesized are slightly toxic. Performed researches have allowed to select two compounds for in-depth study.

SECTION № 2

STUDY OF MEDICINAL PLANTS AND CREATION OF HERBAL MEDICINAL PRODUCTS

STUDY OF TERPENES COMPOSITION FROM EUCALYPTUS VIMINALIS BUDS

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Four supplements of the National Pharmacopoeia of Ukraine (NPhU) harmonized with the European Pharmacopoeia have been implemented in Ukraine. There are some monographs on medicinal plants in NPhU. In particular, according to the NPhU raw materials of eucalyptus are leaves of *E. globulus*, from which the essential oil of eucalyptus (*Eusalypti aetheroleum*) is obtained. However, national plants continue to use *E. viminalis* leaves in the production of drugs, including tinctures and Chlorophilipt thick extract. Imported eucalyptus leaves must comply with NPhU monograph "Eucalyptus leaves", which are normalized by the content of stems (less than 5%) and other impurities (less than 2%). Whereas during the procurement of raw materials buds can get, which affect its quality.

The purpose of our research was to study the terpenes composition of eucalyptus buds, harvested in Abkhazia, to determine the need for normalization of its quantity in raw of eucalyptus leaves.

For obtaining of essential oil from *E. viminalis* buds a method that can extract essential oil with a small amount in plant material was used. For distillation vial "Agilent" 22 ml (part number 5183-4536) with open lid and silicone seal was used. Sample of 2.0-3.0 g of raw material were placed in vial, filled with water to half volume. The vial was closed by the lid with air refrigerator and heated for one hour on a sand bath. To prevent the loss, micro quantities of essential oil adsorbed on the inner surface of the refrigerator, have been washed twice with 1-2 ml of petroleum ether and collected in vial. The yield of essential oil from *E. viminalis* bud was 0.12%

Research of the essential oil's terpenes composition was performed by chromatography-mass spectrometry in the gas chromatograph Agilent Technology 6890 with mass spectrometric detector 5973 by normalization method. Retention indices of components were calculated on the results of analyzes of substances with the addition of a mixture of normal alkanes (C₁₀-C₁₈). The identification of compounds was performed by comparison of mass spectra with the mass spectra of reference compounds with high probability recognition of identification program in the array of spectra databases.

51 Substances have been revealed, among which the major components were felandren (171.33 mg/kg), 1,8-cineole (200.06 mg/kg) terpinen-4-ol (70.18 mg/kg) piperityon (58.10 mg/kg), terpenyl acetate (159.17 mg/kg).

So the qualitative and quantitative analysis of terpenes in the *E. viminalis* bud were analyzed. The content of essential oil in buds was almost 10 times less than in eucalyptus leaves, so buds number must be normalized.

EVELOPMENT AND CLINICAL LABORATORY RESEARCHES OF MEDICINAL FORM "MAODENT"

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Despite the continuous improvement of methods of treating diseases of the mucous membrane of cavity of mouth, the prevention and treatment of therapeutic dentistry are still relevant. For this purpose now, will acquire use herbal medicines that have a wide antimicrobial spectrum and immunotropic action.

The aim of this work to develop an effective composition and conducting clinical and laboratory studies of the medicinal form "Maodent" for the treatment of paradontium and mucous membrane of cavity of mouth. We propose the basis N.E. Kutumov for medicinal forms prepared on basis of infusions of Chamomilla, Salvia, Echinacea: lipophilic base + surfactant + water; vaseline + emulsifier T2 + water (in a ratio of 60:10:30). According to the research was conducted clinical examination of 27 patients with pathology of paradontium: 15 with diagnos "chronic catarrhal gingivitis in the acute stage," 12 with generalized paradontium of 1 and second degree, and 11 patients with pathology of the mucous membrane of cavity of mouth. For medicinal form was determined microbial activity in experiments in vitro: it revealed the highest sensitivity to St. mutans. According to the results of microbiological studies at the molecular level by polymerase chain reaction (PCR) was detected for 24 examined patients Neisseria (meng), Str.epiderm., from 2 - pure culture. In the pathology of the mucous membrane of cavity of mouth, accompanied by violation of its integrity, in cytograms of epithelium of the oral mucosa patients was revealed a large number of segmented neutrophils, sometimes in the form clots (precipitate plaque) - $66,2 \pm 3,2\%$. The number of mononuclear cells grew significantly - $13,6 \pm 2,1\%$. Growth in the cytogramme number of nuclear cells mononuclear deprived cytoplasm indicates a high degree of alteration in the lesion.

Cytogram indicators for patients with paradontium pathology were significantly different from those before treatment: against lowering the epithelial cells of the 1st and 2nd types, was increased the epithelial cells of the 3rd and 4th types. Was decreased amount phagocytose cells, mononuclear, nuclear monocytes. But the most significant decrease was segmented the number of neutrophils - almost 2-times, that indicate the positive dynamics of treatment medicinal form "Maodent".

STUDY OF VOLATILE COMPOUNDS OF HELICHRYSUM ARENARIUM

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Flavonoids containing plants are promising sources of medicines. The creation and optimization of drugs prevents insufficient knowledge about the chemical composition of the herbal drugs. Considering the importance of all active substances in showing the pharmacological activity, there is need for a more complete study of the chemical composition of herbal drugs.

The purpose of study was to comparatively determine the qualitative and quantitative composition of volatile compounds of Immortelle (*Helichrysum arenarium*, family Asteraceae) flowers and stems with leaves. The objects of study were flowers and stems with leaves of Immortelle that were harvested in early flowering in Kharkiv region. The composition and content of volatile compounds was determined by chromatography-mass spectrometric method. Were used the Agilent Technologies 6890 chromatograph with mass spectrometric detector 5973. For calculations the method of internal standard was used.

Researching of composition of biologically active substances of Immortelle flowers found 21 compounds and in stems with leaves – 34 compounds. In flowers have been found 5 monoterpenoids – limonene, camphor, linalool, α -terpinol, α -terpinyl acetate; 2 sesquiterpenoids – 1,4-cis-1,7-trans-acorenone and trans-caryophyllene; 3 aromatic compounds – phenylacetaldehyde, benzophenone and asarone; 3 aliphatic aldehydes – nonanal, tridecanal and tetradecanal. In the quantitative ratio dominated correspondingly – linalool (5.04 mg/kg); 1,4-cis-1,7-trans-acorenone (18.73 mg/kg); asarone (35.55 mg/kg); tridecanal (20.65 mg/kg). In stems with leaves have been found 2 monoterpenoids – α -terpinol and neryl acetone; 11 sesquiterpenoids – shyobunone, α -calacorene, β -farnezen, caryophyllene oxide, 1-isopropyl-4,8-dymethylspiro[4.5]dec-7-one, τ -cadinol, α -cadinol, allo-aromadendrene, ϵ -cadinen, zierone and 1,4-cis-1,7-trans-acorenone; 6 aromatic compounds – 2-octyl benzoate, eugenol, methyl eugenol, cis-methyl eugenol, cis-asarone, trans-asarone; other terpenoid-like compounds – β -ionon and trans- β -ionon-5,6-epoxide; 5 aliphatic aldehydes – benzaldehyde, nonanal, decanal, deca-2,4-dien-1-al and tetradecanal. In the quantitative ratio dominated correspondingly – neryl acetone (6.17 mg/kg); 1,4-cis-1,7-trans-acorenone (106.72 mg/kg); cis-asarone (135.50 mg/kg); β -ionon (2.61 mg/kg); tetradecanal (17.97 mg/kg). The study of composition and content of a variety of biologically active compounds of Immortelle requires further investigation.

ZOSTERA MARINA HERB AS SOURCE OF BIOLOGICAL ACTIVE COMPOUNDS

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One of the areas of creating medicines and dietary supplements is to develop drugs or dietary supplements for the prevention of iodine deficiency disorders. Prevalence of this disorder is very high among the population of Ukraine and due to the low content of iodine in drinking water in Ukrainian daily diet. Well-known alga - Laminaria is now almost inaccessible to the population of Ukraine, and this sea herb comes in a small amount for our country from the Far Eastern countries, and has been treated by different technology, resulting in the loss of biologically active compounds.

In this regard, sea grass (*Zostera marina*), the family Zosteraceae, attracts particular interest for phytochemical research. This plant forms vast underwater thickets along the coast of the Black and Azov Sea and is made in large quantities of storm waves on the beach.

The aim of our research was to investigate the composition of elements, especially iodine.

Zostera herb was collected on the coast of the Azov Sea (Genichevsk) in 2011-2013 year. Dry extracts were prepared by vacuum filtration method in the ratio 1:5 (raw material: solvent). Extractable matters content is 30.50% (solvent- water) and 24.25% (70%-alcohol). To study the elemental composition of marine herb were used the method of atomic emission spectrography at photographic device on a DFS-8.

Analysis of iodine in the samples was carried out by the inversion-voltamperometric measuring the concentration of iodide ions (I⁻) in a solution prepared sample.

It was establish the following regularity for the content of elements in the *Zostera* herb: Na > K > Si > Ca > Mg > Fe > Al > P > Mn > Ni > Mo > Cu > Pb > Zn, and for aqueous extracts of *Zostera* can be represented as follows: Mg > Na > K > Ca > Mn > P > Fe > Ni > Si > Mo > Cu > Pb > Al > Zn, for alcohol extract: Na > K > Mg > Ca > Mn > Ni > Mo > Fe > Si > P > Cu > Al > Pb > Zn.

Using the method of voltamperometry it was determined the level of iodine in *Zostera* herb (more than 0,1%) and extract (0,04-0,07%).

Results of research show that herb and extract of *Zostera marina* are perspective agent in the case of disorder of thyroid function and as a general tonic remedy.

HEMOSTATIC ACTIVITY OF EXTRACTS «PASTORIS SACCULO»

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The large number of complications associated with dismetabolic, toxic, allergenic, immunosuppressive and other negative properties of modern drugs leads to the investigation of active substances by plant origin. The therapeutic effect of medicinal plants occurs due to the presence of biologically active pharmacological substances with high activities, which are contained in different parts of plants. Application grass «pastoris sacco» in medical practice described since ancient times as a styptic. In the official medicine it was introduced in 1883 as a medicine that reduces blood pressure, and having anti sclerotic activity. In modern medicine it applied for the treatment of different gastrointestinal disorders, hypertension, and as analgesic and diuretic, and for the control of bleeding, including uterine. The grass «pastoris sacco» successfully apply if cystitis, pyelonephritis and urolithiasis accompanied by bleeding. Despite these historically proofs of pharmacological effects in Ukraine to date not a single herbal preparation with a strong hemostatic effect. Therefore, a number of studies in this area are an urgent problem in the pharmacy, and that was the **purpose** of this study.

Materials and Methods. Hemostatic activity of polyphenolic complex concentrated extract «pastoris sacco» and diluted extract «pastoris sacco» we studied in experiments in vivo. Finding of a haemostatic effect did by the coagulation time compared with the control - distilled water, and drug comparisons aminocapronic acid. Experiments were carried out on an Althauzena based on the time of the first appearance of fibrin strands. To do this, skimmed a slide struck drop of blood that was taken from the tail vein of rats. Every 15-20 sek. needle carried by a drop of blood, fixing the appearance of the first threads of fibrin. Action product was studied in 20 mg/ml compared with the effect of the drug comparison - aminocapronic acid extract. Experimental results processed by program «Statistika».

Results. Analysis of the data indicates that the extract «pastoris sacco», generates a process of coagulation activation and leads to a hypercoagulable state due to decreasing thrombin time. The most effective dose for the hemostatic activity of the extract «pastoris sacco» is 20 mg/kg. This dose of extract «pastoris sacco» unreliable than conventional comparator - aminocapronic acid in 1.03 times.

Conclusions. Thus, the study showed that the extract «pastoris sacco» has high level of hemostatic activity which is equal to drug comparison aminocapronic acid and is promising for further pharmacological studies.

MORPHOLOGICAL AND CHEMICAL STUDIES OF *ROSA GALLICA* L. FLORES

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Garden purslane – *Rosa gallica* L. belongs to genus *Rosa*, family *Rosaceae*. This species gave rise to the old roses in Europe.

A plant is a perennial well branched shrub. Bush size is 130*100cm, of 90-150cm high. Underground stems are present. The leaves are dark green, oval, pointed, leathery. The blooming is profuse, long termed and single-shot.

Flowers are gathered in inflorescences. On one peduncle 3-5 flowers are present. The single flower is 4-6cm in diameter with 17-25 notched petals. Heart-shaped petals have 2.5cm-3cm in length, 1.5-2.5cm wide with a wedge-shaped base and a twin tip. Average petals are oval or broadly lanceolate with wedge-shaped base and a rounded base. Surface is velvety. Color of petal's base is white or pale pink, color of petal is dark red. Flowers have a rich flavor.

False fruits are round-ovate with sepals. Length is from 1.5 to 2cm, diameter is 1.0-1.6cm. Fruits are brilliant, colour ranges from orange to brown-red. At the top of the fruit a pentagonal areola is present.

The fruit consist of the overgrown fleshy receptacle – hypanthium – within which coccus are present. Coccus are small, spherical with weak pale yellow faces. Very small, dark undeveloped coccus are present. Inside the fruit is lined with stiff bristly hairs. Fruits are odorless. Taste is sweet and sour, astringent.

Rose is a vitamin and general tonic agent. This plant possesses choloretic, anti-inflammatory and wound-healing effects.

By Pharmacopoeia method the content of ascorbic acid in fruits and petals of *Rosa galica* have been determined. In petals the content of vitamin C was 0.06%. In an aqueous infusion of petals the content of vitamin C was 0,055%. The content of vitamin C in fruits was 0.176%.

Rose petals are the source of volatile oil.

The analysis of the volatile compounds of Purslane flowers was performed using chromatography-mass spectrometric method on Agilent Technologies 6890 chromatograph with a mass spectrometer detector 5973. The sample was injected into a chromatographic column in a mode "splitless", rate of the sample injection – 1.2ml/min for 0.2min. Experiment was carried out under the next conditions: chromatographic capillary column INNOWAX with an inner diameter of 0.25mm and 30m long. The gas flow rate (helium) – 1.2ml/min, the temperature of the heater

of the sample input – 250 °C, the thermostat temperature was from 50 °C to 320 °C, the heating rate was 4 °C/min. The detector temperature was 250 °C.

The identification of compounds was performed by comparing the mass spectra of obtained compounds with database of mass spectra libraries NIST05 and WELEY 2007 in conjunction with the identification programs AMDIS and NIST.

The quantification was performed using the concentration of the internal standard and expressed on the herbal drugs.

30 Compounds have been identified and quantified. Among identified dominant volatile components next substances were: β -phenylethyl alcohol – 2,12%; α -evdesmol – 0,98%; 10-epi- α -evdesmol – 4,16%; β -evdesmol – 3,0%; α -evdesmol – 1,83%; quniper-camphor – 0,64%.

The chromatographic profile of Purslane flowers volatile oil is represented on the figure.

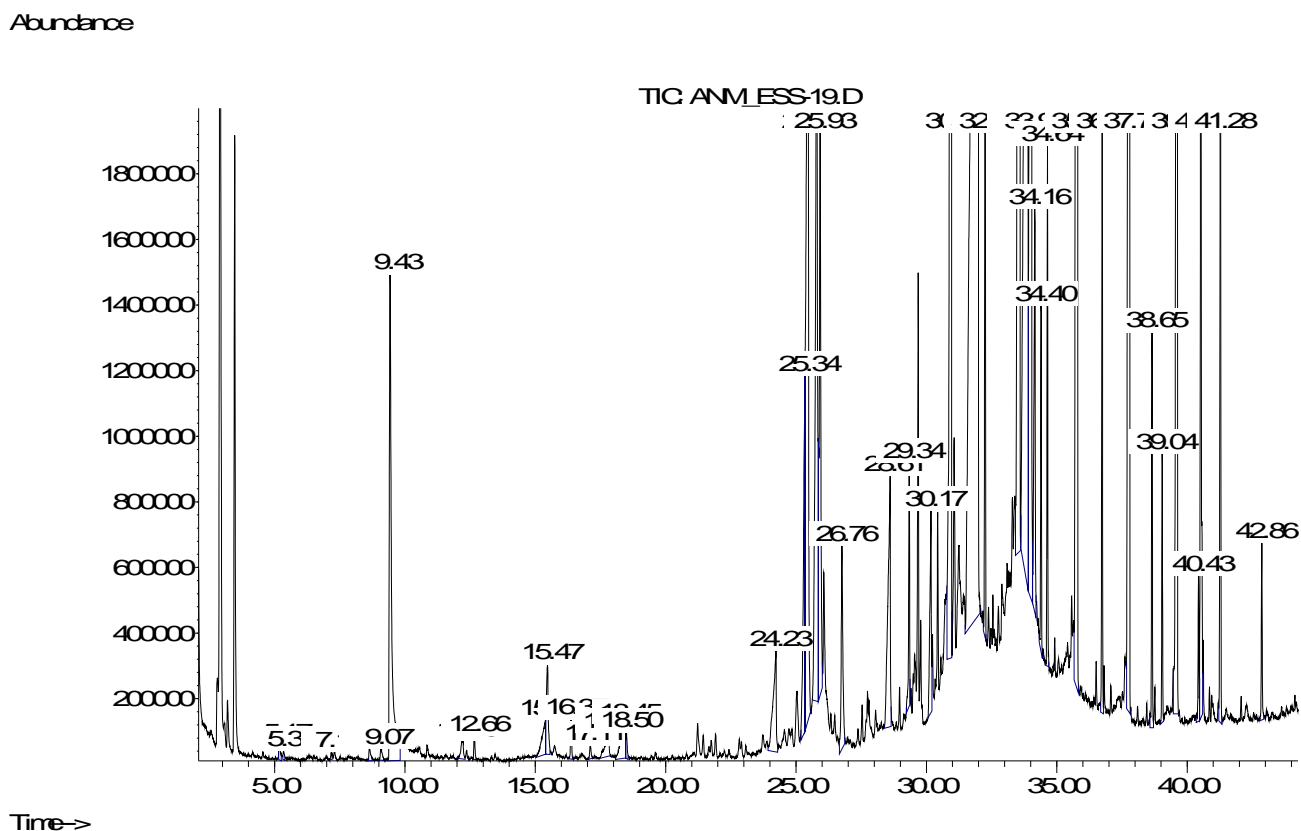


Figure. The chromatographic profile of Purslane flowers volatile oil

Rich chemical composition is the base for further in-depth research of *Rosa gallica* L.

RECEIVING AND RESEARCH OF LIPOPHILIC COMPLEX FROM THE LEAVES AND FLOWERS OF COLTSFOOT

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Nowadays scientists pay a special attention to study of lipophilic complexes and development of medicinal products on their basis. It is well-known fact that LF have saturated and unsaturated fatty acids, carotenoids, chlorophylls, porphyrins and other substances which are the main products of plant biosynthesis. Depending on the structure of the individual components, they have different kinds of biological activity, which makes their use as drugs. The drugs with such structure are antistaphylococcal drug "Chlorophyllipt", anti-inflammatory and antimicrobial ointment "Marigold" and "Vundehil", wound healing oil of buckthorn and rosehip, multivitamin antiulcer agent "Tykveol", an effective hepatoprotector "Esentsyalye".

The aim of our study was receiving and phytochemical research of lipophilic fraction (LF) from the leaves and flowers of coltsfoot.

Materials and methods. Lf were derived from the leaves and flowers of coltsfoot at the Department of Chemistry of Natural Compounds of NUPh. LF were received in the apparatus of Soxhlet using popular method. Chloroform was used as the extract.

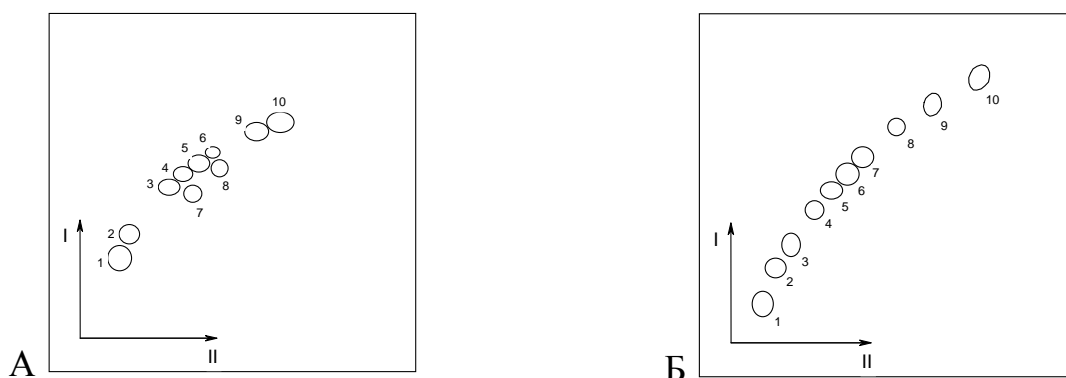
Studying the quality of the received LF was performed by thin-layer chromatography plates "Silufol" in the solvent system hexane-acetone (6:4) – and the direction hexane-acetone (6:2) – the second direction.

In the received lipophilic fractions, we have determined the content of biologically active substances. Determination of content carotenoids was performed by spectrophotometric method at a wavelength of 450 nm. As a reference solution was used hexane. For quantification of chlorophylls used photolorimetric method. Optical density was measured at fotoelektrokolorimetr KPhK-2 red filter in a ditch with a layer thickness of 10 mm. The reference solution was 96% ethanol.

For standardization LF was defined chemical, numerical parameters: acid number, saponification number, iodine value and essential. Determination was carried out by the methods of the State Pharmacopoeia of Ukraine.

The results. The release of chemical lipophilic fraction from the leaves of coltsfoot was 11.56%, with flowers - 10.75%.

Schemes of chromatogram were shown in the picture.



Picture. Schemes of chromatograph in the quality of the LF of leaves (A) and flowers (B) of coltsfoot.

As it is shown in the picture. 1, in both received fractions were revealed at least 10 substances of lipophilic nature. Spots 1, 3, 5, 6 (Fig. 1A) and 2, 3 (Pict. 1B) in daylight had a dark green color, and UV-light they had a bright red fluorescence. Therefore, substances 1 and 3 (Fig. 1A) and 2, 3 (Fig. 1B) were referred to chlorophylls. Spots 5, 6 (Pict. 1A) after treatment with a solution of phosphotungstic acid acquired a pale pink color, which changed to purple and eventually disappeared, and was attributed to porphyrins. Spots 2, 4 (Pict. 1A) and 1, 4, 10 (Pict. 1B) in a daylight had orange color, and UV-light they had brown fluorescence. After processing of chromatogram by 2% solution of p-dimethylaminobenzaldehyde in a mixture of ethanol and hydrochloric acid and heating at 80-90 degrees for 5-7 min, they are painted in pink and purple color and were attributed to carotenoids. Spots 7-10 (Pict. 1A) and 5-9 (Pict.1B) in UV-light were blue, purple and yellow-green fluorescence, which intensified under the influence of ammonia.

The structure of carotenoids in LF with leaves of coltsfoot was 85.66 mg%, with flowers – 12.70 mg% and chlorophyll – 48.27% and 10.75% respectively.

The results of determining chemical amounts in the table.

Table

The results of determining chemical amounts

Object of research	Chemical numerical index			
	acid number	saponification number	essential number	iodine number
LF from leaves	36.92	116.65	79.73	47.84
LF from flowers	49.81	157.07	107.26	22.53

The conclusion. The results tell us about opportunity of creation new effective drugs which are based on LF from leaves and flowers of coltsfoot.

PHARMACOGNOSTIC RESEARCH OF THE HERBAL MIXTURE FOR TREATMENT OF THE CHRONIC GASTRITIS

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The relevance of using the medicinal plants is growing in the last decades. The advantages of phytotherapy are low toxicity, complex effects and the possibility of long-term use without significant adverse events. Diseases of the digestive system in structure of a general disease take the fourth place after the cardiovascular diseases, cancer pathology and respiratory diseases. Chronic gastritis is the main among gastroduodenal disease area (80-85%) and leads in the number of patients. The morbidity of this pathology increased by 19.9% in Ukraine for 5 years, due to the harsh living conditions and the negative impact of the environment - chronic stress, diet violations, long working hours, the lack of disease prevention and population health programs.

The aim of this work was to search for a new herbal mixture for the treatment and prevention of chronic atrophic gastritis type A and also the theoretical and experimental study of its composition. Herbal medicine plays an important role in the treatment of chronic atrophic gastritis type A: in acute phase the medicinal plants used as auxiliary medications in process of medical treatment of the patient, and in the remission phase using them may be more effective and the only allowable medicine. Among the variety of herbs were chosen 4 species that meet all the requirements and have a number of important pharmacological properties, such as expressed anti-inflammatory, reparative, enveloping, sedative, antibacterial and multivitamin effects.

The signature:

Rp.: *Althaeae radices*, *Bursae pastoris herbae*, *Calendulae flores*, *Hippophaës fructus* ana 25.0 Misce, fiat species. D. S. Take 1 tablespoon of mixture, add 300 ml of boiling water, heated on a bain-marie for 10 minutes, infuse in warm for 2 hours, then strain. Take warm the ½ cup 3-4 times a day 30 min before meals.

The commodity analysis of such herbal drugs as *Althaeae radices*, *Bursae pastoris herba*, *Calendulae flores*, *Hippophaës fructus* was done. A determination of the masses of medium and analytical samples of herbal drugs by the method of the State Pharmacopoeia of Ukraine (SPhU) was done, so as the moisture content and amount of impurities; quantitative determination of the polysaccharides, carotenoids, ascorbic acid and flavonoids amount were defined. Also the microscopic, histochemical and microchemical analysis of herbal mixture components was done.

All studied parameters of herbal mixture corresponds with the SPhU. So the given herbal mixture can be used in the acute phase or for the systemic prevention of disease. We expect the significant analgetic, anti-inflammatory and reparative effects on inflamed areas of the stomach, improving of the intestinal motility, gastroprotective and calming effects and a comprehensive vitamin and mineral reducing effects.

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

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According to available references, the study of chemical composition of tubers a Dahlia has not received much attention. In the subterranean organs of some species of Dahlia cultivar we find such groups of bioactive substances as polysaccharides, vitamins, tannic substances, amino acids and mineral substances. For the present study we have chosen Ken's Flame cultivar of the Nymphaeales class. The cultivar is one of the popular in Ukraine, known to be a good source of raw substances.

Organic acids are a group of bioactive substances with manifold pharmacological impact on a human organism. As part of the study of the chemical composition of tubers of Dahlias Nymphaeales of Ken's Flame cultivar, the aim of our study was to examine the qualitative and quantitative composition of organic acids.

Preliminary study of the qualitative composition of organic acids was made by paper chromatography using the solvent system: I - butanol-water-formic acid (5:0,5:2), II - n-propanol-concentrated ammonia (6:4), standards of organic acids. The chromatograms were processed using 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 was defined by chromatography-mass spectrometry applied on a Agilent Technologies 6890. As a result of preliminary studying of organic acids on chromatograms 4 spots are revealed, with 2 spots by values of Rf standards of exemplars are identified as malic acid (I system – Rf 0,55; II system – Rf 0,29) and citric acid (I system – Rf 0,55; II system – Rf 0,29). Malic acid is used in laxatives. Citric acid is used in the treatment of urolithiasis, is an antioxidant and a part of the Krebs's cycle.

As a result of gas chromatography-mass spectrometric studies 9 organic acids were revealed for the first time in the tubers of Dahlias Nymphaeales of Ken's Flame cultivar, among which the largest quantities of malic (2579.5 mcg/g) and citric (3771.8 mcg/g) acids. Among the revealed organic acids were oxalic acid (318.6 mcg/g), succinic acid (267.0 mcg/g) and malonic acid (525.1 mcg/g), which fall into saturated dibasic acids. This group of acids has a stimulating action on the nervous system, anti-inflammatory action, used for the treatment of diseases of the cardiovascular system, in cosmetology. Unsaturated dibasic acids were represented by fumaric acid (99.7 mcg/g). It is used to treat autoimmune diseases, in particular psoriasis. Of phenolcarboxylic acids found in tubers of dahlia were vanillic (60.1 mcg/g) and 4-oxy-dihydrocinnamic (1016.2 mcg/g) acids. Aromatic acids were represented by benzoic acid (33.9 mcg/g).

Thus, the results of a study into qualitative and quantitative composition of the organic acid content in tubers of Dahlia Nymphaeales of Ken's Flame cultivar prove the efficiency of this kind of raw material for the development of new dosage forms with a specific pharmacological effect.

BIDENS TRIPARTITA IS A PERSPECTIVE MEDICINAL PLANT

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The aim of the work is a study of qualitative and quantitative content of substances of *Bidens tripartita* herb.

Research techniques. The herb of *Bidens tripartita* was prepared in the Vinnitsa areas in 2012. We used chromatography on the paper and thin layer of sorbent for preliminary research of qualitative composition of the raw material.

The chromatography on the paper was carried out in the systems of solvents: on the presence of sugars, phenolic acids and phlavonoids cleared n-butanol- acetic acid icy-water (4:1:2); was used on sugars – cleared n-butanol-piridin-water (6:4:3); on organic acids – cleared n-butanol-formic acid-water (4:1:5), cleared ethylacetate-formic acid-water (3:1:1); on phenolic acids and phlavonoids – 2%, 5% and 15% acetic acid. The chromatography in thin layer of sorbent was carried out in the system of solvents by a chloroform-alcohol methyl (9:1).

The quantitative content of extractive substances and polysaccharides was studied by gravimetric method. Sum of oxidative phenols was determined by titration. Sums of fatty acids, free organic and phenol-carboxylic acids were studied by chromatography-mass-spectrometry.

Results. We identified carbohydrates (D-glucose and D-fructose), organic acids (apple, succinic and lemon), phenolic acids (chlorogenic and ferulic) and phlavonoids (kempherol, quercetinum and hyperosid) in the *Bidens tripartita* herb by chromatography on the paper.

The result of the research showed that the raw material contained at least 20% and 3% of extractive substances and sum of oxidative phenols respectively (we used 50% ethanol as an extractant). The quantitative content of polysaccharides, fatty acids, free organic and phenol-carboxylic acids was 3%, 1.4%, 0.01% and 0.4%, respectively.

Conclusions. As the result of qualitative composition research it was detected that the herb of *Bidens tripartita* contains carbohydrates, organic acids, phenolic acids, phlavonoids. We determined the quantitative content of extractive substances, sum of oxidative phenols, polysaccharides, fatty acids, free organic and phenol-carboxylic acids in raw material.

The obtained data will be used in further researches while creating new preparasion from *Bidens tripartita* herb.

DETERMINATION OF THE POLYSACCHARIDES QUANTITATIVE CONTENT IN SHIITAKE, REISHI AND CORDYCEPS MUSHROOMS

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Shiitake, reishi and cordyceps are mushrooms that have long been used in Eastern medicine for tumor treatment. This type of activity is associated with the presence of polysaccharides. Thus the aim of the work was to determine the quantitative content of polysaccharides in shiitake, reishi and cordyceps mushrooms. The study was carried out according to the following method.

20 g of the dried material were placed into a conical flask of 250 ml capacity where 200 ml of water was added. The flask was attached to a reflux condenser and then heated on a water bath with stirring for 30 min. The extraction in the flask was carried out two more times under the same conditions using 200 ml of water for the 1st time and 100 ml for the 2nd. The water extracts were united, centrifuged and decanted to a volumetric flask with 500 ml capacity through 5 layers of gauze which was placed into a glass funnel with 55 mm diameter and preliminarily washed with water. The filter was washed with water and the volume was adjusted with water to the mark (solution A).

25 ml of the solution A were placed to a centrifuge tube where 75 ml of 95 % ethanol were added, then the mixture was stirred, heated on the water bath to 30°C during 5 min. In 1 hour the tube was centrifuged with 5000 rpm during 30 min. The supernatant was filtered under vacuum at a residual pressure of 13-16 kPa, through dried to the constant weight at a temperature of 100-105°C glass filter POR-16 with a diameter of 40 mm. The residue from the tube was quantitatively transferred to a filter, washed successively with 15 ml of 95 % ethanol and water (3:1 ratio), 10 ml of acetone and 10 ml of diethyl ether. Filters with sediments were dried in the air and then at a temperature of 100-105°C to the constant weight.

The polysaccharides content (X , %) calculated on the dry material was calculated using the formula:

$$X = \frac{(m_2 - m_1) \cdot 500 \cdot 100 \cdot 100}{m \cdot 25 \cdot (100 - W)},$$

where m_1 – weight of the filter, g;
 m_2 – weight of the filter with a sediment, g;
 m – weight of the raw material, g;
 W – weight loss on drying, %.

As a result of the experiment carried out the polysaccharides quantitative content in shiitake mushrooms was determined to be 9.07±0.41%, in reishi – 4.96±0.20%, in cordyceps – 7.29±0.32%.

The data obtained might be used at new remedies on the basis of these mushrooms and relevant sections of quality control methods working out.

RESEARCH OF BLUEBERRY PHENOLIC COMPOUNDS

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In medicine and pharmacy Bilberry fruits – *Fructus Myrtilli* – are widely used. Decoction from Bilberry fruits is used as an astringent in colitis, enterocolitis and diarrhea. The astringent effect is caused by tannins of condensed group. According to PhEur fruits contain at least 1% of condensed tannins in terms of pyrogallol. In the pharmaceutical market of Ukraine such drugs as Strix, Optix, Vizio Balans, Bilberry Forte, etc. are represented, which contain biologically active substances of Bilberry fruits. This group of compounds is used to improve vision. In folk and scientific medicine stems and leaves of bilberry are used as a hypoglycemic agent in the form of decoctions and are in composition of hypoglycohaemic drugs Arfazetyn and Mirfazyn. Considering the wide spread of diabetes in Ukraine and a national program "Diabetes", it was advisable to carry out a phytochemical study of blueberry leaves in order to obtain medicines.

As a result of determining of content of extractives in blueberry leaves and chromatographic analysis of the amount of phenolic compounds, the best extractant – 50% ethyl alcohol was chosen. In the extract obtained by this extractant using method of exhaustive extraction content of extractives was 39.12%. The composition of extract was studied using conventional research methods – qualitative reactions, paper and thin-layer chromatography. Hydroxycinnamic acids and flavonoids were studied by two-dimensional paper chromatography in comparison with authentic samples of hydroxycinnamic acids in systems *n*-butanol-acetic acid-water (4:1:2) and 5% acetic acid followed by treatment of chromatogram with ammonia vapor.

Quantification of hydroxycinnamic acid derivatives, flavonoids and polyphenolic compounds was performed by spectrophotometric method. Optical density was measured in the cell layer with a thickness of 10 mm on spectrophotometer Specol 1500 (Switzerland) at the appropriate wavelength. The content of hydroxycinnamic acids derivatives was calculated in terms of chlorogenic acid at 327 nm, the content of flavonoids was calculated in terms of routine – at a wavelength of 417 nm after the formation of complex with aluminum chloride; the content of polyphenolic compounds was calculated in terms of gallic acid – at 270 nm. It established that in blueberry leaves the content of phenolic compounds was – 5.81%, hydroxycinnamic compounds – 1.62% and flavonoids – 3.84%.

Obtained results can be used in the further development of quality control methods for blueberry leaves for the State Pharmacopoeia of Ukraine.

THE INVESTIGATION OF THE ORGANIC ACIDS LEAVES OF VACCINIUM VITIS-IDAEA

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The BAC from the leaves of *Vaccinium vitis-idaea* are used in traditional medicine to treat diseases of the kidneys and urinary tract, bottled stuff, drugs and dietary supplements (complex infusion Pankov, "Fitoren", "Milo -14", "Burdok -S", "Hlyukosyl", "Tsystofit forte") are produced.

The chemical composition of the phenolic compounds of the bilberry usual is described in the literature, but the composition of the organic acids isn't illustrated enough. The purpose of our study was to investigate the chemical composition of the organic acids of bilberry usual.

The study was carried out as follows: The internal standard (50 mg trydekan in hexane) and 1.0 ml methylating agent (14 % BCl_3 in methanol, Supelco № 3-3033) were added to 0.50 mg of the dried minced raw in Vial 2 ml. The mixture was kept in a sealed Vial 8 hours at 65°C . During this time the fatty oil is completely extracted from the plant material and the transesterification of fatty acids is happened. The reaction mixture was poured on the precipitate and diluted with 1 ml of distilled water. For methyl esters of the fatty acids 0.2 ml of methylene chloride was added to obtain the methyl esters of the fatty acids, the mixture was stirred for 1 hour and was subjected to the chromatography.

Introduction of 2 ml sample to the chromatographic column was carried out in a mode splitless (without flow distribution) which allows you to enter the sample without loss to the division and essentially 20 -fold increase in sensitivity chromatography. The speed of the sample - 1 ml/min, term - 0.2 min. The analysis of the methyl esters of the fatty acids was performed using chromatography-mass spectrometer 5973N/6890N MSD/DS Agilent Technologies (USA). Detector - mass spectrometer - quadruples, electron impact ionization method (EI), ionization energy 70 eV, was used to analyze the system for registering the full ion current. For the distribution using a capillary column HP-INNOWAX (30m \times 250mkm) was used for the distribution. Stationary phase is INNOWAX. Mobile phase is helium gas flow rate of 1 ml / min. The temperature of the heater input samples - 250°C . The temperature of the thermostat is programmable from 50 to 250° . The identification of the methyl esters of the acids was performed by calculating the equivalent length of the aliphatic chain (ECL); using data from mass spectra library NIST 05 and Willey 2007 with a total of more than 470,000 spectra, combined with the programs to identify AMDIS and NIST; retention time was compared with the time maintenance of standard compounds (Sigma).

We used the formula to calculate the quantitative determination of the components: $C=K1*K2*1000$ (mg / kg), where: $K1 = P1/P2$ ($P1$ a peak area of the substance, $P2$ – a standard peak area); $K2=50/M$ (50 – a mass of the internal standard, introduced in the sample, μg , M - a sample of the sample, mg), C - fatty acids content in the raw materials, mg/kg.

35 organic acids were found in the leaf. Their quantitative value was found. The dominant compounds are the oleic acid (20,06%), the palmitic acid (14,17%), the linoleic acid (19,75%), the linolenic acid (19,92%), the stearic acid (6,4%), the citric acid (4,49%), the levulinic acid (3,60%) and the p-coumaric acid (2,23%).

TOPICALITY OF USING THE HERBAL MEDICINE IN MYOPIA TREATMENT

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Myopia is one of the dominant pathology in ophthalmology. Nowadays it is a social and clinical problem that is inherent in people of all ages. According to different authors about 35% of the world population suffers from myopia and 49% of them had a high degree myopia. The development of myopia not only affects the quality of life, but also limits the possibility of realization of their abilities in today's society. Issues related to the etiology, pathogenesis and treatment of myopia remain unsolved up to this day. The most promising and rational approach to normalization of vision is the correction using the herbal drugs in the technology of complex treatment of myopia. We have analyzed the published data and found that among the officinal herbal mixtures there are no phytomedications that are recommended for maintenance therapy of vision in cases of myopia. Thus, the making a new herbal mixture for the stabilization of condition at myopia, as well as the pharmacognostic research of this herbal mixture and developing the criteria for quality assessment and introduction of the herbal mixture into medical practice is an actual task. The composition of the herbal mixture to support and stabilize the patient with myopia should include herbs that:

- a) help to strengthen the sclera – those, which contains ascorbic acid;
- b) improve blood circulation – those, which contains nicotinic acid;
- c) increases metabolism in the retina – those, which contains poly vitamins.

So were chosen some herbal drugs that are rich in vitamins: blueberry fruits (*Myrtilli fructus*), wild rose fruits (*Rosae fructus*) and stinging nettle leaves (*Urticae folia*). In ophthalmology the blueberry fruits are mainly used as a part of vitamin and mineral complexes for the prevention and complex treatment of visual impairments. Because of the content of carotenoids, vitamins C and E, the rose hips are used to improve vision, strengthen the blood vessels of the eyes, normalization of its blood supply and in the cases of eye diseases, accompanied by small hemorrhages. Chemical composition of nettle leaves allows referring them to the poly vitamin resources. High content of β -carotene in stinging nettle (twice more than in carrot) improves the condition of the retina, its outlook and increased visual acuity. Especially nettle leaves are useful in treatment of progressive myopia. Such a herbal mixture is non-toxic, does not give significant side effects, not causes addiction. In further studies it is planned to confirm the effectiveness and urgency of using this herbal mixture at myopia treatment.

PHARMACOGNOSTIC RESEARCH OF JUJUBE FRUITS

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Jujube – *Zizyphus jujuba* Mill. (Lam.) belongs to buckthorn family (*Rhamnaceae*). The plant is distributed in the Indian subcontinent, Iran, North Africa. Jujube is cultivated in Japan, Korea, India, Afghanistan, Iran, Italy, France, Portugal.

In Ukraine the plant is cultivated in Nikitsky Botanical garden and in southern regions by amateur gardeners. The plant is undemanding to soils, drought resistant.

Zizyphus jujuba is a shrub up to 3-8 m, branches are sinuous, naked, covered with reddish-brown crust, the thorns are placed on two up to 3 cm definite coriaceous, glabrous, short-petiolar, with the small ovoid prelink, dark green from above, brilliant. The flowers are small (1-2 mm in diameter), green, cabbage inflorescences are on very short pedicels. The fruit is a drupe, pear-shaped or barrel-shaped of red-brown colour up to 3-4 long and up to 2 cm in diameter, with a brilliant smooth or slightly wrinkled surface. The loose is flesh, in some species juicy. The stone is one elongated cigar of shaped form. The odour is the weak and specific. The taste of the fruit is sweet.

Fruits contain sugar (up 36%), fats (to 4.5%), protein (up 2.2%), pectins (up 3%), organic acids, flavonoids: caempferol, miricetin, macro - and microelements (K, CA, Mg, P, and others), vitamins C, B1, K, carotene, tanning substances, steroids, triterpenoids, saponin.

Fruits have hypotensive, sedative, tonic, diuretic, expectorant, anti-sclerotic effects.

The aim of our study was to quantify sugars in infusion and decoction of jujube fruits by refractometric method.

The infusion and decoction have been obtained according to requirements of SPhU. The drugstore drug – 40% solution of glucose was used as a standard. The data were obtained on refractometer “Karat MT ACE-3.140084 # 890268”.

The refractive index of decoction was 1,337 and of infusion – 1,335. By gravimetric method the total content of pectins and polysaccharides were measured – for decoction it was 2.2%, for infusion – 2.9%.

For fruits morphological and microdiagnostic features were established. On a cross section of fruits clearly noticeable large miklin are seen in which caramel shining drops of sugar are noticed what is the main diagnostic feature.

The obtained results can be used for development of the QCT.

PHENOLIC COMPOSITION OF THE DRY EXTRACT FROM *SALVIA OFFICINALIS* LEAVES

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The *Salvia* genus includes approximately 600 species, 24 of which can be found on the territory of Ukraine. The officinal raw material in our country is *Salvia officinalis* leaves. The analysis of literature have shown isoprenoids to be the most well-studied group of biologically active compounds, among which acyclic, mono-, bi-, tricyclic mono- and sesquiterpenoids, phenylpropanoids, di- and triterpenes and fatty acids are present. Regarding phenolic compounds, such flavonoids as apigenin and luteolin derivatives were extracted from *S. officinalis*, *S. verbenaca* and *S. glutinosa*. Besides, pharmaceutical industry uses mainly terpene compounds for the medicines production which indicates the one-sided study of these genus representatives. Thus the study of *Salvia officinalis* leaves is advisable for the medicines on its basis.

The object of our study was the dry extract of *Salvia officinalis* leaves (produced by JSC “Liktravy”, Zhytomyr, series 191213). The phenolic biologically active compounds were extracted with 50 % ethanol.

Liquid-liquid partition, paper chromatography (PC) and thin-layer chromatography (TLC) methods were used for the compounds' extraction and identification. As a result, the preliminary chemical study of the dry extract of *Salvia officinalis* leaves have shown the presence of such groups of phenolic compounds as hydroxycinnamic acid derivatives, coumarins, flavonoids and polyphenolic compounds.

The quantitative content of hydroxycinnamic acid derivatives, flavonoids, polyphenolic compounds was determined by the means of spectrophotometric method.

The quantitative content of the sum of polyphenolic compounds was 30,48 %, flavonoids – 10,02 % and hydroxycinnamic acids – 38,20 %.

Thus, the study of phenolic compounds from *Salvia officinalis* leaves have shown the perspective of its usage in new medicines working out and the advisability to control the content of the sum of polyphenolic compounds (not less than 25%) flavonoids (not less than 7%) and hydroxycinnamic acid (not less than 30%) in the the dry extract for its standardization.

THE ELEMENT COMPOSITION OF *VERONICA LONGIFOLIA* L. HERB

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Veronica longifolia L. belongs to the family *Plantaginaceae*. Many publications based on molecular and phylogenetic contain the information that family *Plantaginaceae* called *Veronicaceae* Durande. Earlier this family belonged to Fig-wort family (*Scrophulariaceae*).

Veronica longifolia L. is a promising species in flora of Ukraine, the areal part of which had been used in folk medicine for a long time as analgesic, anti-inflammatory, expectorant, wound healing, fungicidal, cholagogic remedy and has a large area of distribution.

We have identified rich composition of biologically active substances (BAS): flavonoids, iridoids, terpenoids, coumarins, aliphatic and aromatic acids, tannins, triterpene and steroidal saponins, polysaccharides, amino acids. Iridoids and flavonoids are the most studied groups of BAS of *Veronica* L. genus.

Considering that plants accumulate mineral substances, which are involved in the biosynthesis of various BAS, after entering the human body they are involved in various physiological and biochemical reactions and have high biological activity, and are closely connected with various BAS. Macro- and microelements of *Veronica longifolia* L. attracted our attention because they are not completely studied for today.

The aim of the study was to study elemental composition of *Veronica longifolia* L. herb and to check the limit of heavy metals in plant drug.

Materials and methods.

The object of our study was air-dried herb of *Veronica longifolia* L. harvested in the flowering stage in Kupiansk and Lubotin district of Kharkiv region in June, 2013.

The study of elemental composition was carried out on the base of DNU “STC” Institute for Single Crystals” of NAS of Ukraine by using atomic emission spectrophotometric method.

When this work had been carried out, the spectrograph DFS-8 had been used with a measuring complex for photoelectric registration of emission spectra. The following conditions of powders evaporation have been set: the amperage of arc AC (generator IVS- 28) – 16A, the frequency of igniting pulse – 100 bits per second at 60 seconds exposure.

Spectra have been registered on the photographic film using spectrograph DFS-8 with a diffraction grating of 600 lines/mm and a three-lens system of slit lighting. Lines of spectra have been determined at wavelength of 270 nm to 347 nm in samples comparing with standard samples of mineral elements mixture using microphotometer MF-4.

Obtained results.

In *Veronica longifolia* L. herb 19 elements have been identified and quantified. Of these, 11 microelements (Fe, Mn, Al, Pb, Sr, Mn, Mo, Cu, Zn, Ni, Pb) and 6 macroelements (K, Na, Ca, P, Mg, Si). The total amount of elements in herb was 4997.59 mg/100g. The dominant macroelements (mg/100 g) K (2640), Ca (880), Mg (440), Si (790), P (150) were.

The descending series of chemical elements K>Ca>Si>Mg>P>Fe>Al>Na, Mn>Sr, Zn>Cu>Ni>Pb, Mo, Co>Cd, As, Hg showed the individual characteristics of their accumulation in the studied herbal drug.

The limit of Co (<0.03), Cd, As, Hg (<0.01), which have been present in herb, not inflated, according the State Pharmacopoeia of Ukraine and may be recommended for use in medicine.

Conclusions.

In the *Veronica longifolia* L. herb micro- and macroelements have been identified and quantified, the dominant macroelements (mg/100 g) K (2640), Ca (880), Mg (440), Si (790), P (150) were. The results create conditions for development of new drugs compositions with combined activity, in particular, for treatment and prevention of disease, that related with the mineral imbalance.

PHENOLIC COMPOUNDS OF SOUTHERNWOOD (ARTEMISIA ABROTANUM L.)

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Species of the genus *Artemisia* L. of Asteraceae family and medicines containing raw materials from them are widely used in official and folk medicine in many countries of the world. One of these species is *Artemisia abrotanum* L. (southernwood, lad's love, southern wormwood), which was traditionally considered an antiseptic, astringent, emmenagogue, febrifuge, stimulant, tonic, stomachic, and vermifuge.

Earlier, we have studied the composition of essential oils, fatty and amino acids of *Artemisia abrotanum* L. herb and component composition of lipophilic extracts obtained from it. The aim of presented work was to investigate the composition of phenolic compounds of this medicinal herb.

Materials and methods. For the analysis was prepared methanolic extract of the herb. Dividing the amount of phenolic compounds into individual components was performed by high-performance liquid chromatography (HPLC) using chromatograph Agilent 1200 manned by flow vacuum degasser G1322A, 4-channel gradient pump for low pressure G1311A, autosampler (auto injector) G1329A, column thermostat G 1316A, diode matrix G1315S and refractometric G1362A detectors. For the analysis, we used chromatography column Supelco Discovery C18 size 250×4,6 mm, filled by octadecyl-functionalized silica grains. Chromatography mode: maximum feed rate of the mobile phase 0.7 ml/min, eluent working pressure 100-120 bar (10000-12000 kPa), column thermostat temperature 25 °C, injected sample volume 5-10 ml, chromatography time 50 minutes. Elution mode – gradient, scan time – 0.6 sec, detection range – 190-400 nm, the wavelength – 320, 330 nm (for hydroxycinnamic acids) and 255 nm (for flavonoids). The identification of compounds was performed by retention time of standards and spectral characteristics.

According to results of research it is established that *Artemisia abrotanum* L. herb contains (in mg per 100 g of raw material) flavones apigenin (52.0) and luteolin (55.5), flavonolic glycoside isoquercitrin (99.7), rosmarinic (226.9) and chlorogenic (1013.3) acids.

Thus, in the *Artemisia abrotanum* L. herb were identified and quantified three flavonoids and two hydroxycinnamic acids. These substances are biologically active and significantly contribute to the pharmacological effects of herb and medications obtained from it.

STUDY OF QUALITY MILK OF DIFFERENT BRANDS

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The goal: Study of milk quality of different brands, the development of techniques for the identification of food additives, labeling and study compliance with applicable standard specifications.

Milk is one of the perfect foods, created by nature. Nutritional and biological value of milk is the optimal balance between its components, easy digestibility (95-98 %) and the absolute necessity for the human body (plastic and energy functions). Milk contains all the necessary nutrients for human body, so milk and dairy products are essential in the diet of patients, children and the elderly.

Quality of drinking milk are regulated by national standards - DSTU 2661:2010 "Milk cow drinking. General technical conditions" and the Law of Ukraine № 1870 -IV "About milk and milk products".

For research, samples were taken of drinking cow's milk sold in retail outlets in Kharkiv region: "Balmoloko", " Ukrainian", "Romol", "Dobrinja", "Voloshkove pole", "Zarechie".

Milk samples were tested by organoleptic and physico- chemical parameters, including identification of the fat and protein, the content of antibiotics and some food additives, quality packaging and labeling.

According to the results of the analysis, it was found that out of 6 samples tested drinking milk 3 on different parameters did not meet regulatory requirements, and information on the label as well. One milk sample did not meet the stated information on working life (acidic medium). In two milk samples, fat mass fraction was 2.5 % instead of 2.6% and the next sample - 3.1 % instead of 3.2%. Furthermore, in the same samples revealed the presence in milk of antibiotics. In 2 batches of milk was the integrity of the packaging, as revealed their course.

All six sample were tested about food additives. It was established, that the concentration of soda (sodium hydrocarbonate) were higher than in standard. This fact needs interpretation about the interaction between milk and definite drugs.

Among the six samples of packaged milk, only one had a weight of 500 g, and almost five samples had significant deviations from the norm. All the shortcomings - the result of violations of the conditions of production, low production control and an insufficient level of producer responsibility for the quality of manufactured products.

PHYTOCHEMICAL RESEACH OF KHELLA

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Khella (*Ammi visnaga* or *Visnaga daucoides*) originates from the Nile delta and was used therapeutically by the ancient Egyptians, as is documented in Eber's papyrus. The plant was used in Egyptian folk medicine to treat urinary calculi and bladder stones which was common as a result of widespread bilharzia. The plant's dried umbels are still sold today in markets in the Middle East and the Far East.

The aim of our study was phytochemical research of fruits and herb of *Ammi visnaga* of Lebanon origin.

Herbal drug – fruits and herb were collected in Lebanon from July to September. The fruits are harvested shortly before they are fully ripe, after which they are dried in proper condition.

Preliminary analysis of chemical composition was carried out using thin layer chromatography in different system of solvents compared with reference solution of some phenolic derivatives. Reagents for identification were potassium permanganate solution, solution of potassium hydroxide, Wagner's reagent, tannic acid solution.

As a result were identified the following compounds: furanochromones: visnagin, khellol, khellenin and additionaly 3 furanochromones derivatives, pyranocoumarins: visnadin, samidin and dihydrosamidin, flavonoids represented by quercetin and isoramnetin derivatives.

For isolation of khellin was proposed the next scheme:

1. The seeds and herb are dried, powdered, sieved and extracted in Soxhlet apparatus with solvent ether for several hours.

2. The ethereal extract is concentrated in a rotary thin-film evaporator and stored in a refrigerator for a few days.

3. The cold ethereal extract eventually comprise of three distinct layers: an upper green oily layer; a middle cream coloured fatty layer; and a lower green crystalline layer. The upper green oil is removed by filtration with gentle suction, the middle cream coloured fatty layer is removed by the help of petroleum ether, and the remaining lower solid residue is duly purified by repeated crystallization from methanol to obtain pure khellin.

Preliminary assay about concentration of khellin showed that the in fruits it's slightly more khelin than in herb.

MODERN METHODS OF MICROSCOPIC PLANT ANALYSIS

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The method of light microscopy is the most widely and traditionally used when examining plant objects and in pharmacognostic analysis of medicinal raw materials. Among new promising methods reflecting the microstructure of plants we should notice a method of scanning electron microscopy. Modern scanning electron microscopy allows a wide magnification range which is from 10 fold to 1000000 fold, that is approximately 500 times faster than the best optical microscopes. Applying this method a thin electron bunch of a scanning microscope runs on the surface of a specially fixed and dried plant object coated with a thin layer of metal which is usually gold. The received information is being sent to a cathode ray tube, creating an almost three-dimensional image of examining surface. Among the advantages of scanning microscopy is a large resolving power and depth of definition, the relative ease in the resulting images describing and comparing; the ability to connect additional devices, relatively low requirements for the preparation of plant object.

The method of scanning electron microscopy provides a more complete and reliable information when examining the microstructure, first of all a primary epithelial tissue – the epiderm, which diagnostic features of the structure are widely used in pharmacognostic analysis; in practical and theoretical anatomy of plants, in palynological analysis .

Using scanning electron microscopy we can also provide information about the chemical composition of cells. For example, the method of X-ray microanalysis allows to identify and quantify the content of chemical elements from the spectra arises of X-ray emission. In this case the objects under study should not be covered with a layer of metal.

To method which deserves the attention of research plants and herbal raw materials should be noticed the fluorescent microscopy which allows not only to determine the biologically active substances and their localization in cells and tissues of plants but also identify the physiological state of the algae, as their cells which differ in their physiological state give different color shades and brightness of the glow.

This method gives us the chance of carrying out rather fast and exact assessment of degree of viability of seaweed cultivated by biotechnological methods, including spirulina, widely used as biologically active food supplements.

DETERMINATION OF ASCORBIC ACID CONTENT IN FRUITS AND LEAVES OF BLACK CHOKEBERRY

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Black chokeberry (*Aronia melanocarpa* (Michaux) Elliot) belongs to the apple subfamily (*Maloideae*), the rose family (*Rosaceae* Juss.). It is native to the eastern part of North America. It is widely cultivated as fruit, medicinal and ornamental plant in Ukraine.

Fresh fruits of Black chokeberry are officinal. The principal active substances of Aronia fruits are organic acids (malic, citric, oxalic), carbohydrates, phenolic compounds (phenol carboxylic acids and their derivatives, catechins, anthocyanidins and their glycosides leucoanthocyanidins, flavanols, tannins) and vitamins. They cause hypotensive, spasmolytic, anti-inflammatory, antimicrobial, diuretic and choleric activities of fruits and they strengthen blood vessels.

Phytochemical research of Black chokeberry leaves has been conducted insufficiently. Previously we studied essential oils, amino acids, macro- and micronutrients, polysaccharides and carboxylic acids of fruits and leaves of this plant.

The goal of the present work was to study content of ascorbic acid from Black chokeberry leaves and fruits that were harvested respectively in May and September 2013 in the botanical garden of the National University of Pharmacy.

Determination of ascorbic acid content in the test raw materials was carried out by the high-efficiency liquid chromatography method on a Shimadzu chromatograph equipped with pump LC-20AD, spectrophotometric detector SPD-20AV and system controller CBM-20 ALITE.

As a result of researches content of ascorbic acid in fresh fruits of Black chokeberry was 0.002% (based on dry raw material), in leaves – 0.0001%.

Pharmacognostic study of fruits and leaves of Black chokeberry will be continued.

ANALYSIS OF LEDUM PALUSTRE EXTRACTION CAKE AFTER OBTAINING THE ESSENTIAL OIL

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Wild rosemary (*Ledum palustre*, family *Ericaceae*) has significant area of distribution in Ukraine, which occupies the whole of the northern part from Lviv to Kharkiv regions. All parts of the plant contain essential oil (except the roots), composed mainly by ledol, heranilatsetat and palustrol. In addition, the plant contains flavonoids and tannins, which belong to the original catechins. In medicine, wild rosemary infusion is used as antitussive in acute and chronic bronchitis, as well as spastic enterocolitis. There is evidence *Ledum palustre* use as an insecticide. On the territory of Ukraine it was reported only one drug from this plant - "Ledin," which has antitussive activity. The pharmaceutical industry uses only terpenoid extract, while this plant is rich in other classes of biologically active substances, in particular phenolic compounds.

The aim of our research was to investigate the chemical composition of the extraction cake remained after obtaining the essential oil of *Ledum palustre* shoots, including phenolic compounds for more complex processing of raw materials, and creating new drugs on the basis of the results.

To achieve this we obtained essential oil of *Ledum palustre* shoots by the method presented in the Pharmacopoeia USSR 11-ed. Then 50% ethanol was added to the extraction cake and extracted during the day. The extract was filtered and the volume of filtrate was measured. Quantitative determination was performed by spectrophotometry. The total content of phenolic compounds was determined at wave length 270nm in calculation on gallic acid; hydroxycinnamic acid derivatives - at 327nm in calculation on chlorogenic acid and flavanoids by differential spectrophotometry with $AlCl_3$ at 417nm in calculation on rutin.

It was found that the total content of phenolic compounds in the extract in calculation on absolutely dry raw materials was $1,72\% \pm 0,01\%$, hydroxycinnamic acid derivatives - $1,19 \pm 0,01\%$ and the content flavanosds - $0,069 \pm 0,01\%$.

Thus, we have studied the content of phenolic compounds extracted from cake of *Ledum palustre* shoots remaining after obtaining essential oils and found the possibility of creating a new drug on the basis of the data.

PROSPECTS FOR APPLICATIONS OF SEMI-SOLID MEDICINAL PREPARATIONS BASED ON MEDICINAL HERBS FOR THE TREATMENT OF THE SECOND AND THIRD PHASES OF WOUND PROCESS

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Medicinal plants occupy a significant place in the pharmaceutical field, being one of the most important sources for medicines. The plants have been used for medicinal purposes for centuries. It is known that in the store of medicines that are used in modern medicine due to their beneficial and healing properties, the fourth part is of plant origin. Despite the remarkable progress of modern organic chemistry that produces high quality synthetic biologically active substances used in pharmacy, the popularity of herbal medicines worldwide is not only falling, but rising steadily.

According to the literature, the stimulation of wound healing in medicine remains a pressing problem. Despite the wide range of highly efficient wound-healing, anti-inflammatory and antibacterial medicinal preparations, the conventional treatment of this illness does not always give the desired outcome, and the complication rate can reach 10%. Therefore, the development and application of phytomedications for the treatment of wound processes in the second and third phases is one of the main problems of modern pharmacy and clinical medicine.

Aim. Analyzing and exploring the published data on the use of medicinal plants in traditional and folk medicine, exploring the range of semi-solid medicinal preparations for the treatment of the second and third phases of wound process.

Materials and methods. Object of study: clinical protocols approved by the Ministry of Health of Ukraine, the State register of medicinal preparations of Ukraine, ATC classification and scientific publications. Methods used: information retrieval, compilation and analysis of the literature.

The results showed that such pharmacological groups of medicinal preparations like antibiotics, wound-healing, antiviral and anti-inflammatory medicines are often used for the treatment of wound process. These medicines come mainly in the form of ointments, liniments or pastes. Amount of medicines in the form of gels is limited.

The range of semi-solid medicinal preparations for the treatment of wound process in the second and third phases is presented on the pharmaceutical market of Ukraine mainly by high-priced foreign-made medicines.

Modern biomedical requirements for medicines used in wound healing are as follows: 1) a wide range of antimicrobial activity; 2) medicines have to spread quickly on the wound surface, moisten it and permeate into the wound cavity; 3) the medicine has to ensure continued permeation of substances into inflamed tissues, creating bactericidal concentrations; 4) the medicine should be safe in applications on a wound, especially when it's needed to be used in high doses. Lack of domestic medicines that have positive effect on the formation of granulation tissue and accelerate the process of epithelization gives the opportunity of finding and development new semi-solid preparations for the treatment of wound process.

In recent years the research has been more focused on finding new semi-solid herbal medicines for the treatment of wound process in the second and third phases. The most common medicinal plants for the treatment of this pathology are plantain leaves, yarrow grass, marigold flowers, tutsan grass, sage leaves, arnica flowers and others.

The advantage of the widespread use of herbal medicines is based on the smooth increase of therapeutic effect, low toxicity, the absence or very rare occurrence of adverse side effects, allergic reactions etc. Semi-solid herbal medicines are popular due to their wide spectrum of activity, affordability and efficiency in the application.

Unfortunately, nowadays no semi-solid medicinal form used in clinical practice for the treatment of wound process is up to meet these requirements, although in recent years the range of these medicines has expanded owing to the introduction of synthetic medicines, and new medicines of natural origin.

Conclusion. The range of semi-solid medicinal products based on medicinal plants used for the treatment of wound process in the second and third phases is limited. Herbs promising for further study contain the following groups of biologically active substances: flavonoids, anthracene derivatives and tannins with strong antimicrobial, anti-inflammatory, astringent, wound healing, antiulcer and antiviral activity. Development of new composite semi-solid preparations that would contain the complex of biologically active substances of plant origin is reasonable and relevant.

LOOKING FOR PERSPECTIVE PLANTS THAT CAN BE USED FOR TREATMENT OF GENITOURINARY SYSTEM

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Today the part of men who suffer from diseases of the genitourinary system and reproductive disorders increases compared to previous years. The most common causes that negatively affects on sexual function are different inflammations and hormonal changes in the prostate gland.

Speaking of drugs that are used for treatment of those diseases, much of them have natural origin. Phytomedications usually characterized by a high level of safety, lack of adverse effects on sexual function, they can be used in the treatment for a long time. Popularity of the prostate protectors with natural origin is high due to their adequate performance with minimal risk of side effects, high level of trust of patients, their high tolerance and favorable pharmacoeconomic profile. Ukraine is rich in plant resources which can be raw material for the production of natural origin drugs for the treatment of prostatitis.

Development and implementation of domestically produced prostate protectors is a priority of modern Ukrainian pharmaceutical science. The most effective herbs for infertility treating is *Aralia mandshurica*, *Panax ginseng*, *Echinopanax elatum*, *Eleutherococcus senticosus*, *Leuzea carthamoides*, *Orchis maculata*, *Rhodiola rosea*. These types of herbal drugs are widely used in andrological practice; most of them are part of multicomponent herbal mixtures. But considering the fact that these plants are not growing in Ukraine or cultivated in small scale or listed in the Red Book of Ukraine, the topical issue is to search for new species to develop original Ukrainian prostate protectors. Among the native flora the *Thlaspi arvense* occupies a special place. It has long history being used in folk medicine to stimulate the sexual function of men. However, in Ukraine *Thlaspi arvense* is unofficial raw materials and its chemical composition is studied insufficiently.

We conducted a preliminary pharmacognostic study of *Thlaspi herba* and revealed the presence of derivatives flavonoids, tioglycosides, steroid saponins, alkaloids, lipids, vitamins, micro and macroelements. Those biologically active substances show a wide range of pharmacological effects: antimicrobial, anti-inflammatory, reparative; they can affect to the hormonal and immune balance, reproductive function and so on. So the next step is to make a more detailed phytochemical study of this plant to develop the project of Quality Control Methods.

ANATOMICAL AND HISTOCHEMICAL RESEARCH OF RADICAL ROSETTE, RHIZOMES WITH ROOTS

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In modern medicine, one of the main sources of receiving treatment and preventive medicines are medicinal plants. They are used both independently and receive many valuable therapeutic drugs, that are include more than 25 pharmacological groups medicines and for the most part of them there is no equivalent synthetic analogues.

Geum aleppicum Jacq. - Aleppo avens belongs to the family Rosacea subfamily Rosoideae - grows throughout Ukraine in littered places, in woods, in thickets. Previous chemical investigations of *G. aleppicum* demonstrated the presence of polyphenols, amino acids, fatty acids and other compounds in raw materials, which is inherent antimicrobial, anti-inflammatory and reparative activity.

The aim of this research was to investigate the anatomical and histochemical structure of radical rosette, rhizomes with roots *Geum aleppicum* for identification of medical plants.

For microscopic investigation were used leaves from radical rosette, rhizomes with root, which were collected during 2013-2014 years in the outskirts of Kharkiv.

Aleppo avens is a vigorous herb with thick, short rhizome, radical rosette leaves are long-petiolate, lyre-shaped, pinnately sected or intermittently pinnately parted, lateral parts 3-6(8) couples, they are wedge-shaped, ovate and lobed.

For leaves species-specific anatomical features include trichomes availability and their location; size, number of conductive bunches in the central vein; shape and placement of crystals of calcium oxalate in mesophyll. For root species-specific anatomical features include index of cork rough, endodermis availability, vessels with simple and spiral perforation; location and type of crystalline inclusions, shape and localization of starch grains, presence and density of pigmented idioblasts with red-brown secret.

All things consider, on the basis of morpho-anatomical and histochemical structure of radical rosette, rhizomes with roots *Geum aleppicum* were established diagnostic features for the whole species. The obtained data shows the possibility of usage rhizomes with root *Geum aleppicum* as a raw with tannins. Research of anatomical and histochemical structure of aboveground and underground parts of *G. aleppicum* with the identification of diagnostic features may be need during the development of the relevant sections of quality control methods.

ROSA CINNAMOMEA ROOTS CHROMATO-MASS-SPECTROMETRIC STUDY

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Herbal drugs have several advantages over synthetic ones. In this regard, the search for new sources of medicinal plants containing biologically active compounds is promising. It is known that in terms of pharmacological availability aggregate, herbal drugs have a lot of advantages over individual compounds, therefore it is advisable to use the aggregate substances as multifunctional preventional medicines. Finding primary sources of biologically active compounds among the species of Ukrainian flora that have sufficient herbal drug and have long been used in folk medicine, is a key issue in Pharmaceutical Sciences. The herbal drug is rose fruits (*Rosae fructus*) rich in ascorbic acid, carotenoids, organic acids, phenolic compounds. Under the current standart documents, fourteen species of wild rose are suitable for medicinal use.

At the same time roots of the genus *Rosa* are popular in folk medicine as an astringent and antiseptic, used to treat inflammation of the joints, gout, rheumatism, paralysis, hypertension, heart diseases, digestive disorders, cystitis.

The object of the study were the roots of Cinnamon rose, harvested in October 2013. The study of essential oil components and organic acids was performed by chromatography-mass spectrometry. The spectra were examined on the basis of the general laws of fragmentation under the action of electric shock and by look in mass spectral data base library.

In the herbal drug of cinnamon rose, there is presence of 27 substances belonging to the volatile compounds. Total content of terpenoid substances is 947,44 mg/kg. Volatile components of underground organs of cinnamon rose quantitative content of the following components were found: aliphatic hydrocarbons and hydrocarbon derivatives of aldehyde nature, terpenoid compounds, acyclic monoterpenoids and their derivatives–; monocyclic monoterpenoids, bicyclic monoterpenoids, aromatic compound, acyclic sesquiterpen, triterpen. The dominant components were heksakozan and squalene (as 367.45 mg / kg and 178.76 mg / kg).

In the roots of cinnamon rose have been defined 29 organic acids, 28 of which were identified, including 11 fatty acids. The total content of organic acids was- 33556,5 mg/kg or 3,36%.

These results will be used for the Pharmacognostical study of this herbal drug

SECTION № 3

**THE STANDARDIZATION OF MEDICINES. PHARMACEUTICAL
AND CHEMICAL- TOXICOLOGICAL ANALYSIS**

**ACCEPTABILITY CRITERIA FOR LINEAR DEPENDENCE
WHEN VALIDATING UV-SPECTROPHOTOMETRIC METHODS
OF QUANTITATIVE DETERMINATION
IN FORENSIC AND TOXICOLOGICAL ANALYSIS**

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The purpose of this paper is to analyse the present approaches to acceptability estimation of the calibration model chosen for method description according to the requirements of the international guidances and to form the own approaches to acceptability estimation of the linear dependence when carrying out the validation of UV-spectrophotometric methods of quantitative determination for forensic and toxicological analysis.

It has been suggested to be guided by domestic developments in the field of validation of analysis methods for medicines and, particularly, by the approaches to methods validation in the variant of the method of calibration curve.

The next criteria and the order of acceptability estimation of linearity for UV-spectrophotometric methods of analytes quantitative determination in biological fluids used in forensic and toxicological analysis have been offered:

- acceptability estimation of linear dependence parameters is carried out in two stages – for the lines obtained using model solutions (without matrix) and calibration samples respectively;
- two approaches have been suggested for estimation of parameters of linear dependence obtained using model solutions; they are based on: 1) assumption of equality of the uncertainty related to the procedure of sample preparation of calibration standards and the uncertainty of the calibration curve plotted by model solutions; 2) assumption of insignificance of the uncertainty of the calibration curve plotted by model solutions; for both approaches the acceptability criteria have been offered for residual standard deviation RSD_0^{model} and correlation coefficient R_c^{model} ;
- for estimation of parameters of linear dependence obtained using calibration samples it has been suggested to proceed from assumption of equality of the calibration uncertainty and the uncertainty of measuring the absorbance and sample preparation of the sample to be analysed; within this approach the acceptability criteria have been offered for residual standard deviation RSD_0 and correlation coefficient R_c ; the parameters of within-run (within-day) and between-run (between-day) linearity should satisfy these criteria.

IDENTIFICATION AND QUANTITATIVE DETERMINATION OF FUSIDIC ACID IN THE GEL FOR THE TREATMENT OF THE ACNE VULGARIS OF I-II STAGE

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With comprehensive research, we have proved the gel composition and technology of local action for the treatment of acne I-II stage.

As active substances were selected fuzidiyeva acid as a component with a strong antimicrobial activity and panthenol - like substance that is known reparative action.

At this stage, our objective of the study was to develop a method of high-performance liquid chromatography (HPLC) to determine panthenol developed in gel base.

Identification. In the chromatogram obtained with the test solution retention time peak panthenol must meet the retention time of the peak in the chromatogram panthenol reference solution.

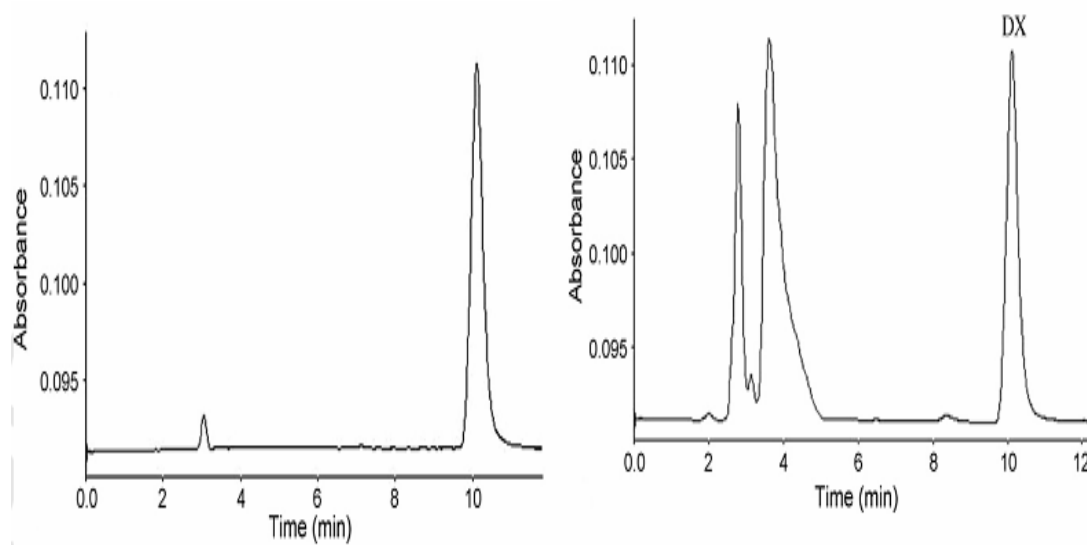


Fig. 1. Chromatogram obtained with reference solution (left) and test solution gel (right) for the identification of panthenol

Quantitative determination. Test solution: about 1.00 g (accurate weight) gel is placed in a volumetric flask of 100 ml, dilute the solution to the mark with the mobile phase, mixed and centrifuged at speed 7000 r / min. for 10 min.

If necessary nadosadkovu liquid was filtered through a teflon membrane filter with a pore size of 0.45 microns. Reference solution: approximately 50.0 mg (accurate weight) Panthenol standard sample is placed in a volumetric flask of 100

ml, dissolved in 30 ml of mobile phase, dilute the solution to the mark with mobile phase and mix. To 20 ml with reference solution and the test solution chromatographed on liquid chromatography with spectrophotometric detector receiving at least 3 chromatogram of the following conditions: column Vydac Protein C4, size 250 mm*4,6 mm, filled with sorbent particle size of 5 microns or equivalent; predkolumna: Vydac Protein C4 mm x 4.6 mm, filled with sorbent particle size of 5 microns or equivalent; mobile phase of 0.1% aqueous trifluoroacetic acid, degassed convenient way, the temperature of the column thermostat OS 30.0, the rate of mobile phase 1, 0 ml / min, detection at a wavelength of 206 nm.

Chromatographic system is considered suitable if the following conditions are met: the efficiency of the chromatographic system is designed for peak panthenol, shall be not less than 2000 volumes, peak symmetry factor triclosan should be not more than 2.0; inrelatively standard deviation of the peak areas panthenol must comply with 2.2. 46 (NPhU1.2).

Panthenol content in mg in 1 g of gel is calculated by the formula:

$$Y = \frac{S \cdot m_0 \cdot P \cdot 100}{S_0 \cdot 100 \cdot 100 \cdot m} = \frac{S \cdot m_0 \cdot P \cdot 0.01}{S_0 \cdot m}$$

where: S – the average peak area from panthenol calculated chromatogram of the test solution; S_0 – the average peak area from panthenol calculated chromatogram obtained with reference solution m_0 – mass of sample NW panthenol, mg P – Fixed substance in OT Panthenol.

Panthenol content in 1 g of gel should be between 47.5 to 52.5

Determination of content of panthenol in the developed formulation is proposed to HPLC under the following conditions : column Vydac Protein C4, size 250 mm x 4.6 mm, filled with sorbent particle size of 5 microns or equivalent ; predkolumna : Vydac Protein C4 mm x 4.6 mm , filled with sorbent particle size of 5 microns or equivalent ; mobile phase of 0.1 % aqueous trifluoroacetic acid, degassed convenient way , the temperature of the column thermostat 30.0 °C , Flow rate 1.0 ml / min , detection at 206 nm wavelength.

Under these conditions, the peak panthenol completely separated from the other components of the gel components.

Data obtained showed that the method is stable and reproducible in different days.

DEVELOPMENT EXTRACTION-PHOTOMETRIC METHOD OF ASSAY OF TIMOLOL MALEATE

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One of the main stages pharmacopoeias analyses is choice of method development and assay of the active substance in the medicinal product. The basis of any quantitative study is an accurate measurement. The content of the active substance is determined individually and as a medicinal product. The conclusion of the quantitative composition of the substance can be done by measuring the mass of the substance, scope solutions or gases, and optical, electrical, magnetic and other physical properties. Among the methods of quantitative determination of drugs using chemical, physical and physicochemical methods.

Timolol maleate substance and formulations based on it included many foreign pharmacopoeias. Requires foreign pharmacopoeias definition timolol maleate carried chemical or physico-chemical methods. With titrimetric methods most frequently used method of acid-base titration with the indicator or potentiometric recording the equivalence point. Among the instrumental methods for the determination of timolol maleate using liquid chromatography, absorption spectrophotometry and others.

Methods for the quantitative determination of timolol maleate extraction photometric method are practically not described.

In this regard, the aim of our work is to develop the extraction photometric methods of quantitative determination of timolol maleate. The drug belongs to the group of selective β -blockers, antiglaucoma agent. In medical practice, timolol maleate is used in the form of tablets and eye drops. In Ukraine registered eye drops under the trade name "Timolol 0.5% to 1 ml dropper tube" and "Timolol-Darnytsya solution of 2.5 mg/ml (5 mg/ml) for 5 or 10 ml bottles."

We recommended the extraction photometric method of quantitative determination of thymol maleate, which is based on the formation of ion associate of methyl orange. As a result of our studies establish conditions for quantitative determination: concentration of timolol maleate, the amount of methyl orange, pH and wavelength.

In the study of subordination solution ion associate timolol maleate with methyl orange Bouguer-Lambert-Beer found that the direct relationship observed in chloroform solution concentration of the active ingredient of $2.0 \cdot 10^{-4}$ to $2.2 \cdot 10^{-3}$ g/ml at length wave 426 nm.

Check the stability of the solution was carried out for 60 minutes. It was established that the analytical solution is stable for hours.

Thus, the results can be possible to use techniques developed by us to quantify timolol maleate in both substance and in finished dosage forms.

ANALYTICAL FEATURES AND VARIETY MERCUOMETRIONS TITRATION

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Methods for the precipitation and redox titration is widely used in the chemical and pharmaceutical analysis, analysis of raw materials, certification of finished products for arbitration analysis and certification of standard samples for major components.

The aim of our work was to study the analytical features and varieties mercuriometric titration where as titrant using a standard solution of nitrate of mercury (I). The salts of mercury (I) to form slightly soluble compounds with halides which are already long used in the analysis. But, in addition for mercury(I) salts are typical redox reaction. In analytical practice used primarily reducing properties of salts of Hg(I).

In 1835 J.L. Gay-Lussac described variants of determination of hypochlorite and chlorinated limes variants of determination hypochlorite and chlorinated limes where standard solution with a reducing properties, along with others was propose a monovalent mercury nitrate. Later, some authors identified salt Fe (III) with titration mercury (I) nitrate. In 1958 he published the first edition of the monograph V.M. Tarayan "Mercuriometric." "

In 1935 M.B. Shchigol proposed mercuriometric for determination of chlorides using as an indicator thiocyanate iron (III). A.S. Vetrov offered for mercuriometric titrations as adsorption indicator diphenylcarbazone. Determination was performed in a wide range of concentrations of HNO₃ (unlike Mercury(II) which described with diphenylcarbazones). It was indicated that the chlorides and bromides titrated in the range concentrations 0.01-0.1N., iodides-0.01-0.025N. (At higher concentrations Hg₂I₂↓ decomposed into HgI₂↓ and Hg↓). These studies are reflected in "The works of the Commission on Analytical Chemistry" of the USSR AS(1951).

Conclusions. Mercuriometric method of precipitation with titration diphenylcarbazone is undervalued in comparison with others. Among the advantages of the method - greater accuracy compared to argentometric definitions halides, the use of less expensive Hg compounds (I), the possibility of direct titration with diphenylcarbazone in highly acidic media and determination in moderately colored and turbid solutions. The main disadvantage of this method is the toxicity of mercury salts which the normative documents attributed to the first class of danger compounds.

APPROACHES TO VALIDATION OF UV-SPECTROPHOTOMETRIC METHODS OF QUANTITATIVE DETERMINATION IN FORENSIC AND TOXICOLOGICAL ANALYSIS: LINEARITY AND RANGE

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Linearity – is the ability of an analytical procedure (within a given range) to obtain test results, which are directly proportional to the concentration (amount) of analyte in the sample (ICH). As regards analytical range of method application, it is the interval between the upper and lower concentration (amounts) of analyte in the sample (including these concentrations), for which it has been demonstrated that the analytical procedure has a suitable level of precision, accuracy and linearity – according to ICH definition.

The purpose of this paper is to form the approaches to the procedure of analytical range choosing and linearity determination, notably to the number of concentration levels within the range, to the number of replicate observations for each level, etc. when carrying out the validation of UV-spectrophotometric methods of quantitative determination for forensic and toxicological analysis.

The following procedure of linearity confirmation for UV-spectrophotometric methods of analytes quantitative determination in biological fluids used in forensic and toxicological analysis has been offered:

- application of the normalized coordinates (normalization by the reference solution, which absorbance is corrected by the value of recovery);
- the application ranges are 25 – 125%, 25 – 150%, 25 – 175%; as 100% the mean toxic or lethal analyte concentration in biological liquid is accepted;
- the number of concentration levels is $g = 5, 6$ or 7 (depending on the chosen application range) in constant increments of 25%;
- the number of «replicates» – replicate experiments – for each concentration level is determined by the results of calculation of $s_{nom,r}$ value, which acceptability estimation is carried out according to the following criterion:

$$s_{nom,r}(sample) \leq \max s_{nom,r} = 0.707 \cdot \max \Delta_{As} \cdot \sqrt{n} / t(95\%, n-1).$$

- each replicate experiment is carried out within individual run/day using the matrix samples obtained from the same source;
- calculation of the parameters of linear dependence is carried out for each run (within-run (within-day) linearity) and by the mean values of replicate experiments (between-run (between-day) linearity).

DEVELOPMENT OF TECHNOLOGY OF QUANTITATIVE ESTIMATION OF PARACETAMOL IN FORMULA OF SUPPOSITORIES WITH ANTIPYRETIC AND IMMUNOMODULATORY EFFECTS

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Temperature rise and febricity development in acute respiratory diseases (ARD) is one of protective reactions of organism, however when temperature rises up to above 38,5°C, the World's Health Organization recommends to apply antipyretic medicines. This group of medicines is the most requested in pediatric practice that caused by a danger of complications development. The rectal application of drugs is the most perspective due to a high drugs bioavailability which is close to injections bioavailability.

The researches of pharmaceutical markets of Kazakhstan and Ukraine have shown that there are not enough medicines with antipyretic and immunomodulatory effects which are intended for use in pediatric practice.

At the Department of Industrial Technology of Drugs, the medicine is being created in form of rectal suppository with antipyretic and immunomodulatory effects for practical use in pediatric. It is supposed to create suppositories on the lipophilic basis (hard fat) with paracetamol (antipyretic component) and herbal extract «Mix-factor» which is glycoprotein oligopeptide composite and has an immunomodulatory effect.

An important stage in drug design is creation of analytical regulative documentation (ARD) for its quality control within manufacturing. One of the most spread methods of ready-made drugs' analysis is an adsorption spectrophotometry.

The aim of our research was development of technology of paracetamol quantitation in lipophilic-based suppositories which contain paracetamol and «Mix-factor». In order to reach the goal stated, it was needed to study spectra of paracetamol absorption in different dissolvents and to find the optimal conditions for quantitative estimation, to define frontiers of subjection to the Beer-Lambert-Bouguer law, to develop technology of sample processing and to characterize the quantitation statistically.

In the ultraviolet spectrum of absorption of water solution of paracetamol standard sample (SS) (Fig.1) a wide intensive line with the maximum in 244 nm is

evident. In the range of 270 nm is a bend of absorption line, which is correspond with the third maximum of absorption of the line of benzene type. The dissolvent substitution to the 0,1 M solution of HCl does not lead to any changes in spectrum parameters, that testifies lack of phenylic hydroxyl dissociation in water solution. Regarding the 0,1 M NaOH solution, the hyperchromic effect and bathochromic shift of the absorption band to 258 nm can be observed. This is connected with the positive inductive effect of phenolate-ion. The calibrating diagram (Fig.2); (Table 1) is ruled in a rage from 0,4 to 2,0*10⁻³%. Specific indicator of absorption $A_{1sm}^{1\%}$ equals 717±4.

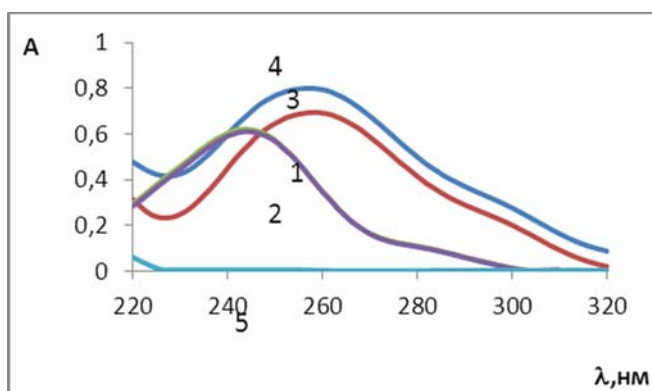


Fig.1

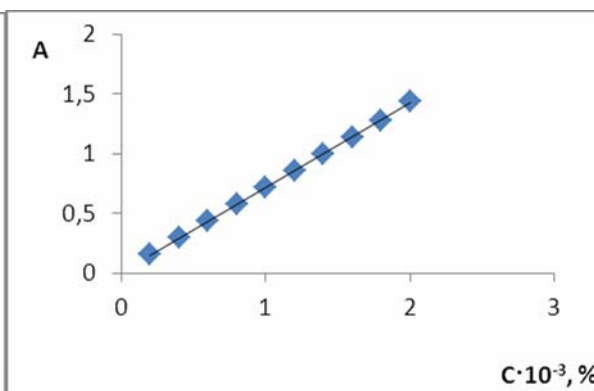


Fig.2

Table 1.

$C \cdot 10^{-3}, \%$	0,2	0,4	0,6	0,8	1,0	1,2	1,4	1,6	1,8	2,0
A	0,155	0,293	0,433	0,573	0,712	0,852	0,997	1,138	1,280	1,438
$A_{1sm}^{1\%}$	775	732	721	716	712	711	711	711	711	719

In case of research, the methodic of sample processing was developed which is consists of paracetamol extraction from suppository by 50% water solution. The absorption spectrum of the preparation's solution does not differ from SS spectrum. The placebo spectrum created analogically reveals the lack of influence of auxiliaries and «Mix-factor» to the medicine spectrum. Statistical characteristic of technology of paracetamol quantitation in suppositories, created by model samples, has shown ability of quantitative measurement of reactant according to this technology. The relative indefiniteness of a certain definition is not higher than 1,6%. The technology created is to be used for creation of Superior pharmacopoeial article based on suppository with paracetamol and «Mix-factor».

DEVELOPMENT OF STANDARD OPERATION PROCEDURES FOR COMPOUNDING PHARMACIES

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In accordance with the modern requirements to the quality assurance (QA) system for compounding preparations development and maintenance of standard operating procedures (SOPs) are obligatory. SOP is a documented set of instructions and step-by-step actions on how to execute a task. It is proved that the development and use of SOPs minimizes variation and promotes quality through consistent implementation of a process or procedure and it helps to ensure quality and minimize the number of errors that occur. There are a lot of advantages of SOPs implementation in compounding pharmacy: assistance in QA; ensuring of consistency; economy of work time; clear lines of accountability; better understanding of the processes; template for the training; additional information for audit.

SOPs in compounding pharmacy should be developed for all daily routine procedures that executed by pharmacists, such as: compounding and quality control of medicines, purchasing, handling of materials, dispensing, cleaning, care for facility and equipment etc. SOPs usually have a clear structure and consist of title, purpose, responsibilities, equipment, materials, procedures, information about the company, implementation, and signatures of authors, reviewer and head of department, information about SOP revisions. In fact, each SOP should contain the answers to the following questions:

- Who participates in the implementation of its requirements?
- What resources are necessary for its implementation?
- Where (In which department) should pharmacist perform SOP?
- When the procedure must be completed?

The most important parts of the SOPs are purpose (areas of work, it should not be over-complex), procedures (a description of the task) and responsibilities (who is responsible for carrying out of the procedure and who ensures that the staff can carry out a procedure). SOPs should be written by the specialist who perform that task and should be annually reviewed by another specialist who involved with the performance of the task and the head of QA department.

Development and implementation of easily readable and clearly specified instructions/SOPs are relevant for practices of compounding pharmacies of Ukraine.

DETERMINATION OF ACCURACY WHEN VALIDATING UV-SPECTROPHOTOMETRIC METHODS OF QUANTITATIVE DETERMINATION IN FORENSIC AND TOXICOLOGICAL ANALYSIS

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The purpose of this paper is to form the determination procedure and criteria for acceptability estimation of accuracy when carrying out the validation of UV-spectrophotometric methods of quantitative determination for forensic and toxicological analysis in the variant of the method of calibration curve.

The following criteria and procedure of acceptability estimation of accuracy for UV-spectrophotometric methods of analytes quantitative determination in biological fluids used in forensic and toxicological analysis have been offered:

- accuracy confirmation of the method is carried out in two directions – by model solutions (without matrix) and by matrix samples;
- verification of the method accuracy by model solutions is carried out by calculation of their concentrations using the respective linear dependence;
- estimation of the method accuracy by matrix samples is carried out at two levels – within-run and between-run – using calibration and model samples;
- determination of within-run accuracy is carried out in the way of calculating the concentrations of calibration samples for each run by individual values of absorbance using the linear dependence obtained for this run;
- determination of between-run accuracy is carried out in two stages – by calculation of the concentrations of model samples and mean concentrations of calibration samples using the linear dependence obtained by the mean values of parallel runs;
- the calculated values X_{calc} , % и X_{calc}^{model} , % are used for calculation of δ and δ^{model} respectively;
- the acceptability criteria have been offered for estimation of value δ^{model} within two approaches based on: 1) assumption of equality of the uncertainty of sample preparation procedure and the uncertainty of analyte quantitative determination in model solutions ($\delta^{model} \leq 4.52\%$); 2) assumption of insignificance of the uncertainty of analyte quantitative determination in model solutions ($\delta^{model} \leq 2,05\%$);
- it is proceeded from insignificance of systematic error for estimation of value δ ($\delta \leq 6.40\%$).

ANALYTICAL CHEMISTRY. THE SEARCH OF ENGLISH EDITIONS FROM DISCIPLINE OF 2000 – 2014 YEARS.

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In our time any higher institution of each country doesn't represent themselves without studying of foreign languages. There are many foreign languages are studied by professors and students in the National University of Pharmacy.

English takes a special place among other languages. It's international language, that the researchers are communicating in many countries of the world.

In 2002 the department of analytical chemistry of NUPh started teaching discipline of "Analytical chemistry" in English for students of second course. During this time the department prepared about 10 editions in English.

The purpose of our work was search of publications "Analytical chemistry" in English.

In 2000 textbook "Modern Analytical chemistry" was issued by D. Harvey. It was reissued in 2008. And in 2009 it was issued electronic versions of this fundamental edition.

The teaching staff of department of analytical chemistry of MSU translated from English to Russian textbook, and reprinted it in 2004. It was recognized as the best of foreign textbook - "Analytical chemistry. Problems and approaches"(ed. R. Kellner & others).

In 2007 publishing house "Springer-Verlage" was represent the textbook of K. Danzer "Analytical chemistry. Theoretical and Metrological Fundamentals". It has a basic knowledge about the analytical process, statistic, calibration, characteristics of analytical methods and others.

A lot of works of the discipline have been republished many times. For example in 2010 was issued 8th edition of the most widely used analytical chemistry textbook – D. Harris "Quantitative Chemical Analysis". In 2014 have been already issued the 9th edition of D. Skoog, D. West, F. Holler, S. Crouch "Fundamentals of Analytical Chemistry". For the last 5 years has increased number of publication dedicated for such modern methods of the analysis as Raman's and Mossbauer's Spectroscopy, Chemical Sensors, X-Ray Crystallography and others.

Conclusions. Search for new foreign publications, especially in English, is an important factor in improving the level of teaching of specialized disciplines in universities. Analytical chemistry is one of fundamental disciplines in the preparing of specialists in Pharmacy.

APPLICATION OF PEROXOMONOSULPFATE AS REAGENT FOR MICRODETERMINATION OF VITAMIN C. POTENTIOMETRIC DETERMINATION OF VITAMIN C IN THE PRESENCE OF SULPHITE

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In view of the widespread use of vitamin C (ascorbic acid) several methods were developed for the determination of ascorbic acid in pharmaceutical preparations. Titrimetric (Visual titration method) and potentiometric using iodine, sodium 2,6-dichlorophenolindophenolate (DCIP) and photometric methods commonly used to assay ascorbic acid. Unfortunately these methods are not applicable to many pharmaceutical preparations containing SO₂ and/or SO₃²⁻ ions.

Although the titrimetric methods are simple to use, difficulties are encountered even with commonly used titrants. Additional problems are met especially with colored samples or in the presence of reducing substances which can bleach the dye and make the analysis nonspecific. Such limitations have encouraged chemists to look for better alternative methods.

On a project on the determination of sulfur compounds it is found that potassium peroxomonosulphate reacts stoichiometrically and quantitatively with ascorbic acid and sulphite-ions but does not react with formaldehyde-bisulphite complex under identical conditions.

A proposed oxidimetric method involves the use of potassium peroxomonosulphate for ascorbic acid mixtures with sulphite-ions. This method requires the masking of SO₃²⁻ ions by formaldehyde-bisulphite complex, which neither reduces the titrant itself nor interferes with the reduction of the titrant by ascorbic acid.



A procedure was developed for determination of ascorbic acid in pharmaceutical preparation for injection 5% (Solutio Acidi ascorbinici 5% pro injectionibus). Resolutions of mixtures of vitamin C with sulphites has been successfully carried out by first potentiometric titrating the vitamin C content with potassium peroxomonosulphate direct or in the presence of potassium iodide. Summary of ascorbic acid and sulphite can be potentiometrically titrated with standard potassium peroxomonosulphate solution or in the presence of potassium iodide visually. The results obtained from commercial preparations were compared with those from an official method titration by iodate standard solution in the presence of iodide ions. No difference was found statistically. This method is really the same as titrating ascorbic acid directly with iodine solution. However, this method is more reliable as the potassium peroxomonosulphate solution is more stable than iodine as a primary standard. The method has comparable precision it is even gave less error percent, it is faster and easier to perform and could be used for routine determination.

THE CHEMICAL STUDY OF BUPLEURUM AUREUM FISCH EXTRACTS

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The questions of standardization and quality control of the medicinal plant raw material and phytodrugs produced in Ukraine continue to be of a vital importance because of the increase of the total amount of phytodrugs, introduction of new types of the medicinal plant raw material into medical practice, as well as medicines based on the previously known medicinal plants of the national flora. Therefore, it is necessary to standardize different types of the raw material and develop the analytical normative documentation, which allows to perform standardization of the medicinal plant raw material taking into account specific properties. Our attention has been drawn by *Bupleurum aureum Fisch* (hare's ear). It contains a lot of flavonoids and since ancient times it has been used for treating pathology of the hepatobiliary system in folk and traditional medicine.

The aim of our work is identification and quantitative determination of biologically active substances in aqueous and aqueous-alcoholic extracts of *Bupleurum aureum Fisch*.

Aqueous and aqueous-alcoholic extracts were prepared from the air-dry crushed overground part of *Bupleurum aureum Fisch* in the ratio of 1:20. To prepare aqueous-alcoholic extracts 30%, 50% and 70% alcohols were used.

The identification reactions conducted indicate the presence of phenols and tannins, substances with the restorative action, steroid compounds, flavonoids and alkaloids in the extracts studied.

The quantitative determination of flavonoids was performed after the reaction of interaction with the solution of aluminum chloride in the alcoholic medium in the presence of the solution of acetic acid by the absorption spectrophotometry method at the wavelength of 411 nm. The results obtained testify that the greatest amount of flavonoids calculated with reference to rutin and the raw material is in 70% alcoholic extract of *Bupleurum aureum Fisch* (2.72%).

After the reaction with phosphomolybdenum tungstic reagent the quantitative content of polyphenolic compounds was determined by the method of absorption spectrophotometry at the wavelength of 760 nm. Simultaneously the optical density of pyrogallol was determined. The content of polyphenolic compounds calculated with reference to pyrogallol (%) indicates that the greatest amount of polyphenolic compounds is in 50% alcoholic extract of *Bupleurum aureum Fisch* (0.97%).

Thus, a great amount of substances with the flavonoid structure in the extracts under study indicates the opportunities of using *Bupleurum aureum Fisch* in traditional medicine.

KINETIC SPECTROPHOTOMETRIC DETERMINATION OF ACETYLSALICYLIC ACID IN DOSAGE FORM "ACELYSIN-KMP"

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Research purpose. To develop a new kinetic spectrophotometric method of quantitative determination of acetylsalicylic acid (ASA) in the selected drug using the indicator reaction of catalytic *p*-phenetidine (*p*-Ph) oxidation by hydrogen peroxide.

Materials and methods. "ACELYSIN-KMP", Kyivmedpreparat – lysini acetylsalicylas is a mixture of DL-lysine acetylsalicylate and glycine with a ratio of 9:1. It has pharmacological properties of ASA, but unlike the latter is easily soluble in water. Our method is based on the system of two coupled reaction: ASA perhydrolysis (reaction with excess of H₂O₂ in a weak alkaline medium with peracetic acid (PA) formation) and following *p*-Ph oxidation by newly generate PA to azodue ($\lambda_{\max}=358\text{nm}$). Its increasing absorbance allows to determine ASA. Kinetic spectrophotometric initial rate method was used for computing.

Results. Optimal conditions for ASA perhydrolysis and thus for indicator reaction was determined, including order of mixing, reagent concentration and pH. In the pH range 8.2–8.5 rate of 4.4'-azoxyphenetol formation directly proportional to the concentration of ASA. It is shown experimentally that the perhydrolysis reaction is the limitative stage of *p*-Ph oxidation in *p*-Ph–H₂O₂–ASA system. Stated kinetic feature of the passing reactions and sufficiently high selectivity of indicator reaction of *p*-Ph oxidation by newly generate PA in the presence of relatively large excess of H₂O₂ is the basis of new developed procedure of quantitative assay of ASA in dosage form "ACELYSIN-KMP". Kinetic curve of 4.4'-azoxyphenetol accumulation in *p*-Ph–H₂O₂–ASA system under optimized reaction conditions was obtained. Sites from 5 to 10min has linear dependence and specify initial reaction rate (A vs. τ dependence tangent angle). The Beer's law was verified from the calibration curve by plotting a graph of concentration vs. increasing of absorbance from the series of ASA concentrations ranging from 22-180 $\mu\text{mol L}^{-1}$. Calibration graph for ASA was obtained: $\text{tg}\alpha=325.5c-0.0004$, ($r=0.9987$), where c is the concentration of analyte, mol L^{-1} , and $\text{tg}\alpha$ is the initial conditional reaction rate, min^{-1} . Standart deviation for the slope ($S_b=21.386$) and intercept ($S_a=0.0023$) was calculated. The limit of quantitation is 12 $\mu\text{mol L}^{-1}$. The relative standard deviation is less than 1.2%.

Conclusion. Thus, a highly selective and sensitive kinetic spectrophotometric method has been developed for the determination of ASA in dosage form "ACELYSIN-KMP". The proposed procedure proved to be selective, simple and rapid (single analysis time does not exceed 10 min) for the quantitative determination of ASA in the selected dosage form in the presence of it hydrolytic cleavage products and compresent components. For five determinations of 44 $\mu\text{mol L}^{-1}$, 88 $\mu\text{mol L}^{-1}$ and 130 $\mu\text{mol L}^{-1}$ ASA the reproducibility has a RSD of 1.18, 1.06 and 0.76% respectively. Hence the proposed method is more sensitive, simple and express in comparance with the well-known one. Dosage form "ACELYSIN-KMP" recovery is 98.95 \pm 1.32% of ASA.

AGE THE ANALYTICAL SCREENING OF GLIBENCLAMIDE FOR CHEMICAL-TOXICOLOGICAL ANALYSIS

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Diabetes mellitus type 2 treatment is based on the usage of oral antidiabetic drugs (ADD), which belong to different compound classes. They are: derivatives of biguanide (metformin), sulfonylureas (glibenclamide, gliclazide, glipizide, glimepiride), glinides (repaglinide), thiazolidinediones (pioglitazone) and others. Sulfonylureas derivatives are the leading group of antidiabetic drug market - about 30% in the CIS countries. Glibenclamide produces in many countries as mono-drugs (Betanaz, Glamid, Glibex, Daon, Euglucon, Maninil) in tablets of 1.5, 2, 3, 5 and 6 mg and in the combination with metformin (Glucovance, Glibomet, Duotrol, Glibofor). According to data of Food and Drug Administration (FDA) and patientsville.com web-site the number of reported cases of glibenclamide poisoning in 2008-2012 were 773. There were 68 reported about death, among them were 27 suicide. Lethal poisoning caused by overdosing and development of lactoacidosis, cardiovascular complications, etc. Lifelong application, growing number of patients with diabetes mellitus (260 million worldwide, 2 million in Ukraine), side effects, combined therapy with other ADD, OTC selling – are factors of toxicological hazards of uncontrolled usage of this drug. Thus, the development of the suitable methods for the chemical- toxicological analysis of glibenclamide is an actual problem.

The aim of our work was to define the conditions for glibenclamide analytical screening for the chemical-toxicological investigations.

Materials and methods: the reactions were made *in vitro* and on the chromatographic plates (1×1cm) with chloroform solutions of glibenclamide. Were used Liebermann`s, Bushard`s, Nessler`s, Dragendorff spray modified on Munier, Wagner`s, Froehde`s, Marqui`s, Erdmann`s, Mandelin`s reagents, 10% solution of FeCl₃, acids: H₂SO₄, HNO₃, irradiation by UV light ($\lambda=254$ nm).

Obtained results: it was revealed, that reagents form with glibenclamide different colors: Liebermann`s (red colour, limit of detection 1 mg), Nessler`s (brown-red → yellow-green → green, 3 mg) Dragendorff spray modified on Munje (brown, 0.5 mg), Bushard`s (orange, 0.5 mg), Wagner`s (red-brown, 0.5 mg), an aqueous solution of CuSO₄ (blue-purple → blue-green, 5 mg), irradiation of UV light (brown, 1 mg).

Conclusions: group and specific reagents for analytical screening of glibenclamide were defined.

DEVELOPMENT OF TECHNIQUE OF RELEASE TRAMADOL OUT OF BLOOD

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Tramadol (tramadol hydrochloride - (1RS,2RS)-2-[(dimethylamino)methyl]-1-(3-methoxyphenyl)-cyclohexanol hydrochloride, CAS- 36282 -47 -0), a synthetic centrally acting analgesic, is a racemic mixture of (+) and (-) isomers, that are involved in analgesic action in a different manner.

The aim of this work is to improve the chemical and toxicological analysis of tramadol isolation out of blood using trichloroacetic acid.

Up to 10 ml of blood 1 ml of an aqueous solution of tramadol (which contained 100, 200, 500 and 1000 mg of drug) was added, stirred with a glass stick and left a day at the room temperature. "Blank" experiment was carried out parallelly. In a day 5 ml of 10 % aqueous trichloroacetic acid was added into the model mixtures. Then the mixture was stirred and left for 2 hours. After that the mixture was transferred to a glass centrifuge and centrifuged for 10 minutes (3000-5000 r / min). The centrifugates were combined, tested for pH (2 - 3) and extracted three times with new 5 ml portions of diethyl ether. The essential layers were separated. The aqueous layer was basified with 50% sodium hydroxide solution to pH 10 - 11 and extracted three times with new 10 ml portions of chloroform. The combined chloroform extracts containing 0.5 g of anhydrous sodium sulfate were filtered through the filter paper.

The obtained chloroform extract was used for detection of tramadol by thin layer chromatography (TLC). Quantitative determination of the preparation was performed by specially developed UV spectrophotometric, photometric extraction and ionometry methods. The results are shown in the table. The table shows that the method can release 35-40% of tramadol out of blood.

Table. Results tramadol isolation from blood using trichloroacetic acid

№	Introduced drug, mg	Highlight drug, mg	Highlight mg drug ,%	Metrological features
1	1000.00	400.00	40.00	$\bar{X} = 37.80$ $S = 1.68$ $S_{\bar{X}} = 0.75$ $\Delta\bar{X} = \pm 2.09$ $\varepsilon = \pm 5.52$
2	500.00	185.00	37.00	
3	200.00	71.00	35.50	
4	100.00	38.50	38.50	

**APPLICATION OF PEROXY ACID AS REAGENT FOR
MICRODETERMINATION OF VITAMIN C. COMPERISION BETWEEN
POTENTIOMETRY AND TITRIMETRY METHODS FOR
DETERMINATION OF ASCORBIC ACID IN THE PRESENCE TIOLS IN
PHARMACEUTICAL PREPARATIONS**

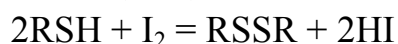
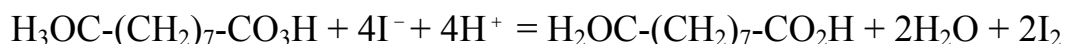
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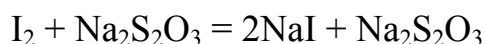
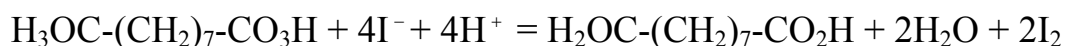
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In view of the widespread use of vitamin C (ascorbic acid) several methods were developed for the determination of ascorbic acid in pharmaceutical preparations. Titrimetric (iodimetric and with 2,6-dichlorophenolindophenolate (DCIP)) and photometric methods commonly used to assay ascorbic acid. Unfortunately these methods are not applicability for ascorbic acid mixtures with thiols. Famous method requires the masking of thiol by cyanoethylating it with acrylonitrile. The cyanoethylated products of thiols do not hamper the reaction and that ascorbic acid could be titrated with chloramine-T using, DCIP as indicator.

Such limitations have encouraged chemist to look for better alternative methods. On a project on the determination of sulfur compounds it is found that potassium diperoxyazelaic acid reacts stoichiometrically and quantitatively with ascorbic acid but does not react at with strong reducing agents like thiol under identical conditions. Resolutions of mixtures of vitamin C with thiols has been successfully carried out by first potentiometric titrating the vitamin C content with diperoxyazelaic acid. Upon dilution of the contents, thiols can be titrated with standard diperoxyazelaic acid solution in the presence of potassium iodide. Thiols are quantitatively oxidized to their corresponding disulfides with diperoxyazelaic acid in the presence of potassium iodide.



This method is really the same as titrating ascorbic acid directly with iodine solution (see Vitamin C method using iodine). However, this method is more reliable as the diperoxyazelaic acid solution is more stable than iodine as a primary standard.



The method has comparable precision it is even gave less error percent. Peroxymetric assay also is faster and easier to perform and could be used for routine determination.

REACTIVITY OF N-[(2-OXOINDOLIN-3-YLIDENE)-2-OXIACETYL]AMINOACIDS ETHYL ESTERS

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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.

The aim of this work was to study the reactivity of ethyl 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.

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 (ЭСИ 43-074) indicator electrode. The reference electrode was a silver chloride electrode (ЭПБ-1). The experiment was carried out at 25°C 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 ethyl 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 ethyl 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.

QUANTITATIVE DETERMINATION OF POTASSIUM HYDROGENPEROXOMONOSULFATE BY VOLTAMMETRY IN THE PRESENCE OF SODIUM DODECYLBENZENESULFONATE

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Many disinfectants consist of surface-active substances (SAS), which provide contact with pathogens oxidant, react with membrane lipids and proteins causing denaturation of the cell membranes. It is known that disinfectant Ecocide S except active substance potassium hydrogenperoxomonosulfate (PMS) contains surfactant sodium dodecylbenzenesulfonate (SDBS).

The aim of the research was to develop a procedure of quantitative determination of PMS in the presence of SDBS by cathodic voltammetry by the method of calibration graph. Electrochemical measurements were carried out in the analyzer ABC-1.1 (Volta, St. Petersburg) with a three-electrode scheme by alternating current mode with square wave modulation in the potential range +1.0...-1.2V, $W=1000\text{rpm}$, amplitude 40mV, $\nu=65\text{Hz}$. Carbosil electrode (CE) was used as a working and an auxiliary electrode, and Ag,AgCl/KCl(sat) electrode type EVL-1M4 as a reference electrode on the background of $0.2\text{ mol L}^{-1}\text{ KHSO}_4$ ($\text{pH}\approx 2$). It was experimentally proved that SDBS leads to an increase of the current peak and the peak potential shifts to more electropositive side (+0.25 \rightarrow +0.3V). The current increase, probably due to relief desorption product recovery from the electrode surface, and the acceleration of electron transfer in the course of electrochemical reactions. The influence of the present SDBS was examined. The current peak increases with the concentration of surfactant up to $1.2\times 10^{-3}\text{ mol L}^{-1}$ and then stays almost constant with the increase in concentration of SDBS above $3.0\times 10^{-3}\text{ mol L}^{-1}$. A method calibration graph for quantitative determination of PMS in the presence of SDBS in disinfectant Ecocid S have been investigated. The linear dependence was observed in the PMS concentration range $(1.8-9.0)\times 10^{-5}\text{ mol L}^{-1}$, the calibration curve equation was $I_p = (4.3\pm 1,1)\times 10^4 c$ ($r=0.998$); RSD were 0.025...0.021 and $\delta = -0.64\text{...}+0.16\%$ respectively ($n=5; P=0,95\%$), $\text{LOD}=6.50\times 10^{-6}\text{ mol L}^{-1}$, $\text{LOQ}= 2.17\times 10^{-5}\text{ mol L}^{-1}$.

Thus, new voltammetric method of PMS determination in the presence of SDBS using CE (glassy carbon) electrode as indicating electrode was developed and the possibility of its quantitative determination was shown.

ZIZIPHORA BUNGEANA AS A VALUABLE SOURCE OF BIOLOGICALLY ACTIVE SUBSTANCES FOR USE IN PHARMACY AND MEDICINE

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The development of the pharmaceutical industry of the Republic of Kazakhstan due to the rational use of natural resources, including plant material is a priority. Extracting of biologically active substances from medicinal plants and the creation of new drugs based on it are relevant to pharmacy and medicine in general.

Under the State program of development of pharmaceutical and medical industry of the Republic of Kazakhstan planned reduction of depending on imports of medicines through better use of its own production facilities, raw materials, and creating new drugs from medicinal plants is an important focus of research in KazNMU named after Asfedniyarov S.D.

The aim of this work is the study of plant materials of *Ziziphora bungeana* for its standardization.

Materials and methods:

1. Aboveground part of plants: twigs, leaves, stems of *Ziziphora bungeana*

2. Pharmaceutical analysis methods of vegetable raw materials:

macroscopic analysis of morphological - definition (external) features raw plants *Ziziphora bungeana* visually.

microscopic analysis, identification of anatomic diagnostic signs with a microscope plants *Ziziphora bungeana*.

phytochemical analysis, conducting qualitative reactions to the main biologically active substances and their quantification.

Expected results: the standardization of herbs *Ziziphora bungeana* in compliance with the State Pharmacopoeia of the Republic of Kazakhstan .

Conclusion: Within pharmaceutical study the following point were examined: impurities (Article 2.8.2), stomata and stomatal index (Article 2.8.3), the content of essential oils (Article 2.8.10). The obtained data will be included in the draft monograph for developing quality certification.

VALIDATION OF UV-SPECTROPHOTOMETRIC METHODS OF QUANTITATIVE DETERMINATION IN FORENSIC AND TOXICOLOGICAL ANALYSIS: RECOVERY

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The validation parameter «recovery» is not used practically in pharmaceutical analysis. Such situation is explainable – the procedure of sample preparation in pharmaceutical analysis does not contain the stages, which require the extraction carrying out (result in the substance considerable losses), which efficiency is characterized by the parameter «recovery».

The purpose of this paper is to form the approaches to the procedure of recovery determination when carrying out the validation of UV-spectrophotometric methods of quantitative determination for forensic and toxicological analysis.

For recovery determination of the methods we suggest to carry out the analysis in the points of 25%, 50%, 100% and 175% (in the normalized coordinates). In this way we provide fulfilment of international requirements (three concentrations levels – low, medium and high) and control additionally the most critical part of the method analytical range – near LLOQ, where differences in recovery values are often observed.

For acceptability confirmation of the recovery value reproducibility we suggest to check fulfilment of two criteria simultaneously:

- the slope for linear dependence $R = f(c)$ should statistically insignificantly differ from zero on conditions the significance of absolute term (the linear dependence $R = bc + a$ goes over $R = a$ in ideal situation), i. e. it is necessary to prove that the value of b is less, and the value of a is more than the confidence interval of its uncertainty:

$$b \leq \Delta_b; \quad a \geq \Delta_a;$$

- the relative confidence interval $\Delta_{R,r}, \%$ should not exceed the extreme uncertainty of analysis Δ_{As} by the value:

$$\Delta_{R,r}, \% \leq \max \Delta_{As}.$$

Thus, the theoretical approaches to determination of recovery when carrying out the validation of UV-spectrophotometric methods of quantitative determination for forensic and toxicological analysis have been formulated; the acceptability criteria for the validation parameter have been suggested and ground.

VERIFICATION OF THE SPECTROPHOTOMETRIC QUANTITATIVE DETERMINATION METHOD OF RIBOFLAVIN IN SUBSTANCE

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Riboflavin (Vitamin B2) takes an important part in the process of carbohydrate, protein and fat metabolism, also plays an important role in maintaining normal visual function of the eye and in the synthesis of hemoglobin. The chemical structure of riboflavin (6,7-dimethyl-9-(D-1-rybityl)-izoalloksazyn) allows to quantitatively determine the substance by the following methods: spectrophotometry, photocalorimetry, fluorometry, alkalimetry.

The literature review revealed the fact that today new methods of quality control for riboflavin methods have been developing: HPLC, electrophoretic extraction, voltammetric. In pharmacopoeial analysis for quantitative determination of riboflavin in substance European Pharmacopoeia, The State Pharmacopoeia of Ukraine (SPhU), the British Pharmacopoeia proposes absorption spectrophotometry method according to the specific absorbance. According to the SPhU, quantitative determination of riboflavin in substance is produced by the spectrophotometry method according to the specific absorbance in a buffer solution at a wavelength of 444 nm. Riboflavin content is calculated using the specific absorption, which is equal to 328. The aim of our work is verification of the spectrophotometric quantitative determination method of riboflavin by specific absorbance.

Characteristics and criteria of acceptability of quantitative determination method of riboflavin such as nominal concentration of the substance in solution by the method, nominal absorbance and requirements for its minimum value, maximum uncertainty of analysis techniques have been theoretically calculated. The linearity parameter was studied at 9 points. The linear dependence graph was constructed in normalized coordinates. Values of b , s_b , a , s_a , RSD_0 and r comply with the parameters of the linear dependence. In the study of the accuracy of parameter systematic error made $\delta=0,72\%$, which meets $\delta \leq 1,00\%$. The study of convergence of the relative confidence interval $\Delta_{As}=0,83\%$ does not exceed the critical value for of convergence results $\Delta_{As}=0,96\%$.

Validational characteristics of the methods do not exceed the critical value of the error and are characterized by qualitative analytical indicators. This method can be correctly reproduced in the laboratory.

COMPARATIVE STUDY OF THE MECHANISMS OF INTERACTION OF NIMESULIDE, MELOXICAM AND IBUPROFEN WITH β -CYCLODEXTRIN SEMI-EMPIRICAL METHOD OF QUANTUM CHEMISTRY

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Introduction. A large number of people around the world taking NSAIDs every day, most of these patients are aged over 60. Among this group of drugs widely used nimesulide, meloxicam - selective COX-2 inhibitors and ibuprofen - nonselective inhibitor of COX-2. Medicines of group of NSAIDs have a number of side effects which, together with poor solubility (class 2 in biopharmaceutical classification system) limit their use. Method of complexation with high-molecular compounds improve solubility and reduce side effects. Given that the problem relates to the solubility of most drugs of NSAIDs important in pharmacy and medicine is the study of common and distinctive features in their interaction with macromolecular compounds that can be used to create new drugs which include this active pharmaceutical ingredients.

Purpose. The aim of study was to conduct a comparative study using semi-empirical quantum chemical method PM3 interaction mechanisms of nimesulide, meloxicam and ibuprofen with β -cyclodextrin (β -CD) and identify similar and different aspects of their behavior in the formation of complexes "guest-host".

Results. In the formation of 1:1 complexes binding energy decreased by 10.21 kcal/mol, 32.04 kcal/mol and 24.62 kcal/mol respectively for complexes of nimesulide, ibuprofen and meloxicam, due to the spatial structure of meloxicam, a molecule which is linear in comparison with molecules ibuprofen, nimesulide and the formation of stronger hydrogen bonds. The energy of intermolecular interactions in 1:2 complexes of ibuprofen - β -CD is -38.32 kcal/mol, in complexes of nimesulide and meloxicam -18.42 kcal/mol and -34.08 kcal/mol, respectively, as a set of ibuprofen - β -CD is more stable. Ibuprofen has only one polar group-COOH as oral β -CD interact better with it than with the molecules of nimesulide and meloxicam in which there are group-SO₂, -NO₂ (nimesulide) and -SO₂, -C = O, -OH (meloxicam).

Conclusion. As follows in complexes with the ratio of 1:1 molecular interaction strength NSAIDs and β -CD and stability of complexes increases in the number of nimesulide < ibuprofen < meloxicam, with the ratio of 1:2 in the number of nimesulide < meloxicam < ibuprofen. Key indicators for evaluation the interaction of β -CD for NSAIDs is linear spatial structure for placement in the oral β -CD, the presence of functional groups capable of forming hydrogen bonds with the secondary hydroxyl groups β -CD and severity of the hydrophobic properties of the molecule NSAIDs.

DETECTION AND QUANTITATIVE DETERMINATION OF ANTIDEPRESSANT CLOMIPRAMINE IN BIOLOGICAL FLUIDS

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Antidepressant poisonings occupy a leading position among the psychotropic drug intoxications in the world. Clomipramine (3-chloro-10,11-dihydro-*N,N*-dimethyl-5*H*-dibenz[*b,f*]azepine-5-propanamine) is a tricyclic antidepressant which is widely used in the modern treatment of the depression disorders. However, the medicine is associated with neurological side effects including worsening depression, other mood symptoms, suicidal thoughts or attempts. Clomipramine was the primary cause of acute and lethal poisonings. The postmortem concentrations were reported: blood 0.21–4.9 mg/L, urine 0.35–25 mg/L. The aim of this study was to develop methods of clomipramine isolation from blood and urine with liquid-liquid procedure followed by the analysis of the extracts obtained with help of colour tests, TLC, UV-spectroscopy, extraction-spectrophotometric methods. Clomipramine was extracted from the biological fluids by chloroform from alkaline medium at pH 11. Concomitant admixtures were separated by extraction with diethyl ether from acidic medium at pH 1–2. When isolating clomipramine from blood previously the protein admixtures were separated by adding 10% trichloroacetic acid solution followed by centrifugation. Reaction with concentrated sulphuric acid, Marqui's test, Frede's test, Erdman's test, Mandelin's test, Liebermann's test were positive for clomipramine. TLC identification was performed using mobile phase: chloroform-dioxane-acetone-25 % ammonium hydroxide solution (47.5:45:5:2.5), Dragendorff spray was used as location reagent, $R_f=0.70\pm 0.02$, the sensitivity is 1 μg of the drug in the sample extract. Identification of clomipramine isolated from the biological fluids was performed with the help of UV-spectroscopy after clean-up step by TLC method. The UV-spectrum of the methanol eluate containing clomipramine was identical to the spectrum of the standard methanol solution of the drug. The wavelength of the principal peak was 251 ± 2 nm. Quantitative content of the drug in the extracts was determined by extraction-photometric method by the reaction with methyl orange, an acidic azodye (linearity was in the range of 5–90 μg in the sample and it was represented by the following regression equation: $Y=0.0137X+0.09$). Recovery (precision, %RSD) of the methods developed were 79% (4%) for urine and 34 (4%) for blood. The results of validation have proven that the methods developed are accurate, precise, sensitive and linear in the range of the expected content of clomipramine in the biological fluids in fatal cases.

QUANTITATIVE ESTIMATION OF NEW BIOLOGICALLY ACTIVE SUBSTANCES OF DERIVATED 4,5-DIMETHOXY-N-PHENYL- ANTHRANILIC ACIDS

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The method for quantitative estimation of 4,5-dimethoxy-N-phenylanthranilic acids was defined by the two-phase titration. Principle of the method consists in direct titration by alkali solution of two-phase system which is compounded of organic phase that encloses substances being analyzed, and of water phase that encloses indicator. The endpoint size of titration is defined according to decolorization of the water layer. The method is characterized by a high accuracy, simplicity, expressiveness. Relative error in the method does not exceed 0.5%.

The aim of research is developing of express method for quantitative estimation of 4,5-dimethoxy-N-phenylanthranilic acids by the method of two-phase titration in a system octanol – water.

Equipment and reagents for quantitative estimation of mefenamic, tolfenamic and 4,5-dimethoxy-N-phenylanthranilic acids by the method of two-phase titration: microburette of class A (capacity – 5ml); glass-stoppered measuring flask (capacity – 100ml); n-octanol; 0.1% alcohol solution of thymolphthalein; sodium hydroxide (0.1M solution). All reagents and solutions were prepared according to demands of SPhU.

Potentiometric titration was conducted in mixed solvent «dioxane - water» (60 volume % dioxane) in ionomer I-160 with application of indicating glass electrode (ESP 43-07) and silver chloride (EVL - 1M4) reference electrode.

The quantitative calculation of the content of 4,5-dimethoxy-2-(phenylamino)benzoic, mefenamic and tolfenamic acids, %, is being performed by the formula:

$$\% = \frac{V \times K \times T \times 100}{m_s}$$

where V – volume of 0.1M solution of the sodium hydroxide, used for titration, ml;

K – correction coefficient to molarity of the 0.1M sodium hydroxide solution;

T – titre of the 0.1M sodium hydroxide solution according to the experimental compound, $g \times ml^{-1}$;

m_s – mass of the experimental compound batch, g.

We have developed the express method for quantitative estimation of 4,5-

dimethoxy-N-phenylanthranilic acids. The method of two-phase titration with the presence of indicator that is not being extracted by organic solvents was taking as a basis. Principle of the method consists in direct titration by a standard water solution of sodium hydroxide of two-phase system which is compounded of the organic phase that encloses salvation of the experimental compound, and the water phase that encloses indicator. There is the extraction disbalance within the titration by sodium hydroxide solution and the sodium salt of 4,5-dimethoxy-N-phenylanthranilic acid rises into water phase. The endpoint size of titration is defined according to decolorization of the water layer.

The optimal conditions for two-phase titration of non-described in literature 4,5-dimethoxy-N-phenylanthranilic acids were determined. N-octanol is being used as an organic solvent which solves well the experimental compounds. The choice of N-octanol as a solvent is caused both by a good solvability, and a usage of the octanol-water mixture as a model one for evaluation of lipophilic activity of biologically active substances. The experimentally founded correlation of volume in the water and organic phases equal 2:1. As indicators 0.1% alcoholic solution of phenolphthalein, 0.04% alcoholic solution of m-cresol purple and 0.1% alcoholic solution of thymolphthalein can be used. According to data it is evident that the alcoholic solution of phenolphthalein is the most acceptable indicator because the ≈ 0.1 g batch of the experimental substances is enough while this solution is being used.

The obtained results of quantitative estimation by the two-phase titration are characterized by the accuracy and representativity. The relative uncertainty of the average result by this method does not exceed 0.5%. The method developed is expressive, easy to use, and reliable. These characteristics is differed this method advantageously from the method of potentiometric titration.

Nature of substitutes and their location in anthranilic fragments of 4,5-dimethoxy-N-phenylanthranilic acids do not affect on the quantitative estimation results.

CONCLUSION

1. The express method for quantitative estimation of 4,5-dimethoxy-N-phenylanthranilic acids by the two-phase titration in a system octanol-water has been defined.

2. The optimal conditions for two-phase titration in a system octanol-water have been determined, the indicator has been chosen, which application let to use less amount of the experimental substance. The method developed is characterized by simplicity, expressiveness, reliability and a high enough accuracy.

VALIDATION OF UV-SPECTROPHOTOMETRIC METHOD OF DOXYLAMINE QUANTITATIVE DETERMINATION IN BLOOD: PRECISION

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The purpose of this paper is to test the approaches to the determination procedure and acceptability estimation of precision when validating UV-spectrophotometric methods of quantitative determination for forensic and toxicological analysis, which have been offered previously, by the example of UV-spectrophotometric method of doxylamine quantitative determination in blood.

Precision of UV-spectrophotometric method of doxylamine quantitative determination in blood has been estimated according to the following order:

- precision confirmation of the method is carried out in two directions – by model solutions (without matrix) and by matrix samples;
- verification of the method precision by model solutions is carried out by calculation of their concentrations using the respective linear dependence;
- estimation of the method precision by matrix samples is carried out at two levels – within-run and between-run – using calibration and model samples;
- determination of within-run precision is carried out in the way of calculating the concentrations of calibration samples for each run by individual values of absorbance using the linear dependence obtained for this run;
- determination of between-run precision is carried out in three stages – by calculation of the difference between the mean «found/spiked» values in different days, and also by calculation of the concentrations of model samples and mean concentrations of calibration samples using the linear dependence obtained by the mean values of parallel runs.

It is noted that the methods with preliminary TLC-purification have better intermediate precision and worse repeatability, than the methods without TLC-purification, that is explained by carrying out the additional stages of sample preparation, which worsen naturally within-run precision (estimates, in the first place, random error associated with sample preparation), but level the influence of changing the origin source of matrix on the results of analysis due to sample purification of high quality (improve between-run precision).

Thus, the offered approaches to precision determination have been tested by the example of UV-spectrophotometric method of doxylamine quantitative determination in blood. The results have shown the adequacy of formed approaches.

STUDY OF THE INFLUENCE ON THE BIOAVAILABILITY OF ANTIBACTERIALS IN THE JOINT PRESENCE WITH ANTACIDS.

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Nowadays the fluoroquinolones are among the most popular antibacterial agents. Pharmacodynamics of fluoroquinolones depends on the peak of serum concentration and the concentration in the tissues, that's why the drugs interactions which can influence for bioavailability of the drug are so important. It has been known that significant changes in the pharmacokinetics of fluoroquinolones observed in the joint use of preparations that containing polyvalent cations. It has been reported at the national and the foreign literature that significant reduction of the bioavailability of fluoroquinolones depends on the formation of insoluble metal complexes. The second Generation of fluoroquinolone, namely ciprofloxacin, is widely used in clinical practice. The presence 4-keto and 3-carboxyl groups in the structure of ciprofloxacin promote the formation of the chelate complexes with metals. For this reason the joint use of ciprofloxacin with antacids is not recommended.

The main aim of our work was study of interaction between ciprofloxacin hydrochloride with salts of calcium, magnesium and aluminum by UV-spectrophotometry. This study was the first stage for proving of complexes formation.

The research was performed by measuring the absorbance of obtained complexes of ciprofloxacin hydrochloride and metal salts in the ratio of 1:2 (CaCl_2), 1:2 (MgSO_4), 1:3 (AlCl_3). As a solvent 0.1 M solution of hydrochloric acid, purified water and purified water with addition of few drops of phenolphthalein and 0.1 M solution of sodium hydroxide until appearance of slightly pink color have been used. Conditions of the gastrointestinal tract were modulated by different selected solvents.

As a result of our work changes of absorbance spectrum of ciprofloxacin hydrochloride with metal salts compared to the solution of pure substance were detected. The absorption maximum of the investigated complex compounds remained unchanged, but there was a significant change of the absorbance intensity of the studied complexes.

In conclusion, the analysis of obtained data has been shown, that the metal complexes, which may affect for the bioavailability of ciprofloxacin hydrochloride, have been formed. These changes may also reduce the pharmacological activity of the antibiotic. So, consequently further research is required.

ELECTROCHEMICAL ANALYSIS KANAMYCIN A SULFATE IN SMALL VOLUMES

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In pharmaceutical practice medicinal dosage forms with a small capital volume to which usual techniques of the ionometric analysis are applied seldom find application. In this regard was of interest to develop a technique of the ionometric analysis kanamycin a sulfate in small volumes with use of usual macroelectrodes and comparison electrodes. For measurements used developed by us earlier kanamycin a sulfate sensitive ion-selective electrode with the plasticized membrane containing as electrode activity substance an ionic associate kanamycin a sulfate with phosphomolybdic acid. As an electrode of comparison was used a silver-chloride electrode of the EVL-1M3 type. Measurement of EMF carried out on I-130 ionomer. For measurements used the device developed by us earlier which is represented by the holder executed in the form of a plate of glass on which two are put in parallel located capillary the channel which are microcameras for analyzed solution. Both of these channels are connected perpendicularly by the salt bridge. Length of vertical microchannels corresponded to diameter of a membrane of an electrode. The horizontal microchannel was symmetrized to the vertical. In points of intersection put on 1 drop of analyzed solution. The internal piece of the horizontal microchannel was filled with analyzed solution and thus electrolytic contact in a chain was provided. For measurement of EMF of a chain to one of points of intersection of microchannels was connected to the ISE membrane, and to another – the electrolytic bridge of an electrode of comparison.

As a result of researches it was established that the ISE function at measurement in 1 drop by means of the developed device remains in the same limits, as at measurements in solution macrovolume. There is invariable her steepness. Use of the device for the ionometrical analysis in 1 drop allows reduce a consumption of analyzed solution.

Therefore this technique can be applied to the analysis kanamycin a sulfate in injection solutions and drops.

DEVELOPMENT AND VALIDATION OF UV-SPECTROPHOTOMETRIC METHOD OF METRONIDAZOLE QUANTITATIVE DETERMINATION FOR PURPOSES OF FORENSIC AND TOXICOLOGICAL ANALYSIS

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Metronidazole is attributed to the group of antiprotozoal medicines and widely used for treatment of infectious diseases, at the same time it is possessed of quite a number of side effects showed by classic symptoms of acute intoxication, especially when interacting with other medicines and alcohol. The concentrations of metronidazole in blood and urine are such high that allow to use UV-spectrophotometry for its quantitative determination. All mentioned above makes actual developing UV-spectrophotometric procedures of metronidazole quantitative determination with the purpose of their further application in chemical and toxicological analysis.

The purpose of this paper is to develop UV-spectrophotometric procedure of metronidazole quantitative determination and validation of the developed procedure using the offered before approaches to the determination procedure and acceptability estimation of linearity, accuracy and repeatability of UV-spectrophotometric methods of analytes quantitative determination in biological liquids applied in forensic and toxicological analysis.

The metronidazole chemical structure supposes its existence in different forms when changing medium pH. The presence of such transformations is confirmed by UV-spectra of metronidazole obtained in different solvents with different values of pH – 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).

The development of procedure of metronidazole quantitative determination was carried out using ethanol as a solvent and wavelength of 310 nm respectively by the following scheme: application of the normalized coordinates (normalization by the reference solution); the application ranges are 25 – 125%, 25 – 150%, 25 – 175%; the number of concentration levels is $g = 5, 6$ or 7 (depending on the chosen application range) in constant increments of 25%.

The metronidazole concentration in the model solution corresponding to the point of 100% in the normalized coordinates was chosen in the way that the absorbance of this solution was 0,4 – 0,6.

Validation of the developed procedure has been carried out by parameters «linearity», «accuracy» and «repeatability» and its acceptability for further application in forensic toxicology has been shown.

SECTION № 4

TECHNOLOGY PHARMACEUTICAL PRODUCTS

PROSPECTS OF APPLICATION PHYTOMEDICINES AT THE PHARMACEUTICAL MARKET OF UKRAINE

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For many years medical and pharmacy specialists and the population are greatly interested in using medicinal plants and medicines obtained on their basis for treating different diseases. Nowadays medicines based on biologically active substances of the plant origin (phytomedicines) comprise 50% of the total nomenclature of medicines, and up to 90 % of these medicines are used for treating cardiovascular, gastrointestinal, nervous diseases.

About 750 plants are described and used in folk medicine, but only 50-60 plants are used in the Ukrainian traditional medicine, while, for example in China, more than 1000 plants are applied, and the USA pharmaceutical firms have in their drugstores more than 500 extracts and compositions from plants.

Approximately 90 medicines of the plant origin in the form of tinctures, oils, syrups, extracts, medicines for injections, solid and soft medicinal forms are produced by the domestic industry. The volume of realization of herbal medicines manufactured abroad is in 2-3 times higher than from home manufacturers at the pharmaceutical market of Ukraine. Therefore, development of this direction by introduction of new phytogenic medicines into medical practice and expansion of assortment of phytomedicines produced not only by pharmaceutical enterprises, but at the chemist's as well is quite perspective. One of the simplest forms of application of medicinal plants are water extractions, among their advantages it should be noted the simplicity of preparation, the complex action and a high bioavailability of biologically active substances containing in the plant raw material, besides, they have a milder effect on the organism. Water extractions (infusions and decoctions) have a wide application in medical practice as mixtures, rinses, lotions, washes, baths and inhalations. At present the classical technology of water extracts is modified due to the application of modern extraction methods, development of new equipment, application of extracts-concentrates. However, the work in this direction is being conducted both using the latest achievements and taking into account the existed experimental data obtained as a result of studying physical and chemical, biological and pharmacological properties of some plants.

Thus, one of the directions of developing phytotherapy is determination of scientific approaches of the rational combination of medicinal plants in order to form the optimal formulation, as well as the search of rational technologies of water extractions with the purpose of achieving the necessary therapeutic effect.

DEVELOPMENT PROSPECTS FOR GEL TREATMENT OF ACNE

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Modern medicine pharmacy poses serious challenges in the creation of new domestic preparations for the topical treatment of acne. Range of medicines for the treatment of this disease is quite wide. However, the practice of medicine feels the need for drugs that can effectively implement differentiated topical treatment of acne in the initial stages. The composition of gels for acne treatment includes active substances belonging to different pharmacological groups.

However, the vast majority - synthetic drugs that exhibit certain drawbacks that limit their use. Given the shortcomings of antibiotic acne topical is conducting the search and creation of a new drug on the basis of the substance of natural origin, developing adequate antimicrobial and anti-inflammatory effects with minimal adverse events. In recent years all over the world there has been increased interest in practical medicine to drugs derived from natural raw materials, in particular - from propolis. One of the biologically active substance is propolis, propolis phenolic hydrophobic drug (FGPP).

Given the high antimicrobial, anti-inflammatory, reparative and other pharmacological features FGPP, the creation of a new drug based on it that meets all modern requirements for drugs for topical treatment of acne is important. The aim of this work is to develop science-based composition, technology and methods of analysis of the gel with a phenolic propolis hydrophobic drug for the treatment of acne first stage, has wound-healing, anti-microbial and anti-inflammatory activity. To achieve this goal, the following tasks.

Explore and summarize current literature data on the treatment of acne and the creation of drugs to treat acne.

Theoretically and experimentally justify the composition and gel technology FGPP having reparative, wound healing and antimicrobial activity.

To study the rheological and physico-chemical properties of the gel.

Conduct research to identify key quality indicators and the development of methods for the analysis of the gel justify kind of packing, storage conditions and shelf-life of the drug.

To carry out microbiological and pharmacological studies for the establishment of a gel and the specific activity of the drug harmless with developed FGPP in gel form.

To carry out a comprehensive study developed biopharmaceutical gel (in vitro, in vivo).

Based on the results to develop analytical documentation and design of production schedules on a gel. At this stage comprehensively study the properties of hydrophilic gel for the treatment of acne, the drug developed analysis techniques, defined terms and conditions of storage.

STRUCTURAL AND MECHANICAL STUDIES OF DENTAL PHYTOGEL

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Medicinal products (drugs) used in the treatment of periodontitis must meet such requirements as antibacterial and anti-inflammatory action and so on. Such requirements can be met, in some cases, in herbal drugs. Proceeding from the relevance of the subject we have developed composition and technology of a new phytogel for dentistry with CO₂ extracts of chamomile and sage. The results of our study have revealed that the optimal basis is a gel containing 1% mixture of xanthan (0.8%) and guar (0.2%) gums. Experimental studies have shown that to the composition of the basis for improving rheological parameters of the gel should be introduced hydrophilic, non-aqueous solvents (HNS) including glycerin, propylene glycol (PG), ethanol. It was established that the addition of glycerol, PG in the amount of 10% though improving the rheological properties of model samples but gives rheograms not fitting in the limits of rheological optimum. Rheogram of model sample containing 5% ethanol provides the basis with optimal physical and mechanical properties. Due to that fact to the composition of the gel may be introduced combination of HNS, we have conducted research to study rheological parameters of model sample containing PG (2.5-10%) with ethanol (5%) and glycerol (2.5-10%) with ethanol 5%. It has been established that optimum is combination of glycerol with ethanol in an amount of 10% and 5% respectively. In order to establish the optimum HNS ratio considering osmotic activity, physical and mechanical properties, we have justified expediency of introduction into the basics of Carbopol (1%) with triethanolamine (0.65%). The additional introduction of the polymer will help to reduce HNS quantity. Thus, rheological studies have established feasibility of introduction this combination that has led to the two-times reduction of HNS.

DEVELOPMENT EXTEMPORANEOUS COSMETIC TOOLS BASED ON BEE PRODUCTS FOR ACNE TREATMENT

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Acne (acne) – an inflammatory disease of the hair follicles and sebaceous glands of the skin. Typically, the affected areas with a high content of sebaceous glands: the face, chest, back. Acne - a chronic disease of the sebaceous glands. Their ducts are sealed and formed inflammation.

Currently in Ukraine lacks extemporaneous cosmetics, skin to get rid of this disease. A detailed study of the problem and taking into account individual patient characteristics are the main principles for the preparation of cosmetic products "extempore".

Search active components was sent to substances that have anti-inflammatory, antibacterial and wound-healing effect, tightens pores and have a drying effect. To achieve these results, was one of the most perspective used components in cosmetology - propolis with unique clinically proven healing properties: antiseptic, deodorizing, analgesic, antioxidant, stimulating metabolism and protective reactions of the organism, as well as wound healing.

Analysis showed cosmetic forms, the acne that for getting the most effective use of the cosmetic form a gel. As a result, the hydrophobic gel was developed, wherein as active ingredients of propolis is used, and in particular FGPP. The analysis was conducted based on the SDA 24-37-103-2004 "Cosmetic gels. ZTU" and developed methods for quantitative analysis and good for active substances.

Given the examination of the regulatory documentation, manufacturing technology and the analysis was developed technological instruction for the extemporaneous manufacturing gel under pharmacies.

RESEARCH OF GRANULES PROPERTIES WITH ANTIDIABETIC EXTRACT FROM HERBAL RAW MATERIAL

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Diabetes mellitus is one of a public health problem and a cause of death, disability, and cost in the Ukraine. Therefore, the development of new antidiabetic drugs 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, which has a specific hypoglycemic activity. The extract has a dark brown color, a faint specific odor, a salty-bitter taste.

The purpose of our work was to investigate technological properties of granules for development of tablets with this soft extract.

Tablets were obtained with the use of the wet granulation method. The soft extract was dissolved in a definite amount of purified water. Then auxiliary matters from the groups of diluents, disintegrants and moisture regulators were wetted with the solution of soft extract. Tablet mass was rubbed through the sieve. The obtained granules were dried at low temperature and calibrated through the sieve with the size of orifices 1 mm. After that granules with soft extract were dusted by magnesium stearate.

The technological properties of granules with antidiabetic extract from herbal raw material were researched. The granules moisture content was 5 ± 0.9 %. The flowability of granules were investigated without lubricant and with magnesium stearate. The antifriction agent slightly increased the flowability of granules. The granules without lubricant had flowability 14.1 ± 0.5 sec/100 g of a sample, with magnesium stearate 12.7 ± 0.5 sec/100 g of a sample (without vibration of an apparatus funnel). The angle of repose was 36 ± 2 °, the Compressibility Index was 17.1 ± 0.02 % and the Hausner Ratio was 1.2 ± 0.03 . The bulk density was 0.4 ± 0.02 g/ml, the tapped density was 0.48 ± 0.01 g/ml.

The experimental results of the technological properties determining of the tablets granulate, as well as the calculated Compressibility index and Hausner Ratio allowed us to estimate the characteristics of the granulate as fair. It was possible to predict the volume of the matrix channel by the value of the bulk density.

Thus as a result of the science-based experiment technological parameters of granules with antidiabetic extract from herbal raw material were defined for further obtaining qualitative tablets.

DEVELOPMENT OF AMLODIPINE BESILATE FAST DISSOLVING TABLETS

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Hypertension and angina pain are ones of the most expressed diseases, with which a practical doctor is to meet. Such diseases and their frequency are so high in lot of countries around the world especially with the elderly people. Worldwide, approximately 1 billion people have hypertension, contributing to more than 7.1 million deaths per year. Overall, approximately 20% of the world's adults are estimated to have hypertension and suffer from angina pain.

Amlodipine is a long-acting dihydropyridine-type calcium channel blocker used to lower blood pressure and to treat angina chest pain. It is of large interest creation of antihypertensive medicines of amlodipine besilate in the form of fast dissolving tablets.

The aim of the current study was to develop the scientifically and experimentally grounded technology of the antihypertensive preparation on the basis of substance Amlodipine besilate in a fast dissolving tablets form.

Much attention is given by the domestic and foreign medicine of the last years to application of medicinal preparations in a rational medicinal form. In connection with this the fast dissolving tablets assumes ever greater importance due to disintegrating or dissolving rapidly in the saliva without the need of water. Fast dissolving tablets have been formulated for pediatric, geriatric, and bedridden patients and for active patients who are busy and traveling and may not have access to water.

With the purpose of tablets composition development we studied crystallography and pharmaco-technological properties of Amlodipine besilate powder that were supplied by "Chemphar», China. Microscope observations have demonstrated, that Amlodipine besilate substance was polydisperse powder of crystalline structure, the particles of which have an anisometric form. The main fraction of powder was 200-315 μm . The investigated substance had very poor flowability (only using vibration 106 sec/100 g of a sample), about what the angle of repose (45°), the Compressibility Index (54.35 %) and The Hausner Ratio (2.19) testified also. The bulk density was 0.22 g/ml, the tapped density 0.48 g/ml.

It predetermined the application of excipients for improvement technological properties of substance when formulating of tablet mass.

The developed tablets correspond to USP on all of indexes.

SEARCH AUXILIARY SUBSTANCES FOR THE CREATION OF A SOLID DOSAGE FORM FOR DIABETES TREATMENT

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The choice of the excipients is an important task for the technologist who working at the modern pharmaceutical production. The correct solution of this task helps not only to create a safe and effective drug tool, but to increase economic efficiency of production, to reduce the cost of the equipment and personnel.

One excipient can have several functions, both positive and negative. For example, the positive effect of the magnesium stearate consists in its lubricating function, which reduces the friction of the punches, but at the same time its high hydrophobicity can make a negative impact on the profile of the release. Microcrystalline cellulose is one of the most widely used excipients. It helps to achieve the desired admixture and friability, but it can also adsorb moisture, as well as the other chemicals. These features should be considered during the process of the creation of a particular recipe.

The purpose of our work is the search for the new excipients for development of the mixture and technology of the solid drug forms for the treating the diabetes.

The modern chemical industry produces combined multi-functional excipients (which consist of several components), for example, the production on the basis of silicate microcrystalline cellulose, which perform multiple functions in the recipe. In some case, such excipients allow to switch from the damp process of the granulation to the direct pressing with those active substances, which traditionally cannot be used in the technology of the direct pressing.

One of the latest developments is the disintegrant and a binder based on microcrystalline cellulose mcc sanaq explosion. This is the example of the one-component of the excipient combining two magnesia for the tablet functions: binder (helps to compress into a recipe directly pill) and disintegrant (contributes to the disintegration of these pills when they ingest in the human's organism).

Formaxx ® CaCO₃ 70 is a «connected» calcium carbonate (70 %) and sorbitol (30 %), it is the first product of the series Formaxx. The «mated» product is the best for the direct pressing; it shows the excellent performance of the admixtures at low pressures.

Cyclodextrins cavamax have the unique ability to protrude as the molecular containers, due to the seizure of molecules in the inner cavity. The complexes which were made in the result of these actions are used in a number of applications in the pharmaceutical mixture. For example, cyclodextrins increase the water solubility medicines, which have the difficulties in the dilution in water, improving their bioavailability of them, they also stabilize the active substances of the drugs.

Thus, on the basis of the analysis of literature data we can conclude perspectivity of application of cyclodextrin, Formaxx ® CaCO₃ 70 and microcrystalline cellulose as auxiliary substances when creating a solid drug forms for treating diabetes.

FORMULATION OF GEL BASED ON HERBAL EXTRACT FOR WOUND HEALING TREATMENT

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Development of new effective drugs for wound healing treatment does not lose its relevance. One of the directions in solving this problem – development of soft medicinal forms based on antimicrobials representing an alternative to antibiotics, in particular, on the basis of medicinal herbs. As promising antibacterial and anti-inflammatory agent of plant origin the extract from *Datura innoxia* leaves is considered.

In the development and preparation of the dosage form it is important to ensure optimal conditions for the release and subsequent absorption of the active ingredients. Topical drugs should provide a local and uniform release of the active pharmaceutical ingredient from the dosage form, making its high therapeutic concentrations at the application sites without significantly increasing medicinal substance level in the systemic circulation. So, the major place in technology of soft medicinal forms belongs to selection of foundation and study of the rheological parameters of the formulation, the definition of which may serve as an objective quality control during production and storage.

The aim of our research is to study the rheological properties of herbal gels with *Datura innoxia* leaf extract on the basis of various gelling agents.

To select the optimal composition of the carrier we have conducted comparative studies of indicators of gel foundation based on hydroxyethyl cellulose, sodium alginate, Aristoflex AVC of the company Clariant, Switzerland, Reolab 200 ST and Reolab 100 XT, Poland.

Due to the varying nature and physico-chemical properties of the above mentioned gelatinizers, as well as mechanisms of gel systems formation, studied foundations were prepared using different technologies. Gelatinizers were injected at concentrations ranging from 1% to 5% and compared by gel rheological properties. Rheological studies of experimental samples were carried out on the rotational Brookfield viscometer, model HB DV-II PRO (USA), spindle SC4-21.

RESEARCH SAPROPEL'S PROPERTY OF THE PRIBICH

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Sapropel – organic sludges, sediments of fresh continental pond. There are three main components: water (60-75%), solid part (sand, clay, carbonates, phosphates, silica, iron compounds, etc.), organic component which has non-uniform structure and are very complexly. Sapropel refers to natural and renewable resources and it is a unique organic raw material. Sapropel uniqueness compared to other therapeutic mud that means that only sapropel goes full cycle of biosynthesis.

Sapropel can not be decomposed and has no odor, and in vivo has regenerative properties that can clean itself. Has a wide range of applications, which includes many diseases of various systems and organs. Experimentally proved that the local application for action is not inferior to traditional methods, have no contraindications, do not cause allergic reactions and complications.

Analysis of published data on the pharmacological activity of sapropel showed the presence of anti-inflammatory, antioxidant, regenerating, the antimicrobial activity of sapropel.

A lot of researches have shown the ability to leverage sapropel in medicine (medicine , pharmacology , mud therapy and cosmetology) . Found that the sapropel treatment improves lymph- and blood circulation, strengthens the vascular wall , stimulated function of the autonomic nervous system. Sapropel in enteral application has a strong antioxidant and healing pharmacology action . Enterosorbent sapropel is effective and can be recommended for use in the complex therapy of acute and chronic poisoning.

The purpose of our research was to study the antimicrobial activity of sapropel which is situated in village of Pribich (Shatsky district, Volyn region) . Investigations were carried out at the Institute of Mechnikov Microbiology and Immunology institute . The antimicrobial activity was studied by the test organisms Staphylococcus aureus strains ATCC 25923 , Escherichia coli ATCC 25922 , Pseudomonas aeruginosa ATCC 27853 , Basillus subtilis ATCC 6633 , Proteus vulgaris ATCC 4636 , Candida albicans ATCC 885/653 .Results of the study indicate the presence of a minor antibacterial activity investigated sapropel all the reference test cultures (except for Staphylococcus aureus).

Wide range of indications for using sapropels clearly shows importance of using for treatment and disease prevention.

THE USE OF MEDICINAL PLANT RAW MATERIAL FOR THE TREATMENT OF THYROID DISEASES

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According to the World Health Organization thyroid disease increases with each passing year. Currently, the prevalence of this pathology in Ukraine is 599 per hundred thousand population and takes a second place after diabetes. According to static data a rise of numbers of thyroid diseases in the world is up to 5 % a year.

15 millions people in our country suffer from thyroid diseases, that is every third in Ukraine. This pathology takes the first place from all endocrine pathologies in child practice. Endocrine diseases lead to high perinatal mortality, birth of mentally retarded children and retarded physical development of children.

Medicines for the treatment of thyroid in Ukraine are produced by 5 pharmaceutical plants. After analyzing the range of industrial and extemporaneous production of medicines for the treatment of thyroid cancer in Ukraine, it was established that the needs of this group of patients are not satisfied. The aim of this work is to study medicinal plants for the treatment of thyroid diseases.

To solve the above problem, it is necessary to expand the range of extemporaneous production, for example, remedies based on medicinal plants.

Previously it was thought that the main condition for the normal functioning of the thyroid gland is adequate intake of iodine. To date, scientists have found new approaches to the treatment of diseases related to the thyroid gland.

German and Belarusian endocrinologists found that regular use of iodine does not lead to the desired result because the thyroid gland decreases slightly and requires the presence of trace elements such as selenium and zinc, as they contribute to the better absorption of iodine and moreover they are involved in the synthesis of thyroid hormones.

Range of raw materials containing iodine, selenium and zinc are presented in following plants: thallus of laminaria - seaweed, grass of european zyuznika and common cocklebur, flax seeds, herb of hypericum, milfoil. These plants have been used for a long time in folk medicine for the treatment and prevention of diseases of the thyroid gland.

Thus for the treatment of thyroid pathologies perhaps it is possible to use medicinal plants above mentioned.

USE OF CRIOMILLED PLANT POWDERS IN THE TECHNOLOGY OF GEPATOPROTECTIVE DRUGS

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Pathologies of liver occupy a leading place among illnesses of digestion organs. From data of World Health Organization in the world - over 2 billion of people have pathology of liver, that in 100 times exceeds prevalence of human immunodeficiency virus.

In Ukraine for the last 10 years prevalence of diseases of liver has been increased on 20,1%.

Phytotherapy has substantial role in the prophylaxis of intensifying liver diseases and prevention of acute process transition to chronic.

Herbs increase biliary excretion, have spasmolytic, antiallergic, antiinflammatory action, promote normalizations of gall-bladder tone.

Possibility to utilize native raw material without the sequential process of extraction comes into the notice of researchers in the last years. Criopowders have become this product, which keep all of the active substances from destroying during milling.

Criopowder is a product, got on criogenic technology, that uses deep-freezing (-180 C) on one or a few stages of production.

In recent work criopowders of Fumaria grass, Calendula flowers, Taraxacum roots, Agrimonia grass, Menyanthes grass, Mentha leaves have been studied.

It has been determined that criopowders had bad flowability, low compressibility. For including of this criopowders in the complement of pills it is necessary to use high-efficiency binder agent. Fluidity can be improved due to wet granulation. As a result of determination of fluidity of these samples, hardness and friability of model pills the use of wet granulation has been grounded.

For the increase of pills hardness, disintegration and friability improvement 5% polyvinylpyrrolidone water solution has been selected for wet granulation. As lubricant 1% of calcium stearate has been used.

Pills correspond to requirements of Ukrainian state pharmacopeia by hardness- $53 \pm 0,4$ N, disintegration – $3,26 \pm 0,02$ min, friability – $0,81 \pm 0,04$ %.

AUXILIARY SUBSTANCES WHEN PRODUCING SYRUPS

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Syrups are the most convenient liquid dosage form for internal use, as in children, still in adults.

Such popularity of syrups explains in addition biopharmaceutical aspects related to the regularity and absorption speed medicinal substances, their distribution and excretion, exception pain when taking drugs, metering accuracy.

Traditional syrup is a concentrated solutions of sugar, to which you have added the appropriate medications and flavors. They are cooked of the highest purification, pure sugar, containing not less than 99.9% sucrose in recalculation to dry substance and not more than 0.4% of water. Depending on the composition of the syrup are divided into taste and medicinal. Part syrups consists of the following groups of auxiliary substances: fillers, sweeteners, preservatives, dyes, stabilizers, regulators pH. In modern pharmaceutical industry as the underlying auxiliary substances apply Compri Sugar® is white granules with a good bulk properties; differs in composition (pure sucrose, or mixed with other auxiliary substances, composition, particle size bulk density.

If you want to minimize the fluidity of solutions consisting of syrups enter the regulators of viscosity. These include: agar, L(+) Tartaric acid; DL - malic acid EMPROVE ® water-soluble starch. And it is also used polyvinyl alcohol, which has a large surface tension, thickening and lubricating properties. In the process of coregents is possible to highlight the following directions: correction of undesirable odour; the correction of taste; giving the medicine attractive appearance.

As correction of taste currently proposed various substances. The maximum effect is observed at the integrated use of syrups with flavoring substances, which in themselves give a feeling of bitterness (orange, cherry, cacao). To fix the bitter taste widely used flavors of apricot, mint, honey, cherry, chocolate, cacao, cinnamon or a combination of orange with raspberries. For sour substances used lemon and orange syrups. In the capacity of coregents, currently offered sugar, raspberry, cherry, orange syrup, sweeteners - saccharose, lactose, fructose, sorbitol, mannitol, sodium saccharin, polysaccharides vegetable origin. The most promising are sorbitol and mannitol - substitutes sucrose, forming a viscous solutions, they also stabilize many drugs that bind metals, prevent the decomposition of active substances, permit thermal sterilization of the finished product. Widely used combination of sucrose, glucose, fructose with sorbitol, mannitol. Just to correct taste use a variety of high-molecular compounds, these include agar, alginates, methylcellulose, pectin. As auxiliary substances, apply vegetable polysaccharides such as shaper, thickeners, correction of taste, stabilizers.

Thus, on the basis of the analysis of literature data we can conclude that rational selection of auxiliary substances required for the development of composition and technology of liquid medicinal forms as syrup. Development of technological process will allow to increase productivity and to achieve maximum therapeutic effect.

THE RESEARCH OF COSMETIC EMULSIONS BASED EMULSIFIER EASYNOV

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Creating of new effective and safe medicines and cosmetics different sets of actions using modern adjuncts is a promising research direction of the Chemist's technology of drugs department National University of Pharmacy.

The aim of our work was obtaining a stable emulsion bases using emulsifier Easynov (octyldodecanol&octyldodecylxyloside& PEG-30 dipolyhydroxystearate) and the research of their physical, chemical and rheological properties.

Peculiarities of the structure, dermatological compatibility with skin lipids as well as moisturizing properties of Easynov make it possible to obtain stable emulsion bases promissory for the production of makeup preparations for sensitive, problem-prone skin and preparations for the correction of involuntional changes of skin.

Experimental samples of emulsions were prepared by cold emulsification. In order to investigate the emulsifying properties of the model samples in Easynov varied content of the oil phase, vaseline oil from 0 to 50% in increments of 5. The concentration of the emulsifier was used as recommended by the manufacturer - 4%. As an experimental emulsion thickener was used Carbopol 980 gelling agent at a concentration of 1%, which was neutralized with 18% sodium hydroxide.

The resulting emulsion was tested by the following criteria: organoleptic and sensory properties, thermal stability, colloid stability, pH, type emulsions obtained, and the structural and mechanical properties.

The researches allowed to receive stable direct emulsions of the type oil-water with satisfactory rheological properties at a concentration of 5-10% paraffin oil from the compulsive use of Carbopol. Also received were stable inverse emulsion water-oil concentration in the oil phase, which was 30-50%.

The reseived emulsion possessed satisfactory touchproperties: they were easily applicate and distributeon skin, they did not create a sticky film, also the emulsions were easily to wash away. Viscosity of the experimental samples increased proportionally to the rise of the concentration of the oil phase.

Conducted physico-chemical and rheological studies show the availability of the emulsifier Easynov. Received emulsion bases may be used in pharmaceutical and cosmetic industry.

POLLEN - NEW PERSPECTIVE SUBSTANCE OF NATURAL ORIGIN

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Pollen most comprehensive - a natural product that has no analogues in the world by the number and variety of biologically active substances. Pollen contains approximately 240 of biologically active substances that are necessary for normal functioning of the human organism. This number can vary, depending on the variety of plants on bee pastures, and can reach 300. Diversity of pollen because the bees fly around different flowers on the spacious grounds from early spring to late fall, and collect them with pollen, which concentrates a large number of biologically active substances. Each plant its medicinal properties.

For example, medicinal herbs for teas, as is known, it is recommended to collect during their flowering as biologically active substances are concentrated most of all it is in the flowering period. To describe the structure of pollen, or, as they call it - the life of the formula, it is easier to use the word "all", "exclusion". Pollen contains all 28 amino acids, including 9 essential that the human body is not able to work independently.

All the vitamins, except B12 (found in meat). It carotene is 20 times greater than carrots. Vitamins are not synthesized artificially, such as those that frequently sold in pharmacies, or those that are added, e.g., in the juice, yogurt, chewing gum, etc. These are vitamins and substances created by nature itself, which the body can be fully used. For example, 40 grams of bee bread is necessary for an adult daily requirement of amino acids. Protein is several times larger than, say, meat, fish or milk. And most importantly - the amino acids that make up proteins, balanced with each other. They are balanced with other components, but in proteins of animal origin does not. Therefore, in comparison with meat, the body will not be clogged decay products, poisons, toxins, toxins, will not be disturbed metabolism. In bee bread are abundant unsaturated fatty acids Omega - 3 (linolenic acid) and Omega - 6 (linoleic acid) in a 3:1 ratio, that is so necessary

for normal functioning of nerve cells, because pollen is the outer shell composition resembles cellulose and protect it from adverse environmental impact, the enzymes of the human body can not split it, and the benefits of pollen limited.

According to research by scientists, this number ranges from 20 - 40 %. People who are prone to allergies, you should be careful. Quite different is the case with bee bread. Placing and compacting pollen combs, bees treated her floral nectar and their salivating. As a result, under the influence of enzymes, bacteria and yeasts, the number of lactic acid. Occurs canning, and the outer shell pollen prolamlivaetsya that gives access to the human body valuable substances of more than 90 %. Use of pollen does not cause allergies. List of diseases that treats pollen very very long, so the best option - consult your doctor - apitherapist.

Healthy individuals may use bee bread prevention, one teaspoon two times a day to enhance immunity to improve vision, memory, ability to concentrate, before or after a meal. Bee larvae fed royal jelly, which is a raw material for pollen, and in just 3 days the larvae gain weight in 1500. In the animal world analogues such rapid growth is not.

Continuously using foodstuffs grown using intensive technology with preservatives, dyes and flavoring agents leads to their deposition in the human body, and undermine the immune system, as well as affect the action of enzymes. Scientific studies have shown that regular consumption of fruits and vegetables grown using intensive technologies will not be able to optimize the amount of vitamins and minerals in the human body.

Pollen in this situation - one of the most effective means. Incidentally, one of the not expensive compared with artificially synthesized chemicals. Ambrosia may be the most complete food supplement, because there is all that is necessary for life. Used separately from food. Do not need to drink water. You must try to chew as carefully as possible to maximize intermingled with saliva. Adult, healthy person to prevent recommended to use two teaspoons per day. That is, 10 g per day.

DEVELOPMENT THERAPEUTIC AND PROPHYLACTIC MEDICINES ON THE BASES OF THE DRONE BROOD

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The development new therapeutic and preventive agents with a wide range of pharmacological actions on the basis of natural raw materials is priority scientific direction of the Chemist's Technology of Drugs Department of the National University of Pharmacy. In a study of such objects used various bee products.

In previous work, we have presented materials about the prospect of creating drugs based on biomass of the moth larvae bee. The result of these studies was the creation of tincture «Gretavosk».

One of such objects of study in our opinion is the drone brood. The beekeepers are used an unusual product - drone larvae for a long time. To date, the prospect of creating as drugs and food additives physiological have insufficiently studied. Primary sources of scientific data are scarce.

Medicinal properties of drone brood described in several works papers (A. Smirnov, K. Chernov, I. Iorish, N. Ilieshiu, V. Alexandru, I. Malaya, E. Ludyanskiy, T. Vahonina et al.).

This product is appreciated for the strongest bio-stimulating properties. In some countries, such as Japan, these bee products are very popular. Various bee products are distributed as healthy food for children in the schools. The drone larvae used in the form of special food, it's cooked, packed in glass and metal containers and sold in the stores. The various dishes prepared from these larvae that count tasty and useful. The drone brood is preserved with soya's sauce and used as a as the spices or fried.

Taking into account the above, we concluded that the drone brood is a promising object of research for development the drugs and physiological food. Given the characteristics of this material, its thermolability, the largest amount of biologically active compounds can be saved only by using gentle technology. At this stage, the researches of the creating freeze-dried substance are carried out. On the basis of a lyophilized powder perspective plan to create a variety of dosage forms.

Given Ukraine's integration into Europe, where safety of medicine's occupies a leading position in the development of drugs, one of the advantages of the developed substance is its safety, as the creation of not only effective, but also the most secure drug is an urgent task of Pharmacy.

RHEOLOGICAL STUDIES OF THE FIRST KIND EMULSION FOR CREATION OF COMPLEX ACTION CREAM

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The effectiveness of any drug is primarily dependent on the rationally chosen carrier of drug substance taking into account all symptoms of the disease. From literary studies it is known that the basis of a soft drug for the treatment of dermatoses should have a soft effect on the skin cover, moisturize and soften it well. Creams, due to the high water content (70%) replenish the lost skin moisture, easily applied to the surface, quickly absorbed without leaving the skin greasy. In addition, the base of the cream should have some structural and mechanical or rheological properties that characterize its spreadability and extrusion of tubes, possess certain osmotic properties and promote the complete release of the active ingredient.

The aim of the work is creation of a cream base, study of its rheological and osmotic properties. The type of basis which suited the task best is oil / water emulsion system. As the oil phase was decided to use mineral oils as they are more stable during storage and do not require additional system stabilizer (antioxidants). For research a range of emulsions was produced, which at the same quantitative value of the oil phase and the same total concentration of emulsifiers of 1 and 2 kinds had their ratio varied expressed through the total value of the HLB of the mixture. Rheological studies of samples have been conducted on viscometer «Rheolab QC» (Anton Paar, Austria) with coaxial cylinders C-CC27/SS. As a result of the studies the influence of the concentration and composition of the emulsifiers mixture on the fluidity of samples and the structural viscosity have been analyzed, the type of flow and the presence of thixotropic properties have been defined.

Structural and mechanical properties are important characteristic that determines the stability of visco-dispersed systems. The study of these parameters is important in drug development, determination of temperature conditions of the process of production and standardization of the finished product.

EXPERIMENTAL STUDY OF CONCENTRATION AND CHOICE OF ROUTE OF ADMINISTRATION OF METRONIDAZOLE AND CLOTRIMAZOLE VAGINAL SUPPOSITORIES IN STOCK

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The main task in developing a new drug is to maximize the therapeutic efficacy of active pharmaceutical ingredients (API) and to minimize their potential adverse effects on the body. Due to the fact that pharmaceutical factors influence the effectiveness of drugs we are justified in pharmaceutical technology considered factors including input method APIs of the drugs.

Research materials were suppositories, metronidazole and clotrimazole and method - a study of antimicrobial activity in vitro method, according to State Pharmacopoeia of Ukraine.

Metronidazole (0.1g) and clotrimazole (from 0.1 to 0.6g) in the basics injected as a solution in DMSO, suspension of vaseline oil and in part directly molten base.

Installed antimicrobial activity depends not only on the concentration of API, but also on the method of introducing them to the ground.

According to the results of microbiological studies found that the greatest area of growth retardation test cultures showed a sample, where clotrimazole (0.4g) injected into the molten part of the base, and metronidazole (0.1g) dissolved in DMSO and injected into foundation.

Such a way of clotrimazole and metronidazole administration of the suppository is optimal, since antimicrobial activity in this case is the highest relative to strains which studied: *S. cerevisiae*, *C. utilis*, *C. Albicans*.

Conducted research on antimicrobial activity of vaginal suppository allowed to choose the optimal concentration API (metronidazole and clotrimazole) consisting of vaginal suppositories and rational way of introducing them to the ground.

MEDICINAL PLANT RAW MATERIAL USED TO TREAT ALLERGIC DISEASES

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Today is actual studying medicinal plant raw material. This is due, first, to the great interest of the population to medicines of plant origin, and secondly, to the prevalence among people traditions of herbal medicine.

Important place among the variety of diseases is given to allergic diseases, including children. Distribution of allergy among children is associated with environmental indicators, genetic predisposition, and insufficient attention to mother's body during pregnancy.

Allergic diseases are natural reactions to exogenous and endogenous allergens, which are due to increased sensitivity of the organism. According to the World Health Organization, the 21st century will be the era of allergy, since the prevalence of allergic diseases has been increasing by 2-3 times every 10 years and has reached epidemic proportions. To allergic diseases of children primarily can be attributed atopic dermatitis, angioedema, urticaria, drug and food allergies, and others. One of the treatment variant of such pathologies is usage of antihistamines of 1, 2 or 3 generations.

Having analyzed the range of antihistamines in Ukrainian pharmaceutical market, we have found that such medicines are presented in the form of tablets, solutions for injections, syrups, oral solutions, drops, lozenges and gels for topical application. Of these dosage forms in pediatric practice most suitable are liquid oral medicinal forms.

The objective of this work is to study medicinal plant raw material that can be used in developing of syrup with antihistamine action.

We analyzed extemporaneous medicines of different dosage forms, containing in their composition herbal ingredients, herbal remedies, species, etc. In the course of this work it was found that for the treatment of allergic diseases most commonly are used such medicinal plant raw material as Marigold herb, Peppermint leaves, Chamomile flowers, Labrador tea shoots and Efedra herb.

Thus, in the course of this work, we have been defined medicinal plant raw material, which can be used in the development of a medicinal plant tea for the treatment of allergic diseases.

DEVELOPMENT OF A COMPOUNDED COSMETIC FOR SKIN XEROSIS TREATMENT BASED UPON APICULTURAL PRODUCTS

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Xerosis (skin dryness) is a permanent symptom of various dermatologic diseases, such as: atopic dermatitis, psoriasis, eczema and others. The problem of skin xerosis is growing from year to year, this stems from the environmental conditions and the incidence of dermatologic diseases.

Nowadays a shortage of compounded cosmetics, that is dedicated to skin xerosis correction, is observed in Ukraine. Thorough examination of problematics and consideration of patients individual traits serve as fundamental principles for the creation of a cosmetic «ex tempore».

The search of active ingredients was focused on those substances, that restore barrier functions of the horny layer and reduce moisture loss.

Powdered honey, one of the most prospective ingredients in cosmetics, that has the unique formula, moistens and nourishes skin, was proposed to be used to achieve these results. Allantoin, that has wound-healing, keratolytic and moisturizing features, that facilitate regeneration, was included to the cosmetic composition to achieve the maximum effect.

The cosmetic forms analysis revealed that the use of such cosmetic form as cosmetic cream is the most efficient for skin xerosis correction. As a result there was created an emulsion type cream of oil/water type, in which powdered honey and allantoin were used as active ingredients. There was performed an analysis on the basis of DSTU (National Standards of Ukraine) 4765:2007 “Cosmetic creams” and there also were developed quantitative analysis methods and qualitative analysis methods for active ingredients.

Taking into consideration the examined regulatory documents, the production technology and the performed analysis, we worked out a standard operating procedure for compounded cream production under the druggists conditions.

The production of powdered honey offers a wide challenge in cosmetic science, as the composition of the received substance fully conforms to natural honey.

EFFECT OF SOLUBLE DILUENTS ON TRIMETAZIDINE DIHYDROCHLORIDE SUSTAINED RELEASE FROM INSOLUBLE ETHYLCELLULOSE MATRIX TABLET

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Sustained release oral matrix tablet is a popular dosage form using which could be achieved the desired in vitro drug release, and corresponding in vivo therapeutic concentration of drug. Therefore, investigation of factors that influence the active pharmaceutical ingredient (API) in vitro release kinetics is an important task. Vasodilator trimetazidine dihydrochloride (TMZ•2HCl) is a freely soluble substance, thus it's attractive as a model substance. Ethylcellulose is one of the most popular polymers among the insoluble matrix formers is used for the experiment. The aim of this work is investigation of the effect of soluble diluents on TMZ•2HCl release from ethylcellulose matrix tablet. Particularly, to investigate influence of popular diluents sorbitol and lactose monohydrate that have different solubility and particle size on TMZ•2HCl release in phosphate buffer solution (PBS) pH 6.8 that mimic intestines conditions.

API: Trimetazidine dihydrochloride (TMZ•2HCl, Sochinaz SA, Switzerland); matrix former: ethylcellulose (Ethocel-10, Ethocel Standard 10 FP; Dow Chemicals, USA); diluents: lactose monohydrate (Sorbolac-400, Granulac-200, Capsulac-60, Meggle AG, Germany), sorbitol (Neosorb P100T, Neosorb P60 W, Neosorb P30/60; Roquette, France); glidant: colloidal silicon dioxide (Aerosil 200 Ph, Evonik AG, Germany), lubricant: sodium stearyl fumarate (Pruv, JRS Pharma, Germany).

The solubility of excipients and TMZ•2HCl were determined using shake flask method. Mean particle size and distribution were determined using the laser diffraction particle size analyzer (Coulter LS 230, Coulter Electronic, Germany). Direct compression method was applied to obtain 200 mg biconvex tablets with 8 mm diameter according to the formulation presented in tab.1 using a mixer (Turbula T2F, Willy A. Bachofen AG, Switzerland) and eccentric tablet press (Korsch EKO, Korsch AG, Germany).

Tab. 1 Tablets formulation.

Formulation	% per tablet
TMZ•2HCl	17.5
Diluent	31.3
Ethocel-10	50.0
Aerosil 200 Ph.	0.2
Pruv	1.0

The drug release from tablets was investigated in a paddle apparatus (Vankel VK 300, Vankel Industries, Edison, NJ, USA) at following conditions: 900 ml of

PBS pH 6.8, 100 rpm, 37°C; (n=3). Samples were withdrawn at predetermined time points, filtered through 0.35 µm filters and measured UV-spectrophotometrically at $\lambda=269$ nm.

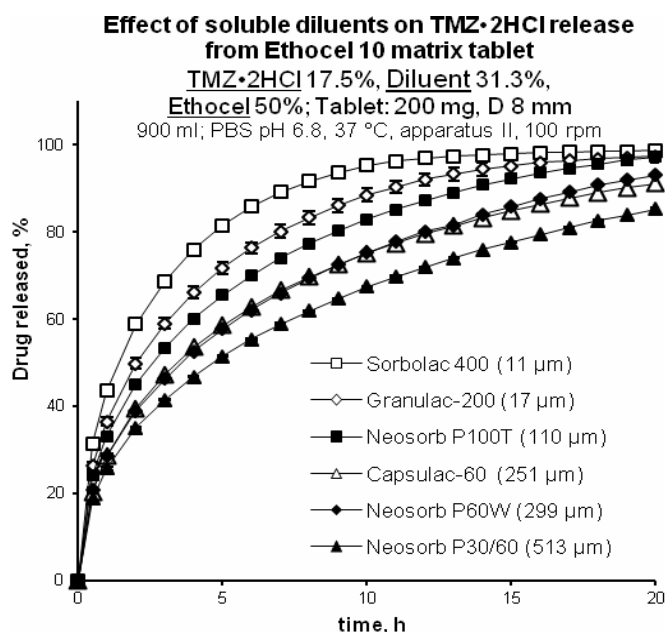


Fig. TMZ•2HCl release from insoluble Ethocel 10 matrix tablets.

Increasing the particle size of lactose monohydrate (from 11 to 251 µm) and sorbitol (from 110 to 513 µm) (Tab. 2) decreased TMZ•2HCl release from insoluble Ethocel 10 matrix tablets (Fig.). This result agrees with percolation theory.

Tab. 2 Ingredient's particle size and distribution.

Ingredients		Mean particle size (µm)	S.D.	D ₁₀	D ₅₀	D ₉₀
1	TMZ•2HCl	20.9	12.5	6.1	19.2	38.4
2	Sorbolac 400	10.5	7.7	1.2	9.3	21.4
3	Granulac 200	16.7	12.2	2.6	14.1	35.7
4	Capsulac 60	250.7	88.0	144.7	245.2	368.7
5	Neosorb P60 W	299.0	183.0	72.1	281.0	553.0
6	Neosorb P30/60	513.0	158.0	331.0	509.0	715.0

Comparing release profile of tablets with diluent Capsulac-60 (251 µm) and Neosorb P60 W (Fig.) was concluded that increasing of diluent solubility from lactose monohydrate to sorbitol (Tab. 3) increased TMZ•2HCl release profile.

Tab. 3 Ingredient's solubility in PBS pH 6.8

Ingredients	Solution's pH	Solubility, mg/ml
TMZ•2HCl	6.7	340
Lactose•H ₂ O	6.5	210
Sorbitol	NA because of high concentration	>4000

ORGANOLEPTIC EVALUATION OF CANDIES WITH L-CARNITINE AND GLUCOSAMINE

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Professional or intense sport is associated with a high load on the joints and the whole body. Therefore, the development of functional food additives (FFA) for the prevention of joints and connective tissues injuries is promising. We have developed FFA in the form of candies with L-carnitine and glucosamine and held its organoleptic evaluation by the method of A.I. Tentsova in two groups of tasters (each of 20 persons) on the five-point schedule. One of them evaluated taste by emerging emotional experiences within the schedule, namely: very nice (5), good (4), not bad (3) bad (2), very bad (1), the second conducted an assessment of the same samples on basic taste sensations: not bitter (salty, sour), slightly bitter (salty, sour) weakly bitter (salty, sour), bitter (salty, sour), very bitter (salty, sour), respectively. From the data obtained determined numerical index of taste and basic taste.

To judge more correctly of the ability of the individual compositions to mask the unpleasant organoleptic sensations compiled "taste map" by the method of I.A. Egorov. The sense of taste has been conventionally signed with letters: K - sour, O - sweet H - bitter, C - salty. To assess the degree of taste used digital indices, namely tints of flavors ("not bitter", "not sour", "not salty" and "not sweet") marked the index 1, index 2 assigned to slightly bitter, slightly sour, slightly salty and slightly sweet taste; index 3 is for bitter, sour, salty and sweet, index 4 marked strong flavor effect ("very bitter", "very sour", "very salty", "very sweet (nauseous)."

In the processed candies citric acid determines the basic taste. In order to establish its optimum concentration we have studied flocculation and melting kinetics (depending on the concentration of citric acid), which has allowed to establish the optimal value of its compositional quantity (0.5 - 1.0 g per 100 g of jelly product). The next stage of our research was to study the influence of citric acid on the organoleptic characteristics of candies. The result of the survey of respondents has become justified choice of citric acid in an amount of 0.5%. At the same time index of taste was O3K2 on five scale, which can be described as very good (5), sweet (O3) weakly sour (K2) taste.

Thus, on the basis of complex studies, we have grounded the amount of citric acid in the composition of candies.

RELEVANCE OF USING ESSENTIAL OILS TO TREAT ACNE

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Acne– it's inflammation, infection and congestion of the follicles, causing an eruption (whiteheads, blackheads, pustules, nobules or cysts) in the skin. As professionals would point out, cause is not so easy to determine. There are several factors involved, with the conditions being different for teenage acne, mostly related to the rise of the androgen hormone during puberty, and adult acne, also having a relationship to hormonal balance, though the cause of the imbalance is quite different.

Essential oils are one of the most effective natural weapons against acne. Topical use of a few specific essential oils can be a first line defense against the bacteria that cause pimples to form. There are also natural skin toning oils that help to close the pores so acne-causing debris are unable to cause inflammation.

Essential oils in general contain some excellent antibacterial properties. However, some of them are not suitable for use on the skin because of their volatile nature. They may either burn the skin or need to be diluted to such a weak solution that they lose their effectiveness. Some of the most powerful antibacterial oils that are also safe and gentle enough for topical use are rosewood, clove, bergamot, lavender and tea tree oil.

Tea tree oil is popular for skin applications due to its gentle nature and rare occurrence of allergic reactions. Some don't care for its rather medicinal smell while others like the distinct aroma. Prior to its use as an acne remedy, it was primarily used to disinfect scrapes and cuts. It may be used as a natural remedy for athlete's foot due to its excellent antimicrobial and antifungal properties. While tea tree oil has many topical applications, it may not be taken orally.

Lavender is an essential oil that may be surprising to some as an acne treatment. Lavender oil also contains several potent antibacterial compounds. It is gentle enough that it can be used topically on the skin without causing irritation. In the proper dilutions, it can be a wonderful addition to an acne skin care routine. It is also excellent as an additive in natural acne skin care products.

Another essential oil that may be one to consider for oily acne prone skin is lemongrass. Lemongrass has a pleasant lemon scent. It is great for oily skin since it acts as a natural astringent without over drying the skin.

Lemongrass also contains antibacterial and antimicrobial components. This combination of astringent and antibacterial qualities makes it an excellent choice for acne prone skin.

RELEVANCE OF COMBINED GEL DEVELOPMENT ON THE BASIS OF BEEKEEPING PRODUCTS FOR TREATMENT OF SPORTS MICROTRAUMA

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In modern conditions with admission of professional sports status, more relevance get the issues of unfavorable factors influence that expect athletes during continuous sports activities associated with significant physical stress or overloading as a whole, as well as new integrated approaches to their pharmacotherapy and rehabilitation after injuries. Treatment of injuries of the locomotor system (LMS) in sports medicine is almost impossible without general and local application of modern chemotherapeutic drugs.

Nowadays in rehabilitation of sports micro traumas are widely used soft dosage forms and particular significance obtains the use of gels, which have several advantages over other soft dosage forms.

In today's pharmaceutical market of Ukraine there is a significant range of local medical products for the prevention and treatment of traumatic injuries.

However, existing drugs are mainly represented by only a few substances, capable to do an anti-inflammatory effect and influence on the inhibition of pain only for a short time.

This applies particularly NSAIDs (diclofenac sodium and its derivatives) which can not fully provide long-term pharmacological effect and effective rehabilitation of athletes.

Considering the lack of domestic combined drugs for the treatment of inflammatory diseases of the LMS and sport micro traumas, which simultaneously exhibit analgesic and anti-inflammatory effects, and the inaccessibility and low efficiency of existing imported medicines, development and implementation in the industrial production of new local drugs is an important task of medicine and pharmacy.

Unabated interest for the modern medicine in this regard represents a development of original drugs for topical application based on natural origin compounds, including bee products.

Undoubtedly, this is due to the growing number of allergic reactions to synthetic drugs that are not only manifested in the skin, but also adversely affect the body as a whole.

Bee products have long been used in folk medicine to treat various pathologies. They confirmed the biological value of basic research of domestic and foreign scholars.

For the treatment are use royal jelly, pollen, propolis, apitoxin.

In addition, the effectiveness and harmlessness of bee products that have long been used to prevent and treat many diseases, today is out of doubt.

Domestic industry produces standardized substance of hydrophobic phenolic propolis preparation (HPPP) (Praeparatum Propolis phenohydrophobum) (RP № UA/4505/01/01, MOH Ukraine № 337 from 07.06.2011), developed at D.P. Salo chemist's technology of drugs department under supervision of Ukrainian Academy of Sciences Academician, Doctor of Pharmacy, professor A.I. Tikhonov.

The substance exhibits a wide spectrum of pharmacological action (anti-inflammatory, antimicrobial, antiradiation, capillary-strengthening et al.).

It is effective in treating a number of diseases in various dosage forms, water and alcoholic solutions, ointments, aerosols, emulsions, patches, pills and other.

On the basis of the compound a number of drugs with different orientation of action has been created, including those produced in industrially in our country: capsules "Apiprost", tablets "Proalor" (LLC "Pharmaceutical company " Zdorovya ", Kharkiv), suppositories "Propolis" (JSC "Lekhim-Kharkiv" Kharkiv) and others.

Given the above, it is feasible to create a soft dosage form in the form of combined gel of anti-inflammatory and local anesthetic action on the basis of standardized substance of a bee products - HPPP and compounds of synthetic origin for the prevention and treatment of LMS (tendons, muscles and joints) and micro traumas specific to sports medicine (bruise, sprains, strains, torn ligaments, tendons, etc.).

By today, its composition and technology have been theoretically and experimentally justified, rational concentration of active pharmaceutical ingredients has been set, the structural, mechanical and technological properties have been studied in order to choose a basis for the investigated gel, the choice and concentration of gelling agent has been performed, and also established QC indices have been included in the MQC project for the designed drug.

Model samples of gel have been put into storage in order to study the stability of the gel and expiry date.

ASPECTS OF DEVELOPMENT AND QUALITY CONTROL OF SUPPOSITORIES ACCORDING TO LEBANESE REQUIREMENTS

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General characteristics, requirements to preparation, registration for dispensing, quality control and packaging of this or that dosage form are given in Pharmacopoeia. Suppositories are represented in the most Pharmacopoeias of the world. Even though the general requirements to them are same, each Pharmacopoeia possesses certain special requirements and peculiarities about their preparation, packing and storage.

One of the tasks of our work was to analyse the requirements of the Lebanese Pharmacopoeia to rectal suppositories.

The conducted research showed that Lebanese Pharmacopoeia has many similar requirements with British and European Pharmacopoeias, and, therefore, with State Pharmacopoeia of Ukraine (SPU), but there are also many peculiarities in it as well.

For example, SPU, ap. 2, in the general article “Medicines for rectal use” regulates packaging generally for all medicines for rectal use specifying that containers for their storage must meet the requirements of the articles “Materials used for production of containers” (3.1) and “Containers” (3.2) if there are no other statements in the separate articles. Terms and conditions of storage especially for rectal suppositories are not given in the general article. In Lebanon, packaging and storage of rectal suppositories is different and includes such rules as: they are usually packed in aluminum, paper or plastic containers and should be stored preferably in a refrigerator, but polyethylene glycol suppositories can be stored at usual room temperature without the requirement of refrigeration.

Thus, the investigated differences to regulation of rectal suppositories preparation and quality control in SPU and in Lebanese Pharmacopoeia allow widening the experience of international pharmaceutical compounding and increasing the quality of their preparation in Ukraine. The work over the full analyses Lebanese requirements is carried on.

DEVELOPMENT OF COMPOSITION AND TECHNOLOGY OF DENTAL FILMS WITH DECAMETOXINE AND CHLORHEXIDINE

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Therapeutic tactics in infectious and inflammatory diseases of the oral mucosa should include prescribing of medicines that have anti-inflammatory, analgesic, anti swelling and hyposensitization effect, local antiseptics. In the treatment of the oral mucosa diseases at all stages antiseptic tools of different groups are widely used. At present, the most effective antiseptics are considered to be surface-active substances (SAS), which mechanism of action is based on the diphillic structure of molecules and ability to cause damaging effects on prokaryotic membrane. Drugs in this class have a wide range of antimicrobial action covering Gram-positive and Gram-negative bacteria, fungi, dermatophytes, yeast-like fungi, protozoa, Chlamydia and even complex viruses (pathogens of hepatitis, HIV). Resistance to these drugs in microorganisms is formed slowly. Typical representatives of ionic SAS are decametoxin and chlorhexidine.

According to the Ukrainian "State Register of drugs" in the domestic pharmaceutical market are registered 44 medicines containing chlorhexidine (28% are solid drugs, 30% are liquid drugs, 42% - soft drugs, of which 20% gel, of 7% are creams and suppositories and 3% - pessaries). Drugs that contain Decametoxin are 12 names. Of these, 33% are solid drugs, 58% - liquid and 9% - drugs with gaseous dispersion medium. Proceeding from the prevalence of the disease and analysis of market research relevant is the creation of stomatological medicines in the form of films with decametoxine and chlorhexidine.

RELEVANCE OF THE CREATION OF A NEW PHYTOTHERAPEUTIC REMEDY FOR THE TREATMENT OF DYSFUNCTIONAL UTERINE BLEEDINGS

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Medical statistics suggest that dysfunctional uterine bleedings (DUB) make about 30% of gynecological diseases, that are diagnosed in women 18-45 years of age. DUB occur due to sexual hormone disorders, are not connected with pregnancy, cancer, inflammatory diseases of the genital organs and blood diseases. They are caused by disorders of ovaries, where not only cyclical germ cells grow, but which also produce female sex hormones directly involved in maintenance of the normal menstrual cycle.

For the treatment of the above pathology hormones (Folliculinum, Non-ovlon, Bisekurin, Rigevidon, etc.) are commonly used, as well as hemostatic agents (Dicynone, Etamsylate, Vikasolum, Aminocaproic and Tranexamic acid, Calcium preparations).

Herbal medicine is also widely used. In this regard, in recent years there has been an increase of the range of scientific research to study properties of herbal medicines and scientific substantiation of the wide introduction of herbal preparations into clinical medicine. This is due to the benefits of herbal preparations in the treatment of various diseases because herbs show a pronounced therapeutic effect and have a smaller range of side effects, allowing to use these preparations without the risk of serious complications.

For the treatment of DUB tinctures and decoctions of such herbs as shepherd's purse, nettle, knot grass, yarrow, St. John's wort, sage, oak, burnet root, field horsetail are used which contain a number of biologically active substances with hemostatic action: ellagotannins, flavonoids, vitamin K and others.

Tinctures and decoctions have a lot of disadvantages: they are not stable during storage, and in most cases are not prepared in pharmacies, but by patients immediately before use. Therefore, the aim of our work is to develop the technology of a finished product — a liquid extract codenamed “Hemofort”, which will have a complex impact on all links of the pathological process.

THE INVESTIGATION OF THE GLIDANTS INFLUENCE ON THE TECHNOLOGICAL PROPERTIES OF TABLET MASS

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The manufacture of the tablets is associated with the use of the excipients regardless of the method of producing tablets. Depending on their destination, all adjuvants can be divided into the several distinct groups: the fillers (diluent), the binders (gliding), the disintegrating (disintegrates), the anti-friction (sliding and lubricants).

The modern researches for the development of the new and improved technologies used for the tablets are multifaceted. The problem of friction during the producing of the tablets, its impact on the manufacturability of the process, the quality of the tablets and ways to leveling the friction with the help of auxiliary substances, is only in the fragmentary studies. This is actualized understanding and systematization of the knowledge regarding the use of the explosives in the manufacture of anti-friction tablets.

During the dosing, the strength of coupling, including sliding friction, between the particles of the components are generally superior to the gravitational force, which leads to the production of stable concentrations impeding the flowability of the material, and as a result, disturbance of uniformity of tablet weight. During extrusion, the internal addition progresses external friction surface of the compressible material to the channel matrix. Part of the compaction pressure is spent to overcome it, is a redistribution of the density adjustment tablets.

Recent years the using of Aerosil as a glidant has increased. It is associated with the variability of the drugs and their properties.

Other adjuvant that effects on increasing the technological properties of the mixtures for the producing of the tablets and encapsulation – Neusilin (magnesium aluminate metasilicate). Despite the fact that Neusilin chemically similar to conventional similar products, it differs from them both structurally and functionally.

The adsorption capacity, the glidants impact on the slope angle and the swing weight tablets were determined during the study. As a result of these studies we can conclude that Neusilin has improved properties compared with Aerosil. Neusilin improves the substances flowability, prevents the agglomeration of the hygroscopic powders, adsorbs oil and the poorly soluble substance perfectly, and stabilizes hygroscopic drugs.

MARKETING RESEARCHES OF DRUGS BASED ON A FLUCONAZOLE FOR A TREATMENT OF VAGINAL CANDIDOSIS

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The frequency of vaginal candidosis for the last 10 years has doubled and is 30-45% in the structure of women`s infectious defeats of the vulva and vagina.

Vaginal candidosis is an inflammation of the vaginal mucosa and is caused by microscopic yeast fungi genus *Candida*.

The purpose of this study was making the analyses of the drugs` range based on fluconazole for the treatment of this disease.

According to the summary data the most effective in therapy of vaginal candidosis is fluconazole - 93.3%.

According to the ATC classification the following subgroup of medicines containing fluconazole are distinguished:

- D01A C - Antifungals for topical use, imidazole and triazole derivatives;
- G01A - Antiinfectives and antiseptics, excluding combinations with corticosteroids;
- J02A – Antimycotics for systemic use.

Pharmacotherapy of vaginal candidosis is divided into systematic and local treatment. According to the State register of medicines in Ukraine 108 drugs containing fluconazole are registered. Depending on a medical form they are subdivided as follows: 26 % of tablets, 57 % capsules, 11 % solutions for infusion, 5 % powders and 1 % gels. Only 2 vaginal medications (1.85%) are available for the local treatment. There are tablets «Venro kit» (made in India, Syncom formulation limited) and «Ginekit» (made in India, Synmedic).

Most of medicines are provided by foreign manufacturers – 72 % (India, Canada, Slovenia, Cyprus, France, Hungary, Turkey, Czech Republic) and only 28 % - by native.

As there is a sharp deficit of vaginal medicines based on fluconazole, it would be promising to create combined remedies that have a wide range of pharmacological action and minimal side effects. To maintain the health of patients it is advisable to use the antifungal agents based on the biologically active substances of plant origin, which do not show a sensitizing action, characterized by a wide spectrum of antimicrobial and antifungal activity, weak resistance towards these pathogens.

MODERN APPROACHES FOR CREATION OF SOLID MEDICINAL FORMS ON BASIS OF CHONDROPROTECTORS

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Creation of medications based on the complex of modern researches: marketing, technological, physical and chemical and economic. In connection with diminishing of efficiency of researches on creation of new medications it was begun to spare greater attention the improvement of properties already known economies, a necessity appeared for using of modern approaches for creation of new medications which will help to promote profitability of domestic pharmaceutical market and reduce the terms of turnover of money facilities.

To modern approaches of creation of medicinal preparations it is possible to take the followings directions: creation of new medicinal forms with the set biopharmaceutical properties (medicines with a modified-release drug on the basis of micro — and nanokapsulami, nanocapsules, homeopathic remedies, powders liposomes, implants, etc.); the search for new molecules or the use of new combinations of previously known pharmaceutical active substances; study of pharmacokinetics of drugs to select new auxiliary substances and optimization of composition; the improvement of existing technologies with the use of modern equipment.

Scientific approach to the study of physicochemical and pharmaco-technological properties of substances and excipients renders a significant influence on the bioavailability and the therapeutic efficacy of the medicinal product.

The creation of medicines in the form of tablets, capsules, powders is one of the most dynamically developing directions in pharmacy, due to a number of advantages of these medicines. These include convenience and ease of use, accuracy of batching, high bioavailability, the stability of the active ingredients and the use of sparing technological regimes at packing.

Today drugs in tablet form, gelatinous capsules, and granulated powders are present in the nomenclature of almost all pharmacological groups, including chondroprotectors. At the moment the production of chondroprotective drugs for Ukrainian companies is a priority, as in the pharmaceutical market of Ukraine these drugs account for about 40 % of the total volume of drugs used in the treatment of diseases of locomotor apparatus. This causes the relevance of further expansion of domestic chondroprotectors in solid dosage forms.

THE RHEOLOGICAL PROPERTIES STUDYING FOR HYDROPHILIC BASED OINTMENTS

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Ointments occupy 11% of all medicinal forms on the modern market of Ukraine. Ointments it is a soft medicinal form, consisting of base and active substances evenly distributed in it. Ointments have a number of advantages over other medicinal forms. It is connected with the possibility of incorporating substances with different properties, consistency, pharmacological activity, and activity type (local or resorptive). For ointments composition development it's important to study the rheological properties.

In accordance with the concept of rheology – it's a science of deformation and flow of bodies. Structural-mechanical properties of ointments include flexibility, structural viscosity and thixotropy. The definition of these indicators is used for the design, manufacture and quality control of soft medicinal forms. That's why, it's necessary to develop ointments with optimal rheological properties.

Rheological properties has a significant impact on technological stages of ointments production (homogenization, rolling, pipeline transport, packaging and others) and also on main consumer characteristics: extrusion from the tube, drawing on the problem area (uniform distribution, adhesive properties), which ultimately affects on the ointments therapeutic effectiveness.

Rheology and rheological research methods have been widely developed in the studying of the disperse systems on polymers base of, and various technological tasks decision. A significant scientific material for the study of rheological properties of soft medicines (especially ointments) is accumulated till nowadays. But it's practical use is complicated by the existence of different methods, devices and conditions for characterizing of the same objects.

The rheological properties studing of ointments on hydrophilic bases which included hydrophobic and hydrophilic extracts was conducted. The experiment was carried out on the "Rheolab-QC" device. The area between ascending and descending gisterthesis loops as indicating about thixotropic properties presence. So we can make an assumption that a studied ointment has a good extrusion capacity and abilitys to spread. It's expedient to continue the researches for development ointments which are correspondent for the high demands of the consumer.

DEVELOPMENT COSMETICS BASED PROPOLIS

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Propolis (bee glue) - this sticky substance that bees collect from tree buds of spring (poplar, alder, birch) and modify their enzymes. Propolis is a resinous residue from the first stage digestion bee pollen. Propolis is burning-bitter taste, has dark brown or yellow. Initially quite soft, but the storage thickens and hardens gradually, becoming brittle mass, like a dark rosin. Propolis is melted at a temperature of 80-104°C, when cooled below 15°C easily crumbled. Soluble in hot alcohol - methyl and ethyl (>70 %), gasoline. Partially soluble in liquid ammonia and a strong acetic acid, as well as special processing is soluble in water or a vegetable or animal oils.

Beekeepers collect propolis special bars or just scraped it with frames and walls. With each hive in the season 50-150 g of propolis collected. Some beekeepers melted propolis collected in a water bath, separating from mechanical impurities, while it is almost completely retains its properties.

Propolis contains almost all trace elements necessary for the person who magnesium, potassium, sodium, iron , zinc, manganese, cobalt, phosphorus, sulfur, aluminum, chromium, selenium, silicon, strontium, titanium, vanadium, zinc, tin, and copper fluoride. Of the minerals essential to man in much greater quantities in propolis is present primarily calcium. Various vitamins also found in propolis, among them especially vitamins B (B1, B2 , B6), vitamin A, C, E, H and R.

Propolis is used in cosmetics as an antibacterial, antifungal and regenerating agent. Very popular lip balms and lipsticks hygiene based on propolis, care of hair and toothpaste. Lipsticks help from cracking and peeling of the skin drying on the lips, herpes warn, nourish and soften the skin. Mascara based on propolis has anti-inflammatory and disinfectant properties, which is very important for especially sensitive eyes.

Propolis tincture is perfect for those who want to get rid of blackheads. Propolis Cream makes the skin smooth and silky, and massage oil on its basis is an excellent way to combat premature aging of the skin.

Propolis contains a large amount of trace elements and vitamins. Its application allows to enrich the skin with oxygen and also contributes to the process of cell regeneration. Almond oil with propolis is perfect for dry and sensitive skin. Masks of this oil make to turn back time - your skin will be firm and clean.

In dermatology widely used application of propolis in the form of pharmaceutical dosage forms. Their action is effective for burns, frostbite, skin nonhealing ulcers. Successfully used ointments and gels of propolis in the vast deep wounds, chronic eczema, itchy dermatitis, furunculosis, fungal diseases on their feet.

SUBSTANTIATION OF MEDICINAL FORMS WITH ANTIPYRETIC AND IMMUNOMODULATORY EFFECT

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The occurrence of fever in acute respiratory infection (ARI) is one of the safety functions of body. However, with an increase in axillary temperature to around 38,5 ° C or more, WHO recommends to take therapeutic measures. In this case children are the most vulnerable to acute respiratory disease, which is associated primarily with weakened or underdeveloped immune system.

On the basis of market research conducted it was found that in today's pharmaceutical market of Ukraine preparations that combine in themselves antipyretic and immunomodulating effects are present in insufficient quantities.

The aim of the study was to choose the optimal dosage form and justify the composition and technology of drug with antipyretic and immunomodulating effects for use in pediatric patients.

As main active ingredients paracetamol as a component of the antipyretic effect and mix factor as a component of immunomodulatory action have been selected. Mix-factor is a glycoprotein oligopeptide composite drug of natural origin.

Based on the processed literature we have selected dosage form of suppositories, which today are widespread in pediatric practice for young children.

Suppositories were prepared by pouring. As the base vehicle used type A hard fat. Paracetamol and the mix factor in the required amount entered to the basis as concentrate. When selecting a temperature mode proceeded from the properties of active substances and excipients. On the basis of thermogravimetical and rheological studies the optimal temperature mode of manufacturing suppositories has been determined. Quality assessment of received suppositories has been conducted in accordance with SPU.

At present, are continuing preclinical studies of paracetamol and mix factor suppositories on animals.

Thus, the research output initiated to justify composition and technology of antipyretic and immunomodulatory action drug in suppository form.

SECTION № 5

MODERN BIOTECHNOLOGY

FISH STEM CELLS AND THEIR APPLICATION

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Stem cells are present in developing embryos and adult tissues of multicellular organisms. Owing to their unique features, stem cells provide excellent opportunities for experimental analyses of basic developmental processes such as pluripotency control and cell fate decision and for regenerative medicine by stem cell-based therapy. Fish stem cells have the potential for use in various biotechnologies. Among them, gene targeting, germ cell transplantation and semi-cloning by nuclear transfer have attracted considerable interest and progress.

The goal of work is to analyze the current status and perspective of fish stem cells investigations and application of their results in the world science. Work with stem cell culture in fish started 20 years ago. Laboratory fish species, in particular zebrafish and medaka, have been the focus of research towards stem cell cultures. Medaka is the second organism that generated embryonic stem (ES) cells and the first that gave rise to a spermatogonial stem cell line capable of test-tube sperm production. Most recently, the first haploid stem cells capable of producing whole animals have also been generated from medaka. Embryonic stem cells have been reported also in zebrafish and several marine species. Recent years have witnessed the progress in markers and procedures for ES cell characterization. These include the identification of fish homologs of mammalian pluripotency genes and parameters for optimal chimera formation. In addition, fish germ cell cultures and transplantation have attracted considerable interest for germline transmission and surrogate production. Haploid ES cell nuclear transfer has proven in medaka the feasibility of semi-cloning as a novel assisted reproductive technology. The first semi-cloned fish in the world was Holly. It was generated by transplantation haploid ES cell nuclei into non-enucleated mature oocytes. Holly showed normal fertility and germline transmission over three generations, providing evidence that mosaic oocytes can generate viable and fertile offspring. In 2013 scientists at the University of Alberta reported that fish stem cells can selectively regenerate damaged photoreceptor cells and restore human vision.

It should be point out, that fish germ cell biology and biotechnology will continue to progress in the near future towards stable culture capable of genetic alterations, cryostorage and germline transmission. Recent progress in fish stem cell culture and transplantation will provide valuable systems and tools for basic research and applications in sustainable aquaculture in Ukraine.

METHODS FOR ISOLATION OF COLIPHAGES FROM NATURAL SOURCES

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In recent years, the problem of acquiring bacterial resistance to antibiotics is becoming increasingly important. Familiar common antibiotics that cured billions of people today are becoming less effective. This is due to the fact that many bacteria have developed resistance to the antibiotic drug. A promising alternative to antibiotics are bacteriophages - viruses that selectively infect bacterial cells. And antibiotics and bacteriophages act directly on microorganisms, antibiotics only affect not only pathogenic, but also the normal microflora, disrupting the natural balance, whereas bacteriophages act only on pathogenic microorganisms. This selective effect due to their nature. Encountering sensitive microbial cell, the phage penetrates her, switches the mechanism of its action on the reproduction of their kind, which, bursting the cell membrane attack other microorganisms. This process becomes spontaneous, and relief from unwanted microorganisms occurs in a matter of hours. An important property of phages is their specificity. Consider coliphages, coliphages - bacteriophage is capable of infecting E. coli and related bacteria it. Because viruses are more resistant to adverse environmental conditions, coliphages continue to manifest themselves even when the bacteria themselves - hosts anymore. Given the higher resistance of coliphages to unfavorable external environment, they are used as an additional indicator of the effectiveness of water, wastewater and groundwater protection . In addition, coliphages proposed as a screening measure possible presence of pathogenic enteroviruses. Definition coliphages may both direct and titration method. Treatment bacteriophages selectively acting is much better than the use of traditional broad-spectrum antibiotics that kill all bacteria that appear on their way and, thus, violate the natural microflora necessary for normal body functioning. But today, only in Ukraine a private limited company " Biopharma " (Kiev) has been producing bacteriophage preparations, namely produces staphylococcal bacteriophage. Today bacteriophages can be purchased in various dosage forms as phages administered to gels, they retain their viability, including gels, sprays. Besides, when phages severe diseases may be combined with various groups of drugs including antibiotics. Thus we see that with the widespread formation of antibiotic resistance in pathogenic bacteria need for new antibiotics and alternative technologies for the control of microbial infections is gaining in importance. Therefore, work on the development of dosage forms of bacteriophages which are conducted at the Department of Biotechnology of the National University of Pharmacy, are relevant.

THE STUDY OF THE SPECTROPHOTOMETRIC CHARACTERISTICS OF WINE MATERIALS IN STORAGE

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The possibility of coculture of *Saccharomyces cerevisiae* W 748 and *Lactobacillus plantarum* (strain A3 8P and 38) during the fermentation of grape juice for the production of red wine is studied at the Department of Biotechnology of National University of Pharmacy for prevention of the accumulation of malic acid, which gives a sharp taste wine. This one is characterized by so-called green acidity. With the transformation of malic acid into lactic, acidity and sharpness in taste of a young wine is reduced – it becomes softer and more harmonious. Previously, there were studies of changes in the number of microorganisms, total acidity and content of ethyl alcohol in the fermentation process.

Besides, one of the specific indicators characterizing the quality of red grape wine is the color of it. The color – is a comprehensive indicator of the chemical composition of wine (the amount of bound and free anthocyanins, which are natural antioxidants), which changes in the process of wine storage. One of the possible deterioration of color is oxidase browning, which affects low-acid young wine materials. In this case wine phenolics is oxidized, condensed and precipitated. The spectrophotometry is used in order to determine the intensity and color hue in wine-making.

At this stage the purpose of the research was to investigate the changes of spectrophotometric characteristics during the storage of wine which were obtained by using a pure culture of yeast and cocultivation *Saccharomyces cerevisiae* and *Lactobacillus plantarum*. The optical density and coefficient of light transmittance was defined at wavelengths of 420, 445, 495, 520, 550, 625 nm by means of spectrophotometer SF - 101. Then color hue and intensity was calculated.

Winematerials were kept during six months in the refrigerator at the temperature of 2-8°C, afterwards the above mentioned indicators were also identified.

The results of the research displayed an increase of optical density at 420 nm with a simultaneous decrease of this parameter at 520 nm, which is explained by transformation of coloring substances in the complex forms. The density at 520 nm is a characteristic indicator of absorption of individual anthocyanins and their changes are expressed in color intensity, in this case it is reduced.

The disappearance of individual forms of anthocyanins in testing wine materials is a result of their transformation into soluble and stable complex forms, thereby the wine retains an individual color.

Research results showed that regardless of the formation of complexes of anthocyanins in the wine materials, investigated objects retain intense ruby color after six months of storage, and color hue is much less than one, as in the case of co-culturing *Saccharomyces cerevisiae* and *Lactobacillus plantarum*, or using a pure culture of yeast. So, we can conclude that the combined use of lactic acid bacteria and yeast does not significantly affect the content of coloring substances in wine materials.

NECESSITY OF STUDYING OF ADHESIVE PROPERTIES OF PROBIOTIC PREPARATIONS

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At the present stage of development of the pharmaceutical market of Ukraine there is a problem to create new, national, complex probiotic preparations. Particular attention should be paid to the methods of monitoring of the specific activity of finished dosage forms. In the section of Analytical Normative Documentation (AND) "Specific activity", in addition to the required parameter for probiotic "The number of viable cells in a single dose of the preparation" the other parameters are also given that determine the therapeutic effect of the finished dosage form of probiotic. The range of positive characteristics of probiotic microorganisms and their favorable effect on the microorganism is distributed each year and accordingly the number of control parameters in the unit of AND "Specific activity" is increased.

One of these properties is adhesive activity, which is determined by various methods: microbiological, light and electron microscopy, biophysical and mathematical. The method with using of human erythrocytes as universal model of cells is the most affordable. There is a glykoforyn on the surface of erythrocytes – a substance that is identical to the glycocalyx of epithelial cells, on which the receptors for adhesins of microorganisms are located. There are two methods – express test method and detailed method, each of them are intended for the solution of the specific tasks. Express method is used for a rapid and simultaneous determination of adhesive properties of a large number of microorganisms' strains. The detailed (test-tube) method is intended to determine the dependence of the adhesion process from the cells properties of micro- and macroorganism and other factors. The degree of adhesion is analyzed in the light microscope. Adhesive properties are evaluated by the average value of adhesion (AVA) – the average number of microorganisms attached to one erythrocyte by counting at least 25 erythrocytes considering no more than five red blood cells in one field of vision. Depending on the value of the index AVA the adhesiveness is considered zero adhesiveness (0-1.0), low adhesiveness (1.01-2.0), medium adhesiveness (2.01-4.0) or high adhesiveness (over 4.0).

Except AVA the adhesion of bacteria is evaluated according to the following parameters: coefficient of the microorganism cells in the adhesion process (C) – the percentage of red blood cells that have adhesive microorganisms on their surface, index of adhesiveness of microorganisms (IAM) – the average number of microbial cells on one erythrocyte involved in the adhesive process.

Adhesion of bacteria to human tissue surfaces is an important initial stage of infection, so the competition for the tissue receptors with pathogens could be the first probiotic effect. Adhesive strains play one of a key role in a probiotic therapy. Therefore it is necessary to determine adhesive properties of probiotic strains before developing of preparation on their base.

FILTRATION IN BIOTECHNOLOGY

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The final stage of any microbiological production is the isolation of the desired product (cell biomass or a product of cell metabolism) from the culture medium and its purification. In most cases, before extraction of the desired product, which is inside the cell, it is necessary beforehand to break this cell. However, this process is not convenient to carry out directly in the culture medium drawn from the fermenter, and with the concentrate after removal of the cell culture fluid. Therefore, regardless of the location of the desired product, the first stage of the isolation of most products of microbiological synthesis is the separation of microbial biomass producers from the culture medium. Thus, various methods can be used depending on the type of microorganisms.

For the separation of bacterial cultures filtration with using various types of filters (vacuum filters, nutsch filters, belt filters, drum filters, chamber filters) are widely used. Filtration of the bacterial suspensions is associated with great difficulties arising from the small size of cells, high viscosity suspensions and the large amount of impurities microparticles, so the development of new and improvement of existing designs filters and filter occurs constantly.

Today there are widely used filters based on fluoroplastic. Fluoroplastics – the name used in industry for any one of a series of fluorine-containing plastics, which are homopolymers of fluorine derivatives of ethylene or copolymers of ethylene fluorine derivatives and, for example, fluoroolefins, olefins, or perfluoroalkyl vinyl ethers. The most important are polytetrafluoroethylene (PTFE), which accounts for 85 percent of the world production of fluoroplastics, and polychlorotri-fluoroethylene (PCTFE). Both are white, crystalline substances that exhibit good chemical and thermal stability, good resistance to cold, weatherproofness, nonflammability, and a number of valuable physical properties. These filter elements with different porosity to liquids and gases (including aggressive) have widest range of applications (energy, oil refining, engineering, electrical, chemical, light, medical, food industries). They are used for filtering of: oils, fuels, acids, alkalis, food, drinking water, medicines, biological media. However, despite these attributes, perhaps the most desired characteristic of this group of plastics is their ability to resist abrasion. Simply stated, here is a chemist's explanation for this unique property: A tightly bonded, impenetrable shield of fluorine atoms surrounds and protects an interior chain of carbon atoms. Unlike other materials, whose molecules lock into each other then break off when sliding takes place, these molecules have very little attraction for other substances. So today at the Department of Biotechnology of NUPh and the Department of Materials Technology of NTUA it is carried out work about possibility the use of porous materials based on PTFE for use in biotechnology.

PROSPECTS OF USING REPRESENTATIVES OF BLUE-GREEN ALGAE IN THE COMPOSITION OF NUTRIENT MEDIA FOR YEAST

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In our time, the problem of finding new components of culture media for cultivation of microorganisms is actual. Every year the production of yeast is growing and there is a need to look for more effective nonfood components with low additional of cell mass. The most important biological growth factors of microorganisms are niacin, thiamine, riboflavin, pyridoxine, biotin, diankobalamin, paraamino benzoic acid, folic acid, choline, hemin (factor X); purine and pyrimidine bases (adenine, guanine, xanthine, hypoxanthine, cytosine, thymine, uracil), amino acids triptofan, lysine, choline, glutamic acid, arginine, methionine, valine, leucine, threonine, histidine, phenylalanine, etc.

In that time the ubiquity of algae in nature and abundant, and sometimes massive, their development in different types of reservoirs on terrestrial substrates and soil determine the importance of these plants, both in everyday life and in his business. Nevertheless, the practical use of algae has not been exhausted, and scientists occur research of new applying these ones.

Algae are lowly plants that don't have true roots, leaves and stems. Today they are used for growing higher plants and fungi. They have a very peculiar chemical composition and contain large amounts of vitamins, mineral compounds and proteins, which in turn are characterized by a wide range of replaceable and essential amino acids. Spirulina and chlorella are representatives of blue-green algae.

Chlorella - a unicellular green alga of Chlorophyta. This alga actively produces proteins, carbohydrates, lipids, vitamins and usually dry biomass of chlorella contains 40-55% protein, 35% carbohydrates, 10.05% lipids and 10% of mineral substance. The protein of chlorella comprises more than 40 amino acids, including all essential them. Macro- and microelements of chlorella are: calcium, phosphorus, magnesium, potassium, copper, iron, sulfur, zinc, cobalt, manganese, zirconium, rubidium and others. It accumulates a lot of iodine. Approximately 80% of the total fatty acids of chlorella are unsaturated fatty acids which are precursors of prostaglandins.

Spirulina is a blue-green multicellular spiral algae kind of Arthrospora. It is used It includes 60-70% protein which is very easily absorbed. Coefficient of digestibility reaches 65-80%. Furthermore, spirulina contains 18 kinds of amino acids that are essential (valine, isoleucine, leucine, and others). This algae contains vegetable fats with a predominance of unsaturated fatty acids, vitamins, lots of micro-and macronutrients.

Therefore, dietary supplements from these algae can be used for the nutrient media for promoting the growth and development of various microorganisms. Now at the Department of Biotechnology National University of Pharmacy the study the effect of different concentrations of additional components of nutrient media containing spirulina and chlorella on growth properties of yeast *Saccharomyces cerevisiae* are conducted.

EM-TECHNOLOGY IN CROP PRODUCTION

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Currently, there is depletion of soil fertility, as evidenced by decrease in productivity of major crops.

EM-technology based on the use of beneficial microorganisms, called effective microorganisms (EM) and presented in Ukraine in the form of bio-fertilizer "Baikal EM-1 U", which produced by "EM Centre Ukraine" in Kharkiv region in Lipty, can restore soil fertility and increase yields of cultivated plants.

This is stable composition which, when applied to the soil shows a high positive activity, expressed in increasing the population of beneficial microorganisms, in the suppression of pathogenic microorganisms, in rapid mobilization of nutrients in easily digestible form for plants, in rapid growth and cultivation of plants and as a result increases productivity of plants. "Baikal EM-1 U" - a symbiotic community of microorganisms, which proved very effective in many branches of agriculture and successfully used in many countries.

The substance "Baikal EM-1 U" is formulated with about 60 strains of microorganisms. They support each other; so long live in the soil. In concentrate microorganisms are dormant and need a culture medium for their activation. The major groups of microorganisms which are part of this substance include: photosynthetic bacteria, lactic bacteria, yeast, actinomycetes.

But all these favorable changes occur only in the presence of organic substances in soil, some of which used by microorganisms for their own power supply. It should be noted that the activity of microorganisms in general, including beneficial microorganisms depends on many factors of the environment: the presence of moisture, the positive temperature, optimum of the reaction (pH), salt concentration, the presence of radionuclides in the soil.

Benefits of applying EM-technology: not harm the environment; doesn't require high economic costs; effectively restores soil fertility due to processing of organic matter, which increases the amount of nutrients readily available to plants substances; restrains proliferation of harmful microorganisms; accelerates fruiting plants by creating friable soil structure, which retains heat better.

At the Department of Biotechnology in The National University of Pharmacy it is carried out research whose purpose is to study the composition and activity of the preparation "Baikal EM-1 Y".

STUDY OF ANTIMICROBIAL PROPERTIES OF CERTAIN SPECIES OF HIGHER SAPROPHYTIC MARINE FUNGI

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In the modern world there is a necessity in bioactive substances, widely used in pharmaceutical, food, agricultural and many other industries.

The perspective direction is their search among the natural sources, in particular among the representatives of marine microorganisms – microfungi, that responds to living conditions of these microorganisms. A world ocean is the habitat of enormous amount of life-form, existing in the conditions of extreme pressure, pH and temperature. Therefore, coexisting with the different forms of life, marine microorganisms are able to product substance with unusual structure and properties which are not met at terrestrial kinds, and potentially can show antimicrobial properties.

In the region of the Black sea the distribution of marine fungi on large taxon of reign of Fungi corresponds to general law of taxonomical structure of fungi in the World ocean, so qualitative and quantitative composition of mycocomplex is the indicator index of the ecological state of the region. For this reason mycologies of the Odessa Branch of the A.O. Kovalevsky Institute of Biology of the Southern Seas National Academy of Science of Ukraine have conducted the screening of bioactive compounds in more than five thousand marine isolates of bacteria and in more than three thousand marine fungi-micromycete. In this direction the higher marine fungi of the Black sea are studied well enough.

From more than 80 selected and studied kinds, for our aim such traditional kinds for the region of the Black sea as *Arenariomyces trifurcata*, *Ceriosporopsis halima*, *Corollospora maritima*, *Halosphaeriopsis mediosetigera*, *Nia vibrissa* have large interest. These types of marine organisms were provided by Odessa Branch of the A.O. Kovalevsky Institute of Biology of the Southern Seas National Academy of Science of Ukraine after collection of water samples, bed silt, cellulose containing substrates, selection and preparation of pure cultures by the method of accumulation in the form of carposomes of ascomycetes and basidiomycetes which can be stored for 3-5 months in sterile sea water.

Kinds of *Arenariomyces trifurcata*, *Ceriosporopsis halima*, *Corollospora maritima*, *Halosphaeriopsis mediosetigera* refers to the Ascomycota (ascomycetes or

cap fungi), class of Sordariomycetes, order of Halosphaeriales, family of Halosphaeriaceae. The fifth organism – *Nia vibrissa* – refers to the Basidiomycota (basidiomycete or basidium fungi), class of Agaricomycetes, order of Agaricales, family of Niaceae. Along with ascomycetes basidiomycete refers to the higher fungi.

The investigation of the Ascomycetes by a lot of scientists has shown that there are great variations in the morphology and development of both fruit bodies and reproductive organs, and a sharp distinction may be made as to whether the sexual organs, associated with ascocarp formation, occur singly or in groups.

At our microscopic study of Halosphaeriaceae family types it was mentioned the presence of fruit bodies (ascocarp) – a perithecium, containing prototunicate asci with sporules. Perithecium appears on the surface of understratum or partly submerged in it. They are small, round or pear-shaped, often with a long proboscis which is several times more than the diameter of perithecium. Covers of asci which are contained in an ascocarp, – peridia– lyse, and ripen perithecium contain ascospores, submerged in mucus. While swelling of mucus ascospore go out from a perithecium through the narrow opening on the top in the form of mucous drops or long mucus cords. Ascospores are two-celled with sprouts, amount and the location of which depend on the type of ascomycete. *Nia vibrissa* is characterized by the presence of spores in club-shaped structures – basidia.

On this stage of work the study of antimicrobial activity was conducted by the method of joint cultivation of the probed marine fungi with test strains of microorganisms in a liquid growth medium and by the method of diffusion in an agar (by the method of «wells»).

The results of the experiment to study the antimicrobial activity by the first method have shown that the number of series of test strains of microorganisms in the control cultures was 2-5 times more than while co-culturing with marine fungi. Antimicrobial activity, studied by the second method was not detected for any species that may be caused by a variety of nutrients components and temperature conditions which are necessary for growth and reproduction of fungi studied and test strains of microorganisms.

We are planning to repeat these experiments for a longer period of cultivation, we continue to develop new methods for determining of antimicrobial activity of higher marine fungi, taking into account the different culture conditions for the studied species of fungi and test strains (temperature, pH), the different nutritional needs, different terms of cultivation.

THE STUDY OF THE STABILITY OF THE MICROFLORA FERMENTS "SIMBILAKT" AND "BIFIVIT" TO DIFFERENT GROUPS OF ANTIBIOTICS

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Currently the interest in the intestinal microflora and its role in support and prevention of human health is increased. Intestinal microflora has a huge potential and metabolic and performs hundreds of biochemical processes. According to the World Health Organization, each year up to 30% of the population in industrialized countries are exposed to diseases of the gastrointestinal tract of various etiologies. Changing the quantitative and qualitative composition and enzymatic properties of the intestinal microflora leads to dysbiosis. Recent studies have shown that the expression of dysbiotic disorders are more common not only in children but in adults, they are associated with poor compliance nutrition and widespread use of antibiotics, hormonal, immunosuppressant, enveloping, laxative, choleric and other medications, stress and adverse environmental conditions. One way of correcting and preventing dysbiotic disorders is use of functional foods cooked on the basis of live bacterial starter cultures. Today in Ukraine sourdough Vivo widespread, they are produced GP "Institute of Technology bacteria ferments milk and meat "Alba Timm" and they were the objects of this study. "Bifivit" and "Simbilakt" - sourdough fermented drinks recommended for correction of the microflora of the gastrointestinal tract, contain the following types of microorganisms: *Acetobacter aceti*, *Lactococcus lactis* subsp. *diacetylactis*, *Lactococcus lactis* subsp. *cremoris*, *Lactococcus acidophilus*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, *Propionibacterium freudenreichii*. The purpose of this study was investigation of the resistance of some sourdough microflora to different groups of antibiotics, namely, semisynthetic penicillins, polyene, biosynthetic penicillins, carbapenems, aminoglycosides, lincosamides, imidazole derivatives, polyenes, macrolides, rifamycins, tetracyclines, triazoles, cephalosporins, cephamycins, semisynthetic cephalosporin III generation, cephalosporins. «Method of disks» was used to determine the resistance of microorganisms to antibiotics. In the first stage, the microorganisms were in liquid beef-broth nutrient medium (water meat peptone, sodium chloride), they were cultured 18-24 hours at temperature $37\pm 2^{\circ}\text{C}$. After inoculation, the microorganisms were sown on the surface of dense nutrient medium MRS (dry enzymatic peptone, sodium chloride, meat extract (meat cattle)) in a Petri dishes and there paper disks impregnated with the appropriate antibiotics at a concentration of 1 mg/ml were placed. After culturing in an incubator at temperature $37\pm 2^{\circ}\text{C}$ for 48 hours the resistance of microflora ferments to these types of antibiotics was evaluated by the presence of zones around colonies stunting discs.

Research results showed that these sourdough resistant to antibiotics: amphotericin, penicillin, vancomycin, kanamycin, clotrimazole, metronidazole, nystatin, fluconazole. Therefore dairy products based on sourdough "Simbilakt" and "Bifivit" can be recommended for using during antibiotic therapy.

PROSPECTS FOR THE USE OF BACTERIOPHAGES IN COSMETOLOGY FOR THE PREVENTION OF SKIN DISEASES

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Nowadays the most common diseases are the diseases of bacterial etiology; for instance acne, plegmons, dermatitis etc. The main reasons which cause bacterial skin infection developings are violation of the integrity of the skin barrier function, skin biocenoses peculiarities which are formed on the back ground of different dermatosis decrease in the activity of immune reactions, diabetes mellitus, severe somatic diseases,irregularities in the hormone system, psychological and mental stresses,violation of the diet, taking some certain medications, using inappropriate cosmetic. Every cosmetic procedure associated with the use of invasive techniques, such as pilling, injections and different kinds of polishing, has a risk of infectious complications. Skin is one of the most important organ of the human body. That,s why it's diseases like acne bring not only esthetic defects but also psychological discomfort. Diseases also prevent skin to perform its functions. Use of antibiotics in the treatment of those diseases is to no purpose (impractical) due resistance of microorganisms to antibiotics. So the new methods of treatment are needed to cope with illnesses successfully here in after. As claimed by immunologists the use of bacteriophage will become the panacea for diseases. The pathogens are Pseudomonas, Proteus, Klebsiella, Enterobacte–riaceae, Staphylococcus, Streptococcus. The bacteriophages are natural alternative to antibiotics. In serious diseases phage can be combined with various medications, antibiotics including, they are not toxic and don't have any contraindications. Their advantage lies in the fact that they have the immunostimulation effect and can be used as the prevention of infections. The drugs with bacteriophages cause the death of a certain kind of bacteria here with they don't affect the normal flora. The efficiency of these instruments to causative agents of septic diseases is about 75-90%, what is a fairly high rate. Today there is a limited list of drugs with bacteriophages which are especially used in cosmetology. In the Ukrainian market the are drugs with bacteriophages in soft dosage forms used for treatment and prevention of dermatological diseases: "Phagoderm" - a powerful anti-inflammatory and disinfectant for skin (Ltd. SPC 'MicroMir', Russia) which include phages to Staphylococcus aureus, Staphylococcus epidermis, Pseudomonas aeruginosa, Acinetobacter baumannii, Esherichia coli, Streptococcus pyogenes; "Bactériophage Staphylococcous" - the ointment for treatment and prevention of inflammatory diseases (FSUA 'Imbio', Russia) which include phages to Staphylococcus aureus, Staphylococcus epidermis; "Gel-balm With Bacteriophages" - eliminates harmful bacteria, provides rapid healing of injuries, restores the normal flora of the skin ("MIRRA", Russia) which include a concentrate of bacteriophage. The medicine with bacteriophages is only one in Ukraine it is produced by "Biopharma"(Kyiv). Now at the Department of Biotechnology development of compound and the technology of soft drugs containing bacteriophage afor use in cosmetology are conducted.

BIOSKIN - A REVOLUTIONARY DISCOVERY

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Breakthroughs scientific thought occur in many different areas of life, but especially in medicine they are dazzling. It gives hope for healing and near vision of longevity. For example, in transplantation on the basis of new biotechnological developments, this skin can be used for developing tissue and organ engineering. Medical ambitious task is create organs and tissues based on biomaterial. On one of them, scientists have successfully coped – invented and introduced into production bioskin – an artificial material, which helps in the treatment of terminally ill patients.

Designed biomaterial (Bioskin “Hyamatrix”), in contrast to its international counterparts has a high biocompatibility, clinical effectiveness and optimal bioengineering properties. This biomaterial is used at an affordable price for a wide range of consumers. Bioskin “Hyamatrix” won the Zworykin Award 2009 in the category “Innovative Product”.

The aim of this work is acquaintance with the concept of “bioskin” history of the invention, the technology for obtaining the present invention and the scope of such a progressive opening.

Hyamatrixbioplastic material, or bioskin is an unique development of the Russian scientist, based on hyaluronic acid – the main component of the intercellular skin. It is finished with scars from burns, scars and wrinkles. Orenburg Bioskin G-DERM, can replace human skin, recognized as the best of biomedical innovation. An unique development of Orenburg furor in the international community of scientists and put plastic surgery on the threshold of revolutionary breakthrough. The Hyamatrix bio-skin is a bio-plastic material produced by the photochemical nano-structuring of the starting hydrocolloid of the hyaluronic acid. The bio-skin and the innovation in it are the basis of the Hyamatrix cosmetic series. The hyaluronic acid is able to absorb a big volume of water for its molecules form a grid shape. The scientists of the State University of Orenburg set a purpose to produce a bio-material from the hyaluronic acid that looks like an elastic plate (matrix) and has optimal bio-engineering features. To meet this purpose the scientists have chosen the photochemical nano-structuring in order to establish the nano-framework of the macro-molecules.

Scientists plan to improve bioskin second generation, which will be used in many fields of science worldwide.

STUDY BACTERIAL STARTERS USED IN THE PRODUCTION OF FERMENTED MILK PRODUCTS

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It is difficult to overestimate the role of dairy products (fermented milk products, FMP) in human nutrition. They are among the most important components of a balanced diet and bioactive substances for the prevention and treatment of various diseases. FMP have great importance for babies and for older age groups, especially the weak, suffering from gastrointestinal and other diseases. In recent years in Ukraine bacterial starter cultures, on which at home you can produce delicious and healthy products (kefir, yogurt, cottage cheese, sour cream, etc.), have become very popular. The value of such products is very important for Ukraine, in which a significant portion of the population lives in ecologically unfavorable regions, works in conditions of poor and unbalanced nutrition, and are under harmful physical and other detrimental effects. Therefore, the aim of our study was to investigate the effectiveness of domestic bacterial starters “Yogurt VIVO” and “Acidolact VIVO”, as functional food products.

Composition of starters is studied by using differential diagnostic method of Gram’s stain. The microscopic preparations which are received show the presence of lactic acid cocci and rods. The next step was to study microflora antibiotic resistance of ferments using the disk diffusion method. The results of the study showed that the microflora of ferment “Acidolact VIVO” is stable to all the studied antibiotics. The microflora of ferment “Yogurt VIVO” is undersensitive to tetracycline, sensitive to bacitracin and highly sensitive to oleandomycin and erythromycin. These results confirm the possibility of using information about the FMP on the basis of the ferment “Acidolact VIVO” during antibiotic therapy. Whereas the drinks based on “Yogurt VIVO” are recommended to use after the therapy completion to restore the normal microflora of the gastrointestinal tract of humans. The following step was to prepare the FMP yogurt and acidophilus milk according to the manufacturer’s instructions, and to control their organoleptic and physico-chemical parameters. The results show the correspondence of the indicators to standard values. Although it should be noted that for Acidolact has a sourer taste which is the result of formation of larger amounts of organic acids during the fermentation. Thus, we see that the application of the FMP based on the bacterial starter cultures is an effective method of prevention and treatment of dysbiosis occurring as an accompanying factor of using antibiotics in the treatment of infectious and inflammatory diseases.

THE PROBLEM OF TREATING HYPOTHYROIDISM

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Hypothyroidism is a disease resulting from partial or total loss of function of the thyroid gland and, as a consequence, lack of thyroid hormones in the body. The most common cause of primary hypothyroidism is autoimmune thyroiditis, which leads to a decrease in the dynamic activity of the thyroid gland. In most cases it is also have the ability to blockade gland functions, influenced by large doses of thyreostatic preparations during the treatment of hyperthyroidism.

Hypothyroidism is the most common endocrine pathology after the non-insulin diabetes. The overall prevalence of it is from 3 to 8 %, and with the subclinical forms – from 10 to 12 % of the world population, and in recent years there has been a steady growth of this disease in young and middle-aged. Women, especially those older than age 60, are more likely to have hypothyroidism. Hypothyroidism upsets the normal balance of chemical reactions in the body. It seldom causes symptoms in the early stages, but, over time, untreated hypothyroidism can cause a number of health problems, such as obesity, joint pain, infertility and heart disease. in addition to the above, the development of new approaches and the search for effective means to restore thyroid function are needed. For the treatment of hypothyroid conditions synthetic derivatives of levothyroxine (LT4), herbal at alias are used extensively.

But recently to treat many diseases, including hypothyroidism, placenta extract are effectively used. Now it has worldwide recognition. Application of tissue therapy helps normalize pathological processes in the body. The advantage of using tissue and cell biological products is the replacement or restoration of function of the affected organ. Biologically active substances which are included in their composition can influence the metabolism of various components on the cellular level as well as the whole body. This is especially true as the number of diseases associated with an increase in immune and endocrine deficiency increases.

Nevertheless, we can distinguish the fact that sufficiently wide study biological properties of preparations placenta, their influence on the course of various diseases remain open. There are questions about influence of the therapy with placenta preparations on the correction process of thyroid pathologies with a history of hypothyroidism. Today these questions aren't resolved and it is subject of targeted and scientific research.

DISCOVERY AND PROPERTIES OF BACTERIAL AGENTS

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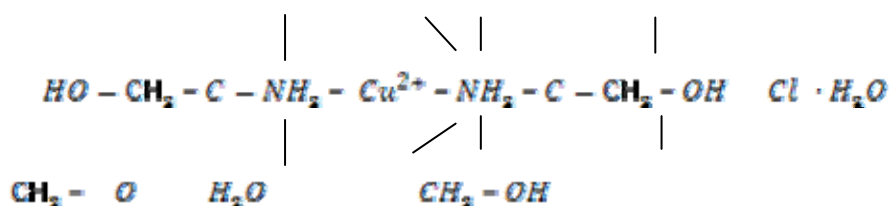
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A method of obtaining an antibacterial agent that includes the processing of tris- (oxymethyl)-aminomethane by cuprous chloride (II) solution has been developed. Fusion reaction is performed at a molar ratio of cuprous chloride (II) to tris- (oxymethyl)- aminomethane 1:2,5-1:4,5 aqueous medium at room temperature. The obtaining of an antibacterial agent involves tris-(oxymethyl)-aminomethane, solution of cuprous chloride (II), and distilled water, washing and filtration means of its crystals: alcohol, acetone or other polar solvent, ceramic filter, vacuum forming and mixing equipment.

According to the chemical analysis of Cu (17), C (25,93), H (6,23), N (7,58), Cl (9,52) received antibacterial pharmacological agents had the following formula: $[\text{Cu} \cdot (\text{Tris}) \cdot (\text{Tris-H}) \cdot \text{H}_2\text{O}] \cdot \text{Cl} \cdot \text{H}_2\text{O}$, де Tris-NH₂C(CH₂OH)₃

By electron, infrared spectroscopy and X-ray analysis structural formula of antibacterial pharmacological agents has been established:



Antibacterial properties of the agent were investigated in a series of microbiological tests, which involved more than 50 strains of microorganisms, including carriers of Escherichia coli and Bacillus aeruginosa, Enterobacteriaceae, coccal flora, etc. Nutrient solutions, such as meat infusion and lactose infusion and blood agars were involved for cultivation of strains. Received solutions of the agent investigated were added to the molten agar. Diurnal cultures of selected strains were serially dissolved in physiological sodium chloride solution, and the initial concentration of microbial cells in these solutions were detected using standard turbidity scales. Using replicator obtained suspension were inoculated on nutrient medium, containing agent investigated at various concentrations and incubated at 37 °C over the time of twenty four hours in an thermostat. Based on the results of inoculation growth (%) it can be concluded that 1 g/l of the agent provides minimal antibacterial effect, and 8 g/l - a complete inhibition of all microorganisms growth studied.

RESEARCH ADHESIVE PROPERTIES OF STARTER FOR PRODUCTION OF FUNCTIONAL FOOD – COTTAGE CHEESE

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At the end of 1980s, new tendency in the food industry, based on production of functional food, had been appeared and developed in the world. This term means systematic use of products of a natural origin which are capable to normalize and regulate separate functions and biochemical reactions both certain bodies and systems, and an organism as a whole. Today among them starters for preparation of cultured milk products in house conditions are wide popular. In the Ukrainian market it is possible to meet starters of such trademarks as "VIVO", "GoodFood", «GENESIS". The main indicators of quality of starter are activity that is controlled by fermentation duration and acidity, purity of starters and a ratio between cultures (qualitative and quantitative structure), existence of foreign microflora, organoleptic indicators of a clot.

The aim of this paper was to study of adhesive properties of the microorganisms which are a part of starts. This indicator isn't included in the standards regulating creation and production of starters, but it is important for determination of efficiency of action of a cultured milk food on its basis as thanks to this property probiotic industrial strains are capable to compete with pathogenic bacteria for binding receptors. Therefore, the criterion of selection of starters forming part of functional food, for their effective action, except high antagonistic properties, should be evaluation of indicators adhesion. As object of research bacterial starter "Cottage Cheese VIVO cultured milk products" of the trademark "VIVO" was chosen. Adhesive properties were studied using an express method on human erythrocytes as universal model of cells of a macroorganism. Adhesive properties of cultures were estimated on the average value of adhesion (the average quantity of microorganisms attached to one erythrocyte at calculation not less than 25 erythrocytes, considering no more than 5 erythrocytes in one field of vision), and the index of adhesiveness of microorganisms (average quantity of microbic cells on one erythrocyte, participating in adhesive process).

Study of adhesion of microorganisms of starter "Cottage Cheese VIVO cultured milk products" showed existence low- and the medium-adhesive strains. This fact shows that producers don't consider ability to adhesion of microorganisms under designing starters for production of cultured milk products that allows recommending this criterion as a necessary under selection of starter strains.

EFFECTS OF PROBIOTICS ON THE CHOLESTEROL LEVEL IN BLOOD

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Cardiovascular disease - the main cause of death and disability among the population, causing the greatest social and economic losses . The most common and significant causes are high blood pressure and elevated cholesterol levels (Cholesterol - lipid is present in the blood and most tissues of the human body, especially in the nervous tissue.).

In recent years, accumulated a significant amount of data that resident and transient flora host, synthesizing, transforming or destroying exogenous and endogenous sterols actively involved in cholesterol metabolism. This allows us to consider as the most important host microflora and metabolic regulator involved in cooperation with host cells in maintaining cholesterol homeostasis.

The analysis of literature data about biologically active compounds produced by probiotic microorganisms showed that hitherto biotechnological potential of anaerobic microorganisms of bifidobacteria, lactobacilli and propionic acid is almost never used. Lactobacills long time attracted the attention of biotechnologists in view of their potential significance for the preservation of health, prevention and treatment of many diseases.

An increasing number of publications about the ability of certain strains of lactobacilli exhibit hypocholesterolemic effect. Numerous clinical studies have shown a positive effect in reducing the cholesterol level in blood serum by the probiotics consisting of following bacteria: *Lactobacillus fermentum*, *Lactobacillus reuteri*, *Lactobacillus rhamnosus*, *Lactobacillus plantarum*, *Lactobacillus bulgaricus*, *Lactobacillus brevis*, *Lactobacillus casei*, *Lactobacillus gasseri*, *Bifidumbacterium bifidum*, *Bifidumbacterium lactis*, *Bifidumbacterium longum*, *Streptococcus thermophilus*.

Relevance of research in the field of microbial ecology, the study of cholesterol metabolism probiotic microorganisms determined by the necessity of creating bio mass consumption to maintain and preserve the health of the population who make a worthy competition medicines. On the basis of the above, at the Department of Biotechnology National University of Pharmacy study the effect of some probiotics on cholesterol levels in the blood serum, and possibility of use for these purpose functional foods are planned, that testify to consider this approach as a promising alternative direction of the hypercholesterolemia pharmacological treatment.

RATIONALE FOR OPTIMUM INACTIVATION METHODS FUNGAL CELLS CANDIDA ALBICANS AND CANDIDA TROPICALIS

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Number of patients with candidiasis in humans and animals has increased dramatically in recent years. Candidiasis is caused by yeast fungi *Candida*. The increase in the incidence of candidiasis associated with irrational use of antibiotics, hormones, steroids, immunosuppressants and other drugs. Candidiasis is manifested in different forms. The greatest danger is posed by systemic and visceral candidiasis. These forms of candidiasis are difficult to treat with modern medication. Urgent need is to develop a vaccine based on the fungi of the genus *Candida* for the prevention and treatment of *Candida* infections.

This article was researched physical, chemical and physico-chemical methods of inactivation of the fungal cell *Candida albicans* and *Candida tropicalis*. The study used a suspension with a concentration 8×10^8 - 8×10^9 in 1 ml of fungi *Candida albicans* strain CCM 335-867 and 8×10^8 - 8×10^9 in 1 ml of fungi *Candida tropicalis* strain ATTC 20336. Physical methods described below. Cells treated separately mushrooms temperature of 50 ± 2 °C for 1 hour in a volume of 100 ml with constant stirring with a stirrer speed of 100 rev/min. The chemical method described below. Formalin was added to the suspensions at a concentration of 40%. The final concentration of formaldehyde in the suspensions was 0.5%. Stirred stirrer speed of 100 rev/min for 5 min and the suspension was kept overnight at 25 ± 2 °C. Physico-chemical method is to combine the above methods.

On Sabouraud nutrient media after cultivation of cells inactivated by natural fungi were found growing colonies of fungi *Candida albicans* 12-17 and 10 *Candida tropicalis* - 15 colony forming units and after chemical methods - *Candida albicans* 9-14 and *Candida tropicalis* 7-12 colony forming units and after physical and chemical methods - have been found growing colonies of fungi. It is likely that the temperature of 50 ± 2 °C is not sufficient to stop cell activity of fungi, and the use of higher temperatures may lead to the weakening or loss of immunogenic properties of fungi. For inactivation of fungi by chemical method is necessary to increase the concentration of formalin, but it can weaken the immunogenic properties of fungi.

According to the obtained results, it was found that the physico-chemical method provides complete inactivation of cells and fungi *Candida albicans* *Candida tropicalis*.

MEDICINAL PROPERTIES OF VEGETABLE CROPS AND THE POSSIBILITY OF THEIR CULTIVATION IN THE IN VITRO

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Medicinal properties of food plants are determined by the presence of active substances, which, unlike synthetic analogues "conflict-free" are included in the processes of human life, and therefore less dangerous in pathological processes. Therefore, edible plants, not just products on our table, but also an invaluable storehouse of useful and medicinal substances, which are key to beauty and health. Edible plants, along with the drug, may be used for the treatment and prevention of various diseases, and can serve as raw material not only edible parts of plants, or otherwise, and the whole vegetable entirety. Intensification of vegetable production to increase production of valuable products sets high requirements to grades hybrids. To consolidate the relevant signs and rapid multiplication of valuable material in the last 10 years been widely and effectively used technology of cultivation of plant cells, tissues and organs in vitro, which was transformed into a complex and large-scale industry of experimental biology. In addition, recent advances in cell mutagenesis and genetic engineering are largely determined by the development of culture methods. Reproduction of vegetable crops in vitro method for conducting a major breeding and seed works. From traditional methods of plant propagation micro cloning has some peculiarities : a) providing a large number of copies with minimal raw material, b) give, depending on the purpose of the study, genetically homogeneous material and somaclonal variants, c) the possibility to choose in vitro plant material with features that interest researchers, and, d) the possibility of obtaining disease-free seed, and e) the opportunity to lead the reproduction of plants throughout the year, as their growth and reproduction in vitro virtually independent of seasonal changes. That such and other techniques and technologies are successfully used in biotechnology laboratories of the Institute of Vegetables and Melons NAASU. The aim of our study was to introduce the detailed basic vegetable medicinal plants in vitro at the base of the institution. Established that crops such as onions, shallots, garlic, peppers, cabbage successfully cloned from meristematic fabric of different zones. Provide good results for the formation of homemade explants of regenerated plants of tomato, carrot roots are obtained by regeneration of somatic embryos ginogennyh callus carrots, etc. However, a range of vegetable crops is huge - more than 1,200 species – and biotechnologists task is not only to develop technologies to produce them under in vitro, but the widespread adoption of these technologies in practice.

SOVEREIGN IMMUNITY - BASE NEW BIOTECHNOLOGY

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Recently found that cells of higher mammals, including humans, have specific genes coding for intracellular autonomous functioning protection factors. These proteins are carried out effectively protect cells from viruses, but it does not fit into the classical schemes of the innate and adaptive immune system.

Already it is identified 28 cell protective factors affecting the different stages of the HIV (human immunodeficiency virus) life cycle. Scientists propose to call this first line of defense against viral aggression sovereign immunity.

Researchers can assume that sovereign immunity is not yet identified part of inducible innate immune system, as in some tissues launch gene expression factors sovereign immunity still depends on the modulating effects of type I interferon.

Inhibition of interferon signaling pathways or Toll-receptor activation by cellular factors IRF (interferon-gamma-induced interferon regulatory factor), STAT (signal transducers and activators of transcription) proteins or NFκB (nuclear factor-κB) proteins – this is a common mechanism by which viruses escape from the action of mammalian innate immunity.

In biology, immunity is the state of having sufficient biological defences to avoid infection, disease, or other unwanted biological invasion. It is the capability of the body to resist harmful microbes from entering it.

Immunity involves both specific and non-specific components. The non-specific components act either as barriers or as eliminators of wide range of pathogens irrespective of antigenic specificity. Other components of the immune system adapt themselves to each new disease encountered and are able to generate pathogen-specific immunity.

In recent years opened a new form of immunity, a new branch of innate immunity – sovereign immunity, which is responsible for an autonomous, private cellular immunity, aimed primarily at the protection against retroviruses.

Modulation factors sovereign immunity using biotechnological methods, off viral genes antagonists using antisense and si-RNA (small interfering ribonucleic acid) will develop new approaches to combat viral infections.

New knowledge about the mechanisms of immune protection may be the basis for developing a new generation of biotech products.

IMPROVEMENT OF THE MEDIUM COMPOSITION FOR THE DELUTION OF RAM SPERM

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Known different medium compositions for the delution and freezing sperm of rams including in its membership disaccharides (sucrose, lactose), polysaccharides (dextrin), chicken egg yolk, tris (hydroxymethyl) aminomethane, trilon-B, acacia, glycerol.

However, these media do not possess sufficient cryoprotectant effect, which leads to the formation of ice crystals destroying membrane integrity, reduced activity of sperms.

As a component of an improved synthetic medium was proposed more effective natural extracellular cryoprotectant animal origin, which neutralizes the harmful effects on sperm deep freeze - bone glue.

This aim is achieved by increasing the duration of the conservation of biological full ram sperm cryopreservation after vledstvie structuring of water around the sperm cell dehydration, lower the freezing point of water and salt crystallization.

For bone glue (collagen) content characteristically high proteids glycine (26%) , proline (14%), hydroxyproline (12%) and 2% polysaccharides. Bone glue having a high molecular weight - 300000 , for inclusion in the composition does not substantially change media osmolality even with significant (20-25%) concentration. In aqueous solutions, bone glue absorbs water, forms several types of gels.

The protective effect of bone glue comprising constructed in synthetic medium is shown that it promotes dehydration sperm and vitrification water absorption directly around them protects sperm from contact with ice crystals greatly reduces the eutectic point of the salts.

Synthetic medium for the cryopreservation of sperm dilution of sheep bone glue contains the following ratio of ingredients , wt . %: lactose 6.0, bone glue 1.8, 0.18 xylitol, tris (hydroxymethyl) aminomethane 0.07, trilon-B - 0.1, glycerin 4.3, chicken egg yolk 14.2 , distilled water 100.

Thus, the proposed medium has higher protective properties in comparison with medium containing dextrin, increases the biological usefulness of semen during cryopreservation and thawing.

PROSPECTS OF DEVELOPMENT OF NEW HERBAL DRUGS

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Plants are important sources of medicines and presently about 25% of pharmaceutical prescriptions contain at least one plant-derived ingredient. In the last century, roughly 121 pharmaceutical products were formulated based on the traditional knowledge obtained from various sources.

Plant derived drugs came into use in the modern medicine through the uses of plant material as indigenous cure in folklore or traditional systems of medicine. The world is now moving towards the herbal medicine or phytomedicines that repair and strengthening bodily systems (especially the immune system, which can then properly fight foreign invaders) and help to destroy offending pathogens without toxic side effects.

Over 80,000 species of plants are in use throughout the world. In India around 20,000 medicinal plant species have been recorded, but more than 500 traditional communities use about 800 plant species for curing different diseases. Currently 80% of the world population depends on plant-derived medicine for the first line of primary health care for human alleviation because it has no side effects.

Calendula one of the most valuable medicinal herbs with an enormous spectrum of healing applications. Cultivated by the Egyptians, Greeks, Hindus and Arabs, calendula grew in European gardens and has been used medicinally since the 12th century.

Calendula was taken internally to treat fevers, promote menstruation and treat cancer. Most importantly, the flowers were made into extracts, tinctures, balms and salves and applied directly to the skin to help heal wounds and to soothe inflamed and damaged skin.

At the moment, there is a large assortment of drugs containing in its composition *Calendula officinalis*. But prospectively direction of modern pharmaceutical science is to create new combined drugs, consisting of both vegetable and mineral components.

As part of this work we planning studies in development of formulation of complex action containing as active ingredients calendula extract and natural clays.

PROSPECTS OF DEVELOPMENT OF NEW DRUGS BASED ON *COMARUM PALUSTRE*

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Comarum palustre is a source of preparation of medicines. The herb contains tannins, flavonoids, volatile oil, gums, organic acids, vitamin C, and various microelements such as phosphorus, potassium, magnesium, copper. *Comarum palustre* (Marsh Cinquefoil) is astringent, anti-fever, antiseptic, styptic, antiviral, anesthetic, diaphoretic, antiphlogistic and wound healing. It can be useful for articular disorders, internal bleeding, haemorrhoids, as astringent for diarrhea, as cholagogue and diuretic, can also be used externally for wounds and mouth inflammations. *Comarum palustre* decoction is used as throat rinsing while tonsillitis and as a mouthwash for oral inflammations and dental bleeding. A diversity of the pharmacological properties of *Comarum palustre* in combination with the activity of biologically active compounds suggests that a range of its dosage forms should be extended.

In our work we investigated the process of extraction of *Comarum palustre* herb by pressurized solvent extraction (PSE) and also developed a technology for obtaining of *Comarum palustre* tincture using Timatic Micro of 0,5 l.

Completeness and speed of extraction of the active ingredients from the herbal raw material depend on technological properties of the material, difference in the concentrations, time of extraction, the nature of extragent and of the other factors which should be considered in the extraction process. Was studied effect of extraction time, number of working cycles, polarity of extragent on quantitative and qualitative characteristics of extract. Were found optimal parameters of process conducting: extragent - alcohol 40%, pressure - 5 atm, number of working cycles 60, extraction time - 7 h. At such conditions was observed maximal yield of extractive substances – 17%. Next stage of our research will be studying of chemical compose of extracts and development of semisolid preparations with obtained extract.

SECTION № 6

**PHYSIOLOGICAL AND BIOCHEMICAL FUNDAMENTALS OF THE
ACTION OF BIOLOGICALLY ACTIVE COMPOUNDS**

STUDY OF ANTIULCER ACTIVITY OF «FENOSIN»

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One of the urgent problems of modern medicine and pharmacy is to improve approaches to the therapy of peptic ulcer.

Taking into account that nowadays the mechanisms of the development of peptic ulcer disease are considered neurohumoral, local activation of lipid peroxidation and free-radical processes, it is appropriate to create a new drug. The components of one would have an impact on all the links in the pathogenesis of peptic ulcer. On the basis of the dry extract of the bark of aspen and bismuth subcitrate was developed new original drug – Fenosin that can be recommended as a mean of adjunctive therapy in the gastro-intestinal diseases: gastritis, peptic ulcer disease.

The aim of the work was to study the Fenosin anti-ulcer activity using the model "stress ulcer". Stress reactions were caused by suspending the animals for nuchal , the study drug was administered intraperitoneally for 3 days and 1 hour prior to stress exposure at a dose of 50 mg / kg .

Antiulcer activity of Fenosin was rated in terms of the macroscopic study of gastric mucosa and blood biochemical parameters.

Modeling of stress ulcers in animals caused marked changes of gastric mucosa. Although were observed redness, swelling, folding disorders, multiple bleeding and ulcers. Found that the model of "stress ulcer" used on animals Fenosin has a pronounced anti-ulcer activity: significantly reduces congestion , edema, ulceration area of the gastric mucosa and improves ulcerative index compared with the control group pathology and drug comparisons . Treatment of animals using the Fenosin helped to reduce the processes of free-radical oxidation and recovery of antioxidant status in comparing with the control group pathology.

The obtained results suggest Fenosin as a perspective drug for the prevention and treatment of peptic ulcer.

CORRECTION OF METABOLIC DISORDERS UNDER EXPERIMENTAL METABOLIC SYNDROME BY AGMATINE ADMINISTRATION

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The metabolic syndrome is a complex of hormonal and metabolic disorders, which increase hazard of type II diabetes and diseases of cardiovascular system development. One of the main pathogenic factors of such consequences is endothelial dysfunction which causes hypertension.

Earlier we demonstrated that experimental metabolic syndrome was accompanied by changes in the nitric oxide metabolism (decrease of arginine, citrulline and nitrites + nitrates content i.e. decrease of NO production). So the aim of present work was to investigate the effect of agmatine, the endogenous NO donator, on metabolic disorders under experimental metabolic syndrome.

Experimental metabolic syndrome was modulated by fructose-rich diet, containing 18.3% protein, 60.3% fructose and 5.2% fat. Experimental rats were divided into 3 groups: 1) the control group received regular rat chow, 2) the study group received fructose-rich diet, 3) the study group received fructose-rich diet with agmatine in therapeutic dose. Plasma glucose, insulin concentration and total level of nitrites and nitrates were determined after 6 weeks of experiment.

Fructose-rich diet provoked a significant increase in body weight, hyperglycemia, hyperinsulinemia and decrease of plasma ($\text{NO}_2^- + \text{NO}_3^-$) content. These data demonstrate the development of obesity, insulin resistance, and disruption of nitric oxide metabolism.

Upon agmatine administration weight loss was observed that can be associated with neuropeptide Y production decrease of and appetite reduction. Agmatine treatment also normalized plasma levels of glucose and insulin possibly due to its ability to increase of glucose uptake by muscle cells and to enhance the sensitivity of cells to insulin. The total content of nitrites and nitrates increased after agmatine treatment. This may be explained by action of agmatine as imidazoline receptors agonist. It's known that agmatine inhibits iNOS and nNOS but activates eNOS reducing blood pressure.

Thus, the data obtained in our experiment indicate that hypercaloric diet caused significant metabolic disorders. Agmatine administration had the protective action, obviously, because of its pleiotropic effects, including the prevention of obesity and insulin resistance and normalization of nitric oxide production.

EXPERIMENTAL STUDY OF ACUTE AND SUBCHRONIC TOXICITY OF DIETARY SUPPLEMENT “IODIS”

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According to the World Health Organization (WHO), pathological conditions caused by iodine deficiency ranks third among 38 most common noninfectious diseases of adults and children as well. Almost 2 billion people in the world live in conditions of iodine deficiency. The aim of our research was to study the acute and subchronic toxicity of DS "Iodis", which is a molecular complex of diiodomethyl-p-tolylsulfone with triethanolamine. The acute toxicity of DS "Iodis" was examined on mongrel white rats after a single application of 10%, 25%, 30% solution in a dose of 2 ml to a previously shaved skin area the size of 2×2cm. The animals had been observed during 14 days. The acceptability was evaluated by the survival, the general condition of the animals and the percentage of dead animals to the total. The studies have shown that at various concentrations of the solution, DS "Iodis" is well tolerated by laboratory animals and, according to the toxicity classification of substances proposed by Sidorov K. K, is referred to low-toxic compounds. Taking into account that DS "Iodis" is supposed to be applied during a month, 1% solution of "Iodis" was daily applied on skin in a dose of 2 ml during 30 days to previously shaved skin area the size of 2×2cm. The indicators of chronic toxicity were the body weight, the general condition of the animals, the biochemical parameters which characterize activity of liver and vital organs, the weight coefficients of the internal organs. The indices were examined in dynamics – before the beginning of the experiment and at the end. As a result of the experiment it was found that DS "Iodis" has no hepatotoxic effects; the activity of indicated enzymes with hepatocyte cytolysis syndrome – ALT and AST were not higher than that of control rats and matched the intact norm. The weight of the internal organs such as heart, kidneys, adrenal glands, spleen and liver of the animals from the experimental groups was not significantly different from the weight of the animals from the control group. In this way we can conclude that 1% solution of DS "Iodis" in a dose of 2 ml with durational cutaneous application (within 30 days) has no toxic effects on the morphofunctional state of the internal organs.

PATHOGENETIC ASPECTS OF PEPTIC ULCER

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Peptic ulcer is a chronic ulcer that usually involves the distal stomach or proximal duodenum. The ulcer results from digestion of the mucosa by acid gastric juice. Persons who secrete large volumes of acidic gastric juice are prone to ulcers.

The initial event is probably a small, superficial erosion of the gastric or duodenal mucosa. Gastric acid and pepsin begin to digest the deeper tissues, which have been denuded of covering epithelium. Attempts at healing in the presence of continuing digestion eventually lead to considerable scarring at the base of the ulcer. Clinically, ulcers produce pain that is usually relieved by ingestion of food or antacids that neutralize the gastric acid.

Helicobacter pylori, the same organism that is associated with chronic gastritis, also plays an important role in the pathogenesis of both gastric and duodenal ulcers. Presumably the organism injures the mucosa and initiates the mucosal erosion that eventually develops into a chronic ulcer. The role of *Helicobacter* in causing a gastric ulcer is understandable, because this is the same organism that causes the mucosal damage leading to chronic gastritis. Its role in causing duodenal ulcers is more difficult to explain because the organism characteristically colonizes gastric mucosa, not duodenal mucosa. Some investigators have speculated that there are small areas of gastric epithelial cells in the duodenum where the organism can grow and damage the duodenal mucosa, making it more susceptible to ulceration. An alternative explanation postulates that the organism does not damage the duodenal mucosa directly, but does so indirectly because the *Helicobacter*-induced gastritis causes the gastric mucosa to secrete excess acid, and it is the hyperacidity that causes the duodenal ulcers. According to this concept, the mucosal damage caused by the gastritis disturbs various functions of gastric mucosal cells that regulate gastric acid secretion and causes the mucosa to secrete excess acid.

Peptic ulcer has complications: hemorrhage, perforation, penetration, malignancy and obstruction. An ulcer may erode completely through the wall of the stomach or duodenum, causing a perforation of the wall through which gastric and duodenal contents leak into the peritoneal cavity, resulting in a generalized inflammation of the peritoneum, the membrane that lines the abdominal cavity and covers the exterior of the abdominal organs (peritonitis). Sometimes the scarring that follows healing of a gastric ulcer may be so severe as to cause obstruction of the outlet of the stomach, called the pylorus, preventing the stomach from emptying properly.

THE STUDY OF VESSEL STRENGTHENING CREAM WITH POLYPHENOLIC CULTURAL GRAPE CONCENTRATE

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Introduction

It is known that under the skin lesions at an early stage of wound healing start vascular changes caused by a disturbance of microcirculation, vascular permeability and integrity of membranes in the mechanism of development of which some biogenic amines play the role, prostaglandins, the initiation of lipid peroxidation processes and decrease of antioxidant defenses.

One of the promising areas of the modern pharmacology is the use of biologically active substances (BAS) of vegetable origin. In particular, there is an interest of the extracts of grape seed culture which contain polyphenols demonstrating reparative, antiinflammatory, antioxidant properties, which can provide the wound healing effect for creating the antipsoriatic means. For getting the concentrates of grape polyphenols in Ukraine, there is a sufficient resource base. These factors have become a prerequisite for pharmacological study of the cream with polyphenol concentrate of Grape cultural codenamed " Enopsor ."

In damaged tissues of the wounds there are the processes with the accumulation of cellular debris with getting oxidized products and microcirculation disorder. In this regard, it has become interesting to study the effect of the cream " Enopsor " on vascular permeability state of the membranes, cytolysis processes, lipid peroxidation and antioxidant protection.

The purpose of this study has been to investigate the vessel strengthening action of the new cream with polyphenol concentrate of Grape cultural.

Materials and Methods

We have studied the effect of the cream " Enopsor " on the vascular permeability of the anterior abdominal wall of the rats by subcutaneous injection of

different phlogauguin agents such as kaolin, histamine, formalin, egg protein, carrageenan. The experiments have been conducted on 40 white male rats weighing 200-220 g. 10 minutes later after the intravenous administration of the dye to increase the permeability of the vessels of the abdominal wall in the area of the abdomen we have injected subcutaneously with various phlogauguin agents: 0.02 ml of a suspension of kaolin, 0.02 ml 0.1 % histamine solution, 0.02 ml of 3 % formalin solution, 0.02 ml of egg white , 0.02 ml of a 0.1 % solution of carrageenin .

The effect on vascular permeability of the cream " Enopsor " has been evaluated by the changing rate of staining the papules under the influence of phlogauguin compared with the control group pathology. The comparator in the study of the pharmacological activity of the cream " Enopsor " has been chosen " Kamagel ".

Results

The analysis of the data indicates that according to the rate of vascular permeability disorders the phlogauguins can be positioned in this order: egg albumen (5.14 min.) , Histamine (5.87 min.) , Carrageenan (6.01 min.) , Kaolin (6.14 min.) and formalin (8.09 min.). The cream " Enopsor " compared with the control group, has helped to reduce the rate of staining papules in 46-138,5 % depending on the type of phlogauguin, indicating varying degrees of severity of this vessel strengthening effect of the active ingredients of this substance. The last fact indicates the speed reduction of papules staining compared to the control group in violation of vascular permeability induced by formalin - by 109.8 % , carrageenan - by 138.5 % , kaolin - by 83.4 % , egg white - 59.9% and histamine - 46.3 %.

Conclusions

Thus, the results of this study confirm the ability of the cream "Enopsor" to inhibit the activity of histamine, serotonin, bradykinin, prostaglandins and thereby reduce vascular permeability and to show vessel strengthening actions that reduce edema and inflammatory process.

STUDY OF ANTIOXIDANT ACTIVITY OF A NEW STRUCTURAL MELATONIN ANALOGUE ON THE BACKGROUND OF ACUTE HEPATIC ISCHEMIA

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It is known that over 30% of adult population suffers from hepatic disorders. One of the most severe hepatic pathologies is hypoxic hepatitis (ischemic hepatitis or liver collapse). Foreign authors consider that hypoxic hepatitis is the most common cause of acute hepatic disorders of intensive care patients, having a prevalence rate of 10%. The level of hospital deaths from hypoxic hepatitis is 61.5%, while the list of medicinal preparations for optimal therapy of this pathology is insufficient.

The actual trend of modern medicine and pharmacy is development, study and introduction of medicinal products with multiple organ action, that is: antihypoxic action, Hepatoprotective action and ability to recover energy metabolism of damaged hepatic cells at treatment and prevention of ischemic and reperfusion damage of hepatic tissue and of microvasculatory bloodstream.

From this point of view, a new preparation can be considered as a perspective compound - 4,3'-spiro[(2-amino-3-nitrile-4,5-dihydropyrano[3,2-c]chromen-5-one)-5-methyl-2'-oxindole] (hereinafter - compound 77), which is a structural analogue of melatonin as of the molecule atomic structure.

The objective is to investigate the antioxidant activity of melatonin structural analogue (compound 77) under acute hepatic ischemia.

Materials and methods. The studies have been performed in white rats of 180-240 g weight. Acute hepatic ischemia has been induced under tiopental-sodium anesthesia (35 mg/kg) by applying a special clamp on the vascular pedicle of liver and on bile passage. Occlusion lasted for 25 minutes. Animals have been separated into the groups as follows: pseudooperated animals; control pathology (25-minute occlusion of the vascular pedicle of the liver and bile canal); animals that received compound 77 in a dose of 5 mg/kg (a dose of maximum antihypoxic effect) intragastrically, daily, during 3 days, last time before ischemia occurrence - 40 minutes; animals that received the comparative preparation melatonin dose of 5

mg/kg in a similar mode. Changes of prooxidant-antioxidant balance verified on the concentration in liver homogenate and serum substances interacting with thiobarbituric acid (TBA-reactants), diene conjugates (DC), glutathione refurbished (GR) and catalase activity.

Results and their discussion. Acute 25-minute hepatic ischemia with subsequent reperfusion was accompanied with significant activation of lipid peroxidation (LPO). Level of TBA-reactants and DC in liver homogenate and blood serum was 1.4-2.6 times more, compared to the one of the pseudooperated animals group, and the activity of the antioxidant system (AAS), as of GR content, was 1.5-1.8 times less.

Melatonin reference product normalizes the imbalance of LPO- AAS system compared to the control pathology group. This way, concentration of TBA-reactants was equal to 172 ± 2.87 mmol/g, DC – 7.57 ± 0.18 mmol/g; GR – 82.9 ± 3.06 ; catalase – 0.27 ± 0.1 mcat/l), which was significantly different from the values in the control pathology indices: TBA-reactants 209 ± 4.95 mmol/g, DC – 8.49 ± 0.21 mmol/g; GR – 72.2 ± 2.80 ; catalase – 0.21 ± 0.02 mcat/l.

Compound 77 showed an expressed antioxidant effect by the way of normalization of LPO-AAS balance. Reduction of LPO processes was verified as of reliable reduction of TBA-reactants (111 ± 4.38 mmol/g) and DC (6.65 ± 0.24 mmol/g). A significant positive aspect of compound 77 antioxidant activity implementation was the restoration of activity and of non-enzymatic link of AAS system (GR 101 ± 1.49 units), and enzymatic (catalase activity: 0.32 ± 0.01 mcat/l). Antioxidant effect of spirocyclic-derived oxindole exceeded the activity of melatonin by all indicators.

Conclusions. On the background of acute 25-minute hepatic ischemia with further reperfusion, a new preparation – compound 77 – has shown an expressed antioxidant activity, which exceeds the effect of melatonin comparative preparation . Pharmacological action of compound 77 has been mainly provided with inhibition of lipid peroxidation together with increase of antioxidant system.

THE RESEARCHES OF THE INFLUENCE OF POLYPHENOL CONCENTRATE FROM GRAPE SEEDS WITH STEVIA ON THE DEVELOPMENT OF DIABETES

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Diabetes mellitus (DM) – is the most common disorder of the endocrine system, which is characterized by disturbance of all types of metabolism and, primarily, the carbohydrate one. Vascular pathologies occupy an important role in this disease, they are as follows: microangiopathy (retinopathy and nephropathy), macroangiopathy (myocardial infarction, stroke , gangrene of the lower limbs), neuropathy. Pathological changes appear in all elements of the vascular wall: endothelium , smooth muscle cells and other cells and structures.

Metabolic disorder of NO is regarded as one of the causes of diabetes mellitus type 2 (DM 2) . NO has a pronounced selectivity for pancreas cells, and its negative effect is realized through the toxic forms of nitrogen oxides (peroxynitrite) .

The purpose of this research has been to investigate the influence of polyphenol concentrate which has been obtained from grape seeds cultural, that contains the extract of stevia, on the work of the insular apparatus and NO-synthase system in the control animals and the animals with experimental DM1 and DM2.

Materials and methods. The experiments have been carried out on the rats of the line Wistar with the weight of 140-200 g , which have been contained on a standard diet of a vivarium . The effects of polyphenol concentrate that has had the stevia extract (PCS) for the content of glucose , insulin , nitrite , arginine and citrulline in the blood of the control rats and animals with DM1 and DM2.

DM1 in the animals has been caused by a single intraperitoneal injection of a solution of Streptozotocin (STZ) ("Sigma", USA) in 1 M citrate buffer pH 4.5 at a dose of 55 mg / kg of the body weight. The development of diabetes has been monitored by measuring the level of glucose and insulin in the rats' blood serum. DM2 in the animal has been caused by a high-calorie diet (45 % saturated fat) with

fructose (2 g per 100 g of the body weight per a day) during 4 weeks. The treatment has been started on 7th day after the injection of streptozotocin and on 14th day after the initiation of high-calorie diet.

Results. Our studies have showed that in the experimental animal with DM1 and DM2 there is the increase of glucose in blood in 4.59 and 2.53 times, respectively, compared to the control animals.

In the experimental animals with DM1, there is also the decrease of insulin levels in the blood in 2.4 times, compared to control animals.

In the experimental conditions DM2, we have observed simultaneous increase of the content of insulin and glucose in the blood of the animals. Furthermore, according to the received data in the present research, the rats that have been kept on a fructose diet, we have observed the reduction of NO and citrulline in the blood and the content of arginine has significantly increased.

Application of the grape seed extract with stevia has reduced glucose and insulin levels in the animals with type 2 diabetes, and positively influenced the indicators of nitric oxide metabolism in the animals with both Experimental Pathology.

Conclusions. Thus, these results suggest that PCS, under the conditions of the experimental diabetes, has a normalizing action on both the work of insular apparatus and system for NO generating. Our studies have shown that polyphenolic concentrates that have been obtained from grape seed cultivars "Merlot" and "Rkatsiteli ", during a long administration to the experimental animals have a normalizing effect on the work of insular system, glucose homeostasis, as well as generating system oxide

During Diabetes mellitus the polyphenol concentrate, which has been obtained from grape seeds cultural, containing the stevia extract, has a moderate hypoglycemic effect and shows a pronounced normalizing effect on the the work of insular apparatus according to the models DM1 and DM2.

MAIN PATHOGENETIC MECHANISMS OF EMPHYSEMA

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Cigarette smoking and atmospheric air pollution appear to be the major factors responsible for the rising incidence of emphysema. Exactly how they exert their destructive effect on the lung is not completely understood. Smoking and air pollution are considered to expose the bronchial mucosa to chronic irritation, eventually producing chronic bronchitis associated with a chronic cough and increased bronchial secretions. The inflammatory swelling of the mucosa narrows the smaller bronchioles, increasing their resistance to expiration and causing air to be trapped within the lung. The leukocytes that accumulate in the bronchioles and alveoli may also contribute to the lung damage by releasing proteolytic enzymes that attack the elastic fibers making up part of the lung's structural framework. Moreover, the mechanisms that inactivate the leukocyte enzymes are less efficient in the emphysematous lung.

Repeated bouts of coughing, with consequent extreme elevations in intrabronchial pressure, cause the alveolar septa to rupture, gradually converting the alveoli into large, cystic air spaces. The lungs become overdistended and lose their normal elasticity. The patient cannot expel air normally from the overdistended lungs because normal lung elasticity is lost and the bronchioli are obstructed; difficulty expectorating the excessive bronchial secretions and poor drainage of secretions and poor drainage of secretions from the bronchi tend to perpetuate the chronic bronchitis, and a vicious circle is created. The diseased lungs are also more susceptible to infection because of impaired pulmonary ventilation, bronchial inflammation, bronchiolar obstruction, and excessive bronchial secretions. Therefore, patients with emphysema frequently have repeated bouts of pneumonia, further damaging the lung tissue.

For the most part, emphysema can be prevented by refraining from smoking and avoiding inhalation of other substances known to be injurious to the lungs. Atmospheric air pollution contributes to the increasing incidence of emphysema and various measures are being undertaken to control this serious public-health problem.

Once emphysema has developed, the damaged lungs cannot be restored to normal. However, several measures can be employed to promote the drainage of bronchial secretions, to improve pulmonary ventilation, and to decrease the frequency of superimposed pulmonary infections. These measures, along with cessation of smoking, will retard or arrest further progression of the disease.

Experimental surgical procedures called *lung volume reduction surgery* are also being investigated. These procedures excise the nonfunctional extremely emphysematous segments of the upper lobes, thereby reduction in lung volumes will allow the remaining less severely affected lungs to function more efficiently.

The following case illustrates the clinical features of a patient with chronic pulmonary emphysema who developed severe respiratory insufficiency that was precipitated by a bout of pneumonia.

THE STUDY OF BIOLOGICAL ACTIVITY OF SYNTHETIC INHIBITORS OF JNK KINASE

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c-Jun N-terminal protein kinases (JNK), also known as stress-activated protein kinases, were originally identified by their ability to phosphorylate the N-terminal of the transcription factor c-Jun and by their activation in response to a variety of stresses (such as heat, pH variation, radiation, redox, osmolality, and chemical stimulation such as growth factors, cytokines, hormones, alterations in nutrient conditions, as well as other environment stresses). Activation of JNK also underlies the development of pathological conditions such as NAFAD, obesity, atherosclerosis. JNK kinases are an important target in the treatment of various dyslipidemic conditions. They belong to the mitogen-activated protein kinase family, and are responsive to stress stimuli, such as cytokines, ultraviolet irradiation, heat shock, and osmotic shock. They also play a role in T cell differentiation and the cellular apoptosis pathway. Activation occurs through a dual phosphorylation of threonine (Thr) and tyrosine (Tyr) residues within a Thr-Pro-Tyr motif located in kinase sub domain VIII. Activation is carried out by two MAP kinases, MKK4 and MKK7 and JNK can be inactivated by Ser/Thr and Tyr protein phosphates. It has been suggested that this signaling pathway contributes to inflammatory responses in mammals and insects. The c-Jun N-terminal kinases consist of ten isoforms derived from three genes: JNK1 (four isoforms), JNK2 (four isoforms) and JNK3 (two isoforms). Each gene is expressed as either 46 kDa or 55 kDa protein kinases, depending upon how the 3' coding region of the corresponding mRNA is processed. There have been no functional differences documented between the 46 kDa and the 55 kDa isoform, however, a second form of alternative splicing occurs within transcripts of JNK1 and JNK2, yielding JNK1- α , JNK2- α and JNK1- β and JNK2- β . Differences in interactions with protein substrates arise because of the mutually exclusive utilization of two axons within the kinase domain. c-Jun N-terminal kinase isoforms have the following tissue distribution: JNK1 and JNK2 are found in all cells and tissues. JNK3 is found mainly in the brain, but is also found in the heart and the testes. Function Inflammatory signals, changes in levels of reactive oxygen species, ultraviolet radiation, protein synthesis inhibitors, and a variety of stress stimuli can activate JNK. One way this activation may occur is through disruption of the conformation of sensitive protein phosphates enzymes; specific phosphates normally inhibit the activity of JNK itself and the activity of proteins linked to JNK activation. JNKs can associate with scaffold proteins JNK interacting proteins as well as their upstream kinases JNKK1 and JNKK2 following their activation. JNK, by phosphorylation, modifies the activity of numerous proteins that reside at the mitochondria or act in the nucleus. Downstream molecules that are activated by JNK include c-Jun, ATF2, ELK1, SMAD4, p53 and HSF1. The downstream molecules that are inhibited by JNK activation include NFAT4, NFATC1 and STAT3. By activating and inhibiting other small molecules in this way, JNK activity regulates several important cellular functions including cell growth, differentiation, survival and apoptosis. JNK1 is involved in apoptosis, neurodegeneration, cell differentiation and proliferation, inflammatory conditions and cytokine production mediated by AP-1 such as RANTES, IL-8

HYPERTROPHIC CARDIOMYOPATHY: GENETICS

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Hypertrophic cardiomyopathy (HCM) is the most common of the genetic cardiovascular diseases, characterized by heterogeneity in its cause, phenotypic expression and management options. The prevalence of HCM in the general population is at least 0.2% (1:500), is transmitted as an autosomal dominant trait, affecting males and females equally. HCM occurs worldwide, has been reported from all continents and more than 60 countries. The disease is caused by mutations in a variety of genes encoding proteins of the cardiac sarcomere.

Clinical presentation/course

HCM is characterized by variable clinical presentation and natural history, ranging from preventable sudden death, from ventricular tachyarrhythmias, to progressive heart failure, to the consequences of embolic stroke. Patients with HCM may display a variety of symptoms. Exertional dyspnea, exercise intolerance and fatigue reflect heart failure and may be associated with chest pain (which can be typical angina pectoris, even in the absence of coronary artery disease). Such symptoms of exertional dyspnea are usually due to 3 possible mechanisms: (1) Left ventricular (LV) outflow obstruction which produces elevated LV intraventricular pressures and wall stress; (2) diastolic dysfunction and impaired LV filing from the noncompliant and thickened wall; and (3) myocardial ischemia from the small vessel disease. However, it should be emphasized that HCM is also frequently compatible with normal life expectancy, often without disability or the need for major interventions to achieve that outcome. The diagnosis of HCM is most commonly made following onset of symptoms.

Genetics of HCM

HCM is transmitted in an autosomal dominant pattern of inheritance. Therefore, an individual carrying a disease-causing HCM mutation has a 50% chance of transmitting the mutation to a child, either male or female. Molecular genetic studies have defined HCM as a disease of the sarcomere, the contractile unit within the cardiac myocyte that is comprised of thick and thin filaments.

HCM has proved to be a genetically heterogeneous condition and to date 18 disease-causing genes and >500 individual mutations have been identified (Figure 2 and Table 1). Mutations in these genes have been identified in 40-60% of HCM cases (the majority of which are missense mutations with amino acid substitution). Many of these mutations have proved to be unique to individual families. Mutations in β -

myosin heavy chain (MYH7) and myosin-building protein C (MYBPC 3) account for the majority of identified mutations.

Genes involved in HCM	Gene Name
ACTC	Alpha Cardiac actin 1
CAV3	Caveolin 3 (Muscular dystrophy)
GLA	Galactosidase alpha (Fabry)
LAMP2	Lysosome-associated membrane protein 2
MTTG	Mitochondrial transfer RNA glycine
MTTI	Mitochondrial transfer RNA isoleucine
MTTK	Mitochondrial transfer RNA lysine
MTTQ	Mitochondrial transfer RNA glutamine
MYBPC3	Cardiac myosin-binding protein C
MYH7	β – Myosin heavy chain
MYL2	Regulatory myosin light chain 2
MYL3	Essential myosin light chain 3
PRKAG2	Noncatalytic AMP-activated protein kinase gamma 2
TNNC1	Troponin C
TNNI3	Cardiac troponin I
TNNT2	Cardiac troponin T
TPM1	Tropomyosin 1
TTR	Transthyretin (Amyloidosis)

Genetic testing for Hypertrophic Cardiomyopathy (HCM) and its utility:

Diagnostic genetic testing can be considered for patients who clinically manifest with symptoms of HCM and for patients who are asymptomatic but are within a family with a known mutation. Testing should be performed first on the family member who is symptomatic, i.e. has clinical manifestations of HCM. Preferably, the youngest of most severely affected family member should be tested first. The three possible outcomes of genetic testing are: positive, negative, and variant of unknown clinical significance (VOUS). Identification of a mutation in the family can lead to genetic identification of at risk family members who are clinically asymptomatic and who may have normal echocardiograms. Family members who test positive for the familial mutation should receive regular echocardiographic surveillance. Alternatively, a negative genetic test result for the familial mutation would obviate the need for repeated follow-up examinations. Genetic testing may be useful when discerning “athlete’s heart” from HCM. Genetic testing can be used for prenatal diagnosis. All patients who undergo genetic testing should receive pre-test and post-test genetic counseling to understand the implications of testing.

THE STUDY OF HEPATITIS PROTECTIVE PROPERTIES OF THE EXTRACT FROM THE LEAVES OF PLUM ORDINARY

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On the basis of these studies, in the result of which we have been established the antioxidant properties of extracts from plums ordinary leaves, it would examine the hepatoprotective properties of the substance on a model of acute liver tetrachlorinemethane injury. The application of Silibor and the extract from the leaves of plums conventional have led to regressive changes in the development of disease, as evidenced by a significant decrease in MCP and positive changes in the biochemical parameters.

In terms of preventive administration of the extract from the leaves of plums ordinary, the content of TBA- active products and diene conjugates in the liver tissue has decreased to 1.25 times. The application of plum extract has led to regressive changes in pathology (mass reduction factor of the liver). The content of reduced glutathione in the liver homogenate has increased. There has been the normalization of catalase activity.

In the animals that have been treated with the extract of grape leaves, the content of reduced glutathione in the liver tissue has increased by 53.6 % compared to the untreated animals and corresponded to the level of this indicator in the intact animals. Under the action of te extract from the leaves of plums ordinary there has been the normalization of catalase activity.

Introduction of the extract from the leaves of plums has been accompanied by the usual decrease of cytolytic syndrome that resulted from the inhibition of the investigated substance the peroxide decomposition membranes of hepatocytes, and turned out to be the hyperenzymemia of ALT decrease by 43.4 % compared to the untreated animals. Plum extract has reduced the activity of GGT, ALP and cholesterol content in the blood serum.

Thus, the extract from the leaves of plums ordinary shows the hepatoprotective properties and not inferior to the severity of the therapeutic effect of the drug comparison Silibor. Hepatoprotective effect of the studied substance has been detected by its ability to inhibit peroxide destructive processes and stabilize the antioxidant defense system, resulting in the improved functional status of the organ: there is the inhibition of cytolytic processes more clearly than under the influence of a reference drug.

THE STUDY OF ANTI-INFLAMMATORY ACTION OF THE EXTRACT FROM THE LEAVES OF PLUM ORDINARY

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The inflammatory process is one of the major pathogenesis components of a liver disease, that's why it is justified to use the drugs based on conventional leaf plums, which, along with other types of pharmacological activity exhibit anti-inflammatory properties.

The evaluation of anti-inflammatory activity of the extract from the leaves of plums conventional has been studied according to the influence of the studied extract on the development of carrageenin foot edema in the rats.

The animals of the control group during the aponeurosis of the hind limb have been injected with 0.1 ml of 1 % solution carrageenin. The animals of the second and third groups have been administered intragastrically with the studied extract at a dose of 25 mg / kg and Silibor at a dose of 25 mg / kg. The animals of the fourth group have been injected with at a dose of 8 mg / kg. The degree of swelling has been assessed in 3 hours after the carrageenin injection – the point of maximal inflammation. It is known that the leading role comes to the PG in the pathogenesis of carrageenin inflammation in 1,5-5,5 hours. after the injection with phlogogen, it allows us to say about the influence of the studied substance on cyclooxygenase system.

We have used ortofen at a dose of 8 mg / kg, and hepatoprotektor Silibor at a dose of 25 mg / kg as the comparison drugs.

Studies have shown that the extract of the study has shown a moderate anti-inflammatory activity and reduced the magnitude of swelling by 25.1 %, yielding expressive antiexudative action of ortofen. Silibor showed no significant effect on the intensity of the inflammatory process. Anti-inflammatory effect of the studied extract is mediated through effects on synthesis of inflammatory mediators by inhibiting cyclooxygenase and lipooxygenase systems.

INVESTIGATION OF FUNCTIONAL AND BIOCHEMICAL INDICATORS IN THE RATS UNDER GLUTAMATE TOXICITY

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One of the main causes which generally leads to increasing of morbidity in the population is the eating large amounts of food which contains the flavor enhancers (such as monosodium glutamate (MSG)). In the present work the glutamate influence on organism was investigated and biologically active substances for the prevention and treatment of the glutamate toxicity searched as the relevant issue of the modern pharmacy. An experimental research has been carried out on rats weighing 180-220 g. Grouping were as follows: the group of intact animals (n=6); the group of control's pathologies animals which treated sodium glutamate at doses 4 g/kg daily throughout 30 days (n=6); the group of animals treated with the polyphenols complex from grape cultural (CPG) at a dose of 90 mg/kg for 40 minutes before daily dosing of monosodium glutamate. The functional performance of central nervous system by open-field test and state of lipid peroxidation-antioxidant system (LPO-AOS) have been investigated.

It has been established that the administration to rats's food ration sodium glutamate excess at a dose of 4 g/kg resulted to development of excitotoxicity which characterized primarily by significant disruption of the central nervous system functional activity on indicators of open-field test. The development of oxidative stress was established on the LPO products increasing (increase of thiobarbituric acid reactive substances by 2.1 times, diene conjugates by 1.8 times) and decreased activity of the AOS (reduced glutathione refurbished by 1.5 times, α -tocopherol by 2.4 times).

Adding to the food ration of grape's seed concentrate has reduced of excitotoxicity. All studied parameters of central nervous system (locomotor and research activity and autonomic responses) were within the physiological range, and as the increase urination then it can not be explained to the diuretic effect of the CPG. The administration of CPG normalized all indicators prooxidant-antioxidant balance in the study group.

On the basis of this investigations has been following recommendations: necessary to minimize the content of monosodium glutamate in the daily food ration.

One of the effective ways to preventing of the glutamate toxicity development is the addition to the food ration the grapes polyphenols complexes, possibly in the form of dietary supplements.

CO-ENZYME Q10 AN ALTERNATIVE WHEN TREATING CANCER.

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Cancer known medically as a malignant neoplasm is a broad group of diseases involving unregulated cell growth. In cancer, cells divide and grow uncontrollably, forming malignant tumors, and invading nearby parts of the body. The cancer may also spread to more distant parts of the body through the lymphatic system or bloodstream. Not all tumors are cancerous; benign tumors do not invade neighboring tissues and do not spread throughout the body. There are over 200 different known types of cancer that affect humans.

Cancer can be detected in a number of ways, including the presence of certain signs and symptoms, screening tests, or medical imaging. Once a possible cancer is detected it is diagnosed by microscopic examination of a tissue sample. Cancer is usually treated with chemotherapy, radiation therapy and surgery.

Adverse effects of these treatments on our vital organs lead to sleeplessness, pain, loss of life and chances of survival are slim. These effects made scientists look for alternative treatment to protect humans from adverse effects of cancer treatment and CoQ10, Co-Q10, vitamin Q10 was suggested as a new means.

CoQ₁₀ is a substance made naturally in the body and found in most tissues. It is used by the body to help to produce energy within the mitochondria — "the energy power house" of body cells. It can also be artificially made in the laboratory and sold as a dietary supplement. As an antioxidant, it helps protect cells from oxygen damage. It is found in meats, fish and many foods.

Coenzyme Q10 was first identified in 1957. Particularly high amounts were found in heart tissue, which is why researchers became interested in the connection between CoQ10 and heart disease. Studies in the 1960s found a possible link between cancer (especially breast cancer) and lower levels of CoQ10 in the blood. However,

CoQ10 levels naturally drop as people get older, which is also when people are more likely to get cancer. No normal range of CoQ10 in the blood has been defined.

Some laboratory studies suggested that CoQ10 might have a role as an immune system booster. Since then, researchers have been testing CoQ10 supplements for treating heart disease, cancer, and other conditions. Still, no firm conclusions have been reached about its usefulness in treating any disease and it's given in form of tablets, capsules or oil-based gel capsules and water soluble preparations.

Ubiquinone protects normal tissues from free radical damage and oxidation caused by certain cancer treatments. Production of free radicals regulate cell growth in humans is a function of the body also sometimes killing bacteria, fungi. Other potential benefits of CoQ₁₀ include treatment of gum disease, muscular dystrophy, migraines, renal disease and early Parkinson's disease. There is evidence Co Q₁₀ may improve function in athletic performance.

Doses may range from 60mg to 390mg per day. The artificial form may be absorbed better if eaten with a meal high in fat or if the supplement is made with natural Vitamin E. It may take 1-4 weeks to notice results.

Side effects are rare, but have been reported in high doses (600-1200mg/day). Side effects include heartburn, nausea, headaches, fatigue, dizziness, sensitivity to light, irritability, involuntary movements, diarrhea (mild) and skin reactions.

Finally, because CoQ10 is a strong antioxidant; there are theoretical reasons to suspect that it might interfere with the effectiveness of chemotherapy and radiation therapy. At least one study showed that when mice with implanted human lung cancer were treated with radiation and given CoQ10, they had less slowdown in tumor growth than mice that were treated with radiation alone. This question has not been adequately studied in human clinical trials. CoQ10 did not affect the ability of doxorubicin (a chemotherapy drug) to kill breast cancer cells in laboratory dishes, but its effect on chemotherapy in patients remains uncertain.

RESEARCH OF TOXIC PROPERTIES OF OINTMENTS BASED ON EXTRACTS OF SEEDS DAUCUS CAROTA

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Besides different investigations of pharmacological activity, new drugs are receiving increased requirements for their safety. So, research of acute toxicity and local irritant effect of the two samples of ointment made of seeds DAUCUS CAROTA became necessary stage of work.

Acute toxicity research of the two ointment samples which made of seeds DAUCUS CAROTA was conducted with the method of cutaneous application. Rats were used as experimental animals. On shaved area of the skin, larger than 50% of the total skin area, the ointment was applied at the rate 6 g / kg of body weight. During the two week observation after the rats signs of intoxication were not detected: animals were movable, active, food reflexes were normal, skin of all animals were normal, they did not lose weight. Results of toxicological research show us no toxic activity of the two ointment samples which made of seeds DAUCUS CAROTA using a single cutaneous application on rats. Local irritant effect of the two samples of ointment made of seeds DAUCUS CAROTA was investigated according to methodical recommendations. 1 drop of an aqueous solution of ointment was entered into the conjunctival sac of guinea pig eye. The other eye served as a control. Entering of the study drug (ointment) was one-off. Mucous membrane reaction was studied during the certain period of time: 15 min, 1 h, 24 h. Into account were taken the degree of congestion, edema, the amount of bleeding. Evaluation of damaging action was carried out with using the point system.

As a result of research of local irritant effect of ointment made of seeds DAUCUS CAROTA found that the entering of an aqueous solution of ointment in the amount of 1 drop in the conjunctival sac of guinea pig eyes did not cause visible changes of mucous membrane, which corresponds to 0 points. Animal's ophthalmic status was normal.

SECTION № 7

PRECLINICAL PHARMACOLOGICAL STUDY OF NEW MEDICINES

STUDY OF THE INFLUENCE OF RECOMBINANT ANTAGONIST OF INTERLEUKIN-1 RECEPTOR ON THE COURSE OF ALLOXAN DIABETES IN RATS

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Diabetes mellitus (DM) occupies an important place in the structure of mortality and disability among the causes of the violation and the deteriorating quality of life. Therefore, optimization of diabetes therapy is one of the most pressing health problems. Anticytokine therapy is one of the most promising directions of optimization of diabetes therapy.

The task of this work is the experimental study of hypoglycemic properties of the recombinant receptor antagonist IL-1 interleukin obtained in St. Petersburg Research Institute of Pure Biochemicals on the model of alloxan diabetes in rats. Pathology model was reproduced by single subcutaneous injection of alloxan in a dose of 20 mg per 100 g body weight white mongrel female rats. Interleukin in a dose 7 mg/kg and the reference drug anakinra in a dose 8 mg/kg were injected subcutaneously, the second reference drug metformin in a dose 30 mg/kg - intragastrically once a day for 10 days, starting 4 days after reproduction model pathology. Hypoglycemic action of the drugs was evaluated by animal survival and dynamics of basal serum glucose after 3 hours, 3 and 14 days after the alloxan injection.

The survival rate was 62.5% in the group of control pathology and group treated by anakinra. The survival rate was 75% in groups of animals treated by metformin and interleukin. Administration of all study drugs decreased the level of basal glucose in the blood serum of experimental animals. Under the action of interleukin and anakinra on the 14th day of the experiment the level of glucose in the blood serum of animals was significantly decreased in 2 times, under the action of metformin - in 1.4 times relative indicator in the control group pathology.

Thus, on the model of alloxan diabetes in rats the original recombinant interleukin-1 receptor antagonist has hypoglycemic action for which expression is not inferior to anakinra and superior to metformin. We can assume that the hypoglycemic effect of interleukin is the result of the blockade of IL-1 receptors in the pancreas and the subsequent protection of β -cells from the damaging effect of alloxan.

Research results indicate the prospects of further experimental study of anti-diabetic properties of interleukin for subsequent inclusion of the drug in the complex therapy of type I diabetes.

MODULATED EFFECT OF DERIVATIVE OF 3,2'-SPIRO-PYRRHOL-2-OXINDOLE COMPOUND R-86 ON FORMATION OF CEREBROCARDIAC SYNDROME IN THE COURSE OF EXPERIMENTAL HAEMORRHAGIC AND ISCHEMIC INSULT

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Objectives. To conduct monitoring of functional indices of cardiac performance and neurologic status in conditions of a modal intracerebral hemorrhage (ICH) when Derivative of 3,2'-Spiro-Pyrrhol-2-Oxindole is used as pharmacoprophylactic treatment with a view to perspectiveness of its further in-depth study as a cardioprotector.

Materials and Methods. Modulated effect of Derivative of 3,2'-Spiro-Pyrrhol-2-Oxindole Compound R-86 has been evaluated on forming of cerebrocardial syndrome in the course of ICH and ischemia-reperfusion (IR) of rats which were simulated by injection of autoblood (20 ml/100g) into the brain inner capsule and setting clamps on both internal carotid arteries under propofol anesthesia for 40 min. Derivative of 3,2'-Spiro-Pyrrhol-2-Oxindole Compound R-86 was administered as a prophylactic mode every 24 hours during 3 days up to pathology simulation in a conditionally-effective dose of 10 mg/kg of intragastric administration – a dose that provides the highest implementation of its antihypoxic action. As a drug preparation for comparison Corvitin 100 mg/kg intraperitoneal was chosen that has both cardioprotective and cerebroprotective effects in the course of haemorrhagic insult. A control pathology group got 0,9 % solution NaCl (2 ml/kg) as a therapy. Neurologic status evaluation, ECG changes, changes in central venous pressure and a degree of arterialization were chosen as criteria of cerebrocardiac syndrome development and efficacy of therapy with investigated substance. Monitoring in the course of ICH was performed in twenty-four hours after reperfusion had been performed.

Results. Conducted research has shown that ICH and IR are accompanied by development of neurologic deficit of intermediate degree of severity, significant aggravation of central circulatory dynamics and functional disorder of cardiac performance testifying about forming of cerebrocardiac syndrome. Pharmacoprophylactic use of Derivative of 3,2'-Spiro-Pyrrhol-2-Oxindole Compound R-86 as well as Corvitin prevented the development of cerebrocardiac syndrome that manifested itself in the prevention of development of neurologic deficit and stabilization of cardiovascular activity functional data.

Conclusion. Investigated Derivative of 3,2'-Spiro-Pyrrhol-2-Oxindole is a perspective biologically active substance for the further in-depth study of its cardioprotective characteristics.

HEPATOPROTECTIVE ACTIVITY LIPOPHILIC AND HYDROPHILIC LIME LEAVES EXTRACT RESEARCH

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Paracetamol is the one of the most used non-prescription drugs in Ukraine. As one of the most effective analgesics and antipyretics, paracetamol is nevertheless a potential hepatotoxic agent.

Not only overdose of paracetamol, but even its long-term use contributes to the development of drug hepatitis, especially for people with hepatitis of various etiologies or patients with diabetes mellitus.

Paracetamol hepatotoxicity caused not only by the result of covalent binding of its highly reactive metabolite N-acetyl-4-benzohinonimin with macromolecules of hepatocytes, but also by activation processes of free-radical oxidation (FRO) with enzymatic and non-enzymatic dysfunction of antioxidant systems.

The purpose of the research. Hepatoprotective activity lipophilic and hydrophilic lime leaves extract research.

Materials and methods. This work is devoted to the experimental research of the hepatoprotective properties of hydrophilic (PL-1) and lipophilic (PL-2) lime leaves extracts. Investigations have been carried out on the paracetamol hepatitis model of rats. White mongrel male rats with weight 180-220 g have been used in this research.

Obtained results. As a result of these experiments revealed that the use of PL-1 and PL-2 in drug-induced hepatitis caused by paracetamol reduces the intensity of cytolytic and free radical processes in the liver, increases the activity of the antioxidant system of hepatocytes and contributes to the normalization of carbohydrate, protein and lipid metabolism, and recovery processes bile production and secretion.

Efficiency of researched extracts is 20% higher on average than the efficiency of the reference drug silibor in the intensity of the hepatoprotective action.

Summary. Conducted research testifies the advisability of further preclinical lime leaves extracts studies to create new domestic plant hepatoprotector on their basis.

A STUDY IN CHINOLINE PERADORINE EFFECT ON LYMPH SYSTEM COAGULATION ACTIVITY UNDER CARDIAC INFARCTION

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Violation of lymph outflow from cardiac muscle damage area leads to development of interstitial edema, aggravates microcirculation disturbance in coronary vessel obliteration area.

The object of work is to study the effect of chinoline peradorine (chinoline derivative of carboxylic acids) on lymph circulation wrapping activity and lymph drainage function of cardiac muscle under acute cardiac infarction.

Research material and methods Experiments were performed on 45 rats with weight of 180 – 200 g. In 5 rats the lymph coagulation condition and lymph outflow rate (lymphorrhagic syndrome) was studied in intact condition.

In the rest of animals acute cardiac infarction was imitated by tying upper third of anterior interventricular artery. The dynamics of acute cardiac infarction progress was monitored by ECG registration and determination of creatine phosphokinase (CPK) in blood serum by spectrophotometry using Chemaiol standard reagent set. The blood was taken from auricular limbic vein. ECG was registered in intact condition and within 30 days, CPK at the beginning of experiment as well as within 7 days after imitation of infarction.

Results and discussion In animals of Group 2 after administration of chinoline peradorine substance the course of infarction was more favorable. Alterations of lymph coagulation were marked by reduction of heparin tolerance by 69%, more than 1.6 times decrease of prothrombin index as compared with control group, substantial increase of heparins and thrombin time (221 and 233% respectively), fibrinogen concentration was reduced 2.5 times. Lymph outflow velocity increased more than 4 times as compared with controls (0.141 ± 0.015 mL / min) which was indicative of intensified lymph drainage, thus, better removal of cardiac metabolism toxic products.

Conclusion It must be noted that within the following periods of study heparin and thrombin time values were higher than initial ones, whereas prothrombin index and fibrinogen concentration remained reduced up to the end of observation. Consequently, we may state that chinoline peradorine administration has an expressed hypocoagulation effect and stimulated lymph anti-coagulation activity. Chinoline peradorine showed an expressed hypocoagulation effect in experiment as well as assisted in acceleration of cardiac lymph draining function.

EXPERIMENTAL STUDY OF THE CEREBROPROTECTIVE PROPERTIES OF NEW OLIGOPEPTIDES HOMOLOGOUS TO PRIMARY SEQUENCE OF AKTH 15-18

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The high prevalence of cerebrovascular pathologies, as well as insufficient effectiveness of medicines used to correct their consequences, it makes necessary to investigate researches for new neuroprotective agents. Peptidergic drugs have an important place among cerebroprotective agents. In the 80 – 90 the last century the concept of creation of neuroactive substances by chemical modification of the polypeptide chain of cerebral sections of hormones and neurotransmitters - AKTH, vasopressin, etc. was developed and experimentally proved (Л.В. Антонова, 1989). Proceeding from this concept in «State Research Institute of Highly Pure Biopreparations» (St. Petersburg) the panel of conformationally restricted tetrapeptides homologous to primary sequence AKTH 15-18 was established. They all contain the D- or N- methylated form of lysine and arginine. The experimental data show their high resistance to blood peptidases that provides long duration of action. Also the oligopeptides are characterized by the absence of cytotoxic properties.

The purpose of this investigation was to evaluate the cerebroprotective properties of oligopeptides on the models of acute cerebrovascular disease (ACD), normobaric hypoxic hypoxia with hypercapnia (NBHHH), and to determine antagonism with the toxic effects of ethanol.

Experiments were carried out on random white rats (ACD) and white mice of both sexes, which were obtained from the vivarium of the central research laboratory of NUPh. During the investigation "European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes" (Strasbourg, 1986) was used. Peptides were administered intranasally at a dose of

0.02 mg/kg once a day for 4 days (ACD) and prophylactically at the same dose on the models of NBHHH and antagonism with ethanol .

On the ACD model Acetyl-Lys-Lys-(D-Arg)-Arg-amide (KK-3) peptide demonstrated the highest efficiency, preventing death of animals with ischemia during 3-day postocclusive period. Peptides Acetyl-Lys-Lys-Arg-Arg-amide (NP- 4), Acetyl-(D-Lys)-Lys-Arg-Arg-amide (KK -1), Acetyl-Lys-(D-Lys)-Arg-Arg-amide (KK-2), Acetyl-Lys-Lys-Arg-(D-Arg)-amide (KK-4), Acetyl-(D-Lys)-Lys-(D-Arg)-Arg-amide (KK-5), Acetyl-(D-Lys)-(D-Lys)-(D-Arg)-(D-Arg)-amide (KK-9), Acetyl-(D-Arg)-(D-Arg)-(D-Lys)-(D-Lys)-amide (KK-10) also were effective. All of them showed better results in comparison with reference drugs mexidol (i/v, 100 mg/kg), piracetam (i/v, 400 mg/kg) and semax (i/n, 0.02 mg/kg), which increased the survival rate to 66.7 - 83.3%.

On the model of NBHHH peptides KK-6, KK-7 and KK-10 exerted prohypoxic properties, reducing the lifetime of mice in the hermetic chamber by 11.1 - 19.4%. Only KK-1 and NP- 4 peptides significantly increased this value by 13.5 and 24.3% respectively, comparing with the control group ($p < 0.05$). Other peptides showed only a tendency to antihypoxic action. This dissociation of the results may be explained by different mechanisms of the protective effect on the pathogenetic links of ischemic brain stroke.

Peptides KK-1 and KK-5 showed significant antagonism with ethanol. They demonstrated better results than reference drug semax. These peptides significantly reduced the duration of anesthetic phase of ethanol intoxication by 34 and 34.2% respectively ($p < 0.05$ comparing with the control group).

So, the obtained data substantiate the cerebroprotective effect of the neuroactive peptides on the models of ischemia, anoxia and ethanol intoxication. Effectiveness of the peptides KK-6, KK-7 and KK-10 dissociates on the different models of cerebral injury. Investigation of this phenomenon is our aim for the nearest future.

CHRONORHYTHMS OF ACTION OF CARRAGENIN AND VOLTAREN

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For many years carragenin induced paw edema has been one of the classical models for studying the antiexudative activity of nonsteroidal anti-inflammatory drugs (NSAIDs). Modern chronobiology, chronobiology and chronopharmacology put forward a task to study the temporal features of the action not only drugs, but also agents that are used in modeling this or that pathology.

We have studied features of action of carragenin and voltaren during autumn and winter. The obtained data showed that after the introduction of 1% solution carragenin female rats at 22:00 in autumn, acrophase (maximum value) of inflammatory edema was observed at the fifth hour after florigene, and the amplitude amounted to 55.6 units. In the winter carragenin was introduced at the same time, but the acrophase of its activity shifted and was observed on the fourth hour. The amplitude of inflammatory edema amounted to 51.5 units.

Also we carried out a study of the activity of voltaren dose of 8 mg/kg when it's introduced 1 hour before inflammatory edema acrophase. The drug activity in autumn in the first 2 hours after its introduction averaged 65% and in winter – 63.6%, respectively.

The obtained data confirm the fact that inflammatory processes are most pronounced in the autumn period, and dosage of NSAIDs in autumn and winter are similar, which is confirmed by the comparable activity of the drug in these seasons.

The findings suggest the need to study the temporal features of the proinflammatory agents' action as well as the development of the most rational appointment of NSAIDs.

CORRECTION OF PHYSICAL STAMINA AND METABOLIC CHANGES WITH DIACAMPH HYDROCHLORIDE UNDER CONDITIONS OF IMMOBILIZATION STRESS AGAINST THE BACKGROUND OF MODELLED DIABETES MELLITUS

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Introduction. Diacamph hydrochloride (DH) being a derivative of benzimidazole exerts no effect on normal glucose content in blood however it reduces excessive glucose levels, stimulates regeneration of pancreatic β -cells, decreases insulin resistance, exerts anti-oxidative effect and demonstrates antihypoxic and cerebroprotective features in various models of cerebral lesions. That complex of pharmacologic activity types gives grounds for expectations that the new substance may have actoprotective features particularly under conditions of diabetes mellitus (DM).

The Study Objective The study objective is to make a comparative assessment of actoprotective features of DH and bemithyl under conditions of experimental DM. The assessment to be performed on the basis of physical stamina changes and behavior characteristics of metabolic processes in various organs of rats with a modelled stress induced by chronic immobilization (CIS).

Materials and Techniques. Stress-protective features of DH were assessed in rats with alloxan model of DM against the background of two-week immobilization induced by putting the animals into tight boxes. DH was used in conditionally effective intraperitoneal (i/p) dose of 25 mg / kg and compared with bemithyl used in i/p dose of 50 mg / kg. Actoprotective activity of both drugs was studied using forced swimming test under various temperature conditions (24-27 °C; 10-12 °C and 38-40 °C), rod rotating test (15 rpm) and treadmill run test (42 m /min belt speed and 10° inclination angle). Appropriate biochemical studies were performed upon therapy completion to assess metabolic changes. The animals were narcotized, then decapitated and musculus quadriceps femoris, hepar, heart and brain were isolated. Indices of energy metabolism (glycogen, lactate, pyruvate, adenosine triphosphate (ATP) and adenosine diphosphate (ADP)) and those of oxidative stress (content of TBK-reactants, proteins' carbonyl groups (PCG) as well as activity of NADPH-oxidase and superoxide dismutase (SOD)) were being determined in organs. The results were being statistically processed using Statistika 6.0 software and Student's test.

The Findings. Physical stamina of rats is considerably reduced in alloxan model of DM. DH (25 mg / kg) demonstrates distinct actoprotective features being superior to bemithyl (50 mg / kg). According to results of three exercise tolerance tests DH as actoprotector appeared to be likely superior to bemithyl. Substantial metabolic disorders emerge in skeletal muscles, heart, hepar and brain of rats with CIS against

the DM background. The processes of oxidative phosphorylation and its conjugation with tissue respiration are inhibited, hypoenergy state is being formed (ATP content in brain and heart is being reduced by 25% and 22% respectively while ADP level is being increased by 43% and 41% at the average respectively), reserve of glycogen is being decreased in hepar and skeletal muscles, anaerobic pathway of glucose metabolism prevails and lactate-acidosis is being developed. At the same time balance of prooxidant-antioxidant enzymes is impaired: activity of prooxidant enzyme NADPH-oxidase is being increased (by 16% at the average) and activity of antioxidant enzyme SOD is being decreased (by 21%), processes of free radical type oxidation of lipids and proteins are being activated in hepar, myocardium and brain. DH and bemithyl facilitate activation of oxidative phosphorylation and its conjugation with tissue respiration in brain and myocardium, they also contribute to inhibition of glycogenolysis and increasing of glycogen reserves in skeletal muscles and hepar, activation of aerobic pathway of glucose metabolism and reducing of lactate-acidosis in hepatocytes, restoration of prooxidant-antioxidant balance and inhibition of processes of peroxidation of fat and proteins in brain, myocardium and hepar of rats. Favourable metabolic effects of DH under conditions of CIS against the background of diabetes mellitus are more evident than influence of bemithyl. DH showed antihyperglycemic effect decreasing level of glucose in blood by 39.9% while bemithyl decreased it only by 18.9% ($p < 0.05$). DH facilitated increasing of glycogen content in hepar and skeletal muscles of rats by 68.8% and 46.4% respectively while relevant indices of bemithyl appeared to be likely inferior (by 49.4% and 27.8% respectively). Clear impact on energy metabolism in the brain and myocardium was demonstrated by DH, increasing the level of ADP by 58.2% and 60.4% versus 40.5% and 39.6% respectively against the background of bemithyl. DH also reduced the lactate content and lactate / pyruvate ratio by 69.9% and 70.4% respectively, while bemithyl by 63% and 56%. Levels of TBK-reactants and PCG appeared to be trustworthy lower when compared with control pathology (by 19% and 12% in brain, by 8.3% and 13% in heart and by 15% and 14% in hepar respectively) than in case of treatment with bemithyl. DH inhibited NADPH-oxidase by 26% and increased activity of SOD by 66.1%, activity of the enzymes under study was being changed by 16% and 48% respectively against the background of bemithyl. All differences mentioned above were statistically significant ($p < 0.05$). More evident actoprotective effect of DH correlates with its more powerful corrective influence on energy metabolism and anti-oxidative action as compared with bemithyl.

Conclusions. DH as antihyperglycemic drug used in half dose as compared with bemithyl under conditions of CIS against the background of DM appeared to be trustworthy better than bemithyl in terms of animals' physical stamina enhancement, normalization of indices of carbohydrate metabolism, energy metabolism and prooxidant-antioxidant balance.

AN INFLUENCE OF THE NEW DENTAL GEL «LIZOSTOM» ON A RECOVERING TIME IN RATS WITH EXPERIMENTAL GINGIVITIS

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Inflammatory periodontal disease remains one of the urgent problems of modern dentistry. Currently, there is an increase in the number of patients with periodontal disease with prevalence in their structure of generalized forms of gingivitis and periodontitis.

The aim of our study was an experimental rationale for the use of new dental gel based on lysozyme in experimental gingivitis .

Material and methods. Experimental work was carried out on 40 white nonlinear rats of different sexes weighing 180-220 g animals were divided into 5 groups: 1 – intact group, 2 – experimental gingivitis, 3 – experimental gingivitis + "Lizostom", 4 – experimental gingivitis + Metrogyl Denta. Experimental gingivitis was modeled preliminary evocation oral dysbiosis by intragastric administration of lincomycin and subsequent local lesion of the gums and tissues of the mouth vestibule applications of the suspension of bee venom .

Results of the study. In experimental gingivitis together with the intensification of proteolysis noted activation of lysosomal enzyme – acid phosphatase (both in serum and in homogenates of periodontal tissue), indicating that the damage and destruction of periodontal membranes of cells. Normalization of acid phosphatase activity in serum and periodontal tissue in untreated control occurred only on day 20 of the experiment. Rats treated with "Lizostom" normalization of this parameter in the blood serum was observed on day 10, using Metrogyl Denta – on day 15. As the acid phosphatase is one of the markers of inflammation, reduction of its activity under the influence of dental gel based on lysozyme indicates its positive effect on the inflammatory process in the periodontium, which is manifested earlier period of convalescence. In addition, "Lizostom" reduces the severity of local and systemic signs of inflammation (redness, swelling, leukocytosis, ESR), which confirms its effectiveness in the treatment of periodontal disease.

Conclusions. "Lizostom" reduces the recovering time in rats with experimental gingivitis by 10 days compared with untreated control and 5 day group compared to animals treated with the gel Metrogyl-Denta.

PRE-CLINICAL STUDY
OF ACUTE TOXICITY AND HYPOGLYCEMIC ACTION OF
N,N'-(ETHANE-1,2-DYYIL)BIS(QUINOLINE-2-CARBOXAMIDE)

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The relevance of studying the problems of diabetes mellitus (DM) is determined by extremely rapid growth of morbidity as well as high degree of disability. The ambiguity of certain aspects of the pathogenesis of diabetes and its complications, together with complexity of pharmacotherapy requires constant studying of this problem and searching for new antidiabetic drugs.

N,N'-(ethane-1,2-dyyil)bis(quinoline-2-carboxamide), a compound containing the fragments of the chemical structure of imidazoline receptors type I₂ blocker – (2-(4,5-dihydroimidazol-2-yl) quinoline hydrochloride), known by BU 224 code, has attracted our attention. There are no hypoglycemic drugs of such chemical structure now. There is no data about the impact of the investigated compound on carbohydrate metabolism. However, on the basis of chemical structure, it may be assumed that N,N'-(ethane-1,2-dyyil)bis(quinoline-2-carboxamide) can affect imidazolin receptors and, consequently, influence the mechanisms of carbohydrate metabolism regulation. In literature there are data concerning anticancer properties of this compound in vitro, due to the strengthened apoptosis and activation of caspase-3.

(N,N'-(ethane-1,2-dyyil)bis(quinoline-2-carboxamide) was synthesized by Candidate of chemical sciences Paponov B.V. (V.N. Karazin Kharkiv National University).

Objective. This study aimed to investigate the hypoglycemic action of N,N'-(ethane-1,2-dyyil)bis(quinoline-2-carboxamide) as a prospective hypoglycemic agent on the model of alloxan-induced diabetes and on the normoglycemic rats to determine the “dose of effect” dependence as well as acute toxicity in different routes of administration.

Materials and methods. The acute toxicity of N,N'-(ethane-1,2-dyyil)bis(quinoline-2-carboxamide) was determined on the white rats using intraperitoneal and intragastric administration of the investigated substance. LD₅₀ was calculated by the method of Litchfield-Wilcoxon using the probit analysis. Hypoglycemic effect was investigated on the white random-bred male rats with the body mass equal to 0.20±0.02 kg. DM was modelled by the subcutaneous administration of alloxan monohydrate (Sigma, USA) once at a dose of 150 mg/kg as a 5% solution in the acetate buffer, pH 4,5. Animals previously were deprived of food for 24 h, but had

free access to water. After 10 days the rats with the basal glucose level higher than 11 mg/dl were selected. Glucose was determined in the blood samples which were taken from the vessels of tip of the tail, by the glucose oxidase method using diagnostic kits ("Filicit", Ukraine).

In order to study pharmacological activity, N,N'-(ethane-1,2-diyil)bis(quinoline-2-carboxamide) was administered as an aqueous suspension, stabilized by polysorbate 80 at a dose of 1.5 mg/kg intraperitoneally. This dose possesses an antitumor effect. Intragastrically N,N'-(ethane-1,2-diyil)bis(quinoline-2-carboxamide) was given in a broad range of doses as the aqueous suspension stabilized by polysorbate 80. As a reference drug metformin (Sigma, USA) at a dose of 100 mg/kg was used. Plasma glucose content was determined by glucose oxidase method before and 90 min after drug administration. ED₅₀ was calculated by the method of G.N. Pershyn. Statistical differences were analysed using Wilcoxon criterion \check{T} and Student t test.

Results and discussion. By the classification of Hodge H.C., Sterner J.H., N,N'-(ethane-1,2-diyil)bis(quinoline-2-carboxamide) administrated intraperitoneally belongs to moderately toxic substances (III grade of toxicity, LD₅₀ = 10.005 mg/kg), administrated intragastrically – to low-toxic compounds (IV grade of toxicity, LD₅₀ = 633.45 mg/kg).

As to pharmacological activity, N,N'-(ethane-1,2-diyil)bis(quinoline-2-carboxamide), at a dose of 1.5 mg/kg intraperitoneally has pronounced hypoglycemic effect, lowering the level of glycemia at 57.2% that exceeds the antidiabetic effect of metformin that equal 44.0% at a dose of 100 mg/kg. In the intragastric administration N,N'-(ethane-1,2-diyil)bis(quinoline-2-carboxamide) has a dose-dependent hypoglycemic effect in range of doses 7.92-31.67 mg/kg, with non-linear dependence "dose-effect". The maximal hypoglycemic effect is provided by the dose of 15.84 mg/kg. ED₅₀ equals 11.64 mg/kg.

The therapeutic index at intragastric administered equals 54.42, indicating a wide therapeutic window and the respective safety of the compound. In normoglycemic rats N,N'-(ethane-1,2-diyil)bis(quinoline-2-carboxamide) at a dose of 15.84 mg/kg statistically significantly lowers blood glucose by 24,9%, while at doses of 3.96-7.92 mg/kg hypoglycemic effect is absent.

Thus, the effect of N,N'-(ethane-1,2-diyil)bis(quinoline-2-carboxamide) can be defined as antihyperglycemic in significantly lower dose compared with metformin both in intraperitoneal and intragastric administration with a sufficiently high level of safety. The latter is verified by the therapeutic index that was calculated using the results of effective dose and acute toxicity determination in intragastric administration.

STUDYING OF CHRONORHYTHMS OF ACUTE TETRAHLORMETAN HEPATITIS COURSE AND CHRONORHYTHMS OF KARSYL ACTIVITY AGAINST THE BACKGROUND.

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The liver and biliary tract pathology takes the leading place among the gastro intestinal tract (GIT) diseases. For the last 20 years there is an increase in the incidence of hepatobiliary system disease, and the cases of death from this disease are doubled. The pharmaceutical market counts 97 brand name medicines for the liver and biliary tract diseases treatment. However, the large range of modern hepatoprotective drugs does not solve the problem of the increasing incidence of liver and biliary tract, because the effectiveness of these drugs is influenced by many factors, including the dependence of their actions on hepatobiliary system biorhythms.

The purpose of these studies was to investigate the circadian hepatobiliary rate system (active cytolytic, cholestatic enzymes, cholesterol and mass liver changes) model of acute tetrahlormetan hepatitis in rats and effect of karsyl in modeling this disease.

Found that in intact animals in the evening (10pm) was significantly higher alanine aminotransferase (ALT) and alkaline phosphatase activity by 31% and 36%, respectively, relative to these indicators in the morning (10 am). A similar trend is evident for aspartate aminotransferase (AST) (19% difference). Cholesterol concentration, indicators De Ritisa and mass liver changes intact rats both morning and evening groups were virtually the same level. Thus, the data confirm the circadian course dependence of physiological and biochemical processes in the liver, in which the important role plays a functional work of microsomal enzymes of hepatocytes.

Amid tetrahlormetan hepatitis the violation of the circadian rhythm of physiological activity of enzymes is observed: ALT and AST cytolysis markers activity is offset, however, alkaline phosphatase activity kept pace (49% of the enzyme activity of the latter is higher in the evening than in the morning).

Circadian activity in karsyl tetrahlormetan hepatitis background was different for alkaline phosphatase activity (a decrease of 38% in the morning group and 57% in the evening). So, karsyl effects the figure more significant in the evening time.

Thus, our study confirms the circadian rhythm presence of hepatobiliary function at healthy rats and hepatobiliary changes of structure and pharmacological action of karsyl in terms of hepatitis.

NEW POTENTIAL OF RHEUMATIC DISEASES IMMUNOBIOLOGICAL THERAPY

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Chronic inflammation in rheumatoid arthritis (RA) and many other systemic diseases of connective tissue extend beyond the joints. Patients with RA have an increased risk of disease development in cardio-vascular system, lungs, eyes, musculoskeletal system. Effective control of inflammation becomes important and is the key to improving outcomes for patients with rapidly progressive RA. Traditional treatments are often ineffective for patients with RA, as they do not completely suppress the inflammation that causes its progression.

Thanks to the appearance of biological agents, especially inhibitors of tumor necrosis UPE-a, there were alternative effective means obtained, which are characterized by high efficiency and ensure rapid and sustained improvement.

The purpose of the research. To study the state of rheumatic diseases immunobiological treatment.

Materials and methods. We have researched the effectiveness of the drug "Rituximab" – Mab-Thera for patients with an inadequate response to the ongoing complex treatment in serum department 27 GKB Kharkov.

Obtained results. Mab-Thera application for 26 patients with RA is accompanied with clinical improvement of state of the disease with a marked reduction in the immune-inflammatory activity. Mab-Thera prescription for patients with systemic lupus erythematosus with active lupus nephritis resistant to basic drugs leads to reduction of the nephritic syndrome and stabilization of the nephritis course. Mab-Thera prescription for patients with Sjogren's syndrome, accompanied by high activity, leads to improved clinical and laboratory parameters of the disease.

Summary. Thus, the use of new biological agents for the treatment of systemic connective tissue diseases can slow the progression of the disease, and also to achieve stable, long-term remission of it in most cases.

THE STUDY OF ANTIULCER ACTIVITY OF BIOFITON[®] «HEALTHY STOMACH»

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The improvement of the methods of extraction of biologically active substances from the plant material is one of the forms of herbal drugs optimization.

The subject of the study has been Biofiton[®] «Healthy stomach» which is produced by «Phytoapteka Chistyakova» and contains: althea roots (13%), cinquefoil rhizomes (11%), plantain leaves (11%), licorice roots (11%), motherwort herb (11%), yarrow herb (11%), marigold flowers (10%), camomile flowers (10%), calamus rhizomes (9%). This drug is made with a unique modern technology of cryomechanic activation of the plant material, which is completely different from all known methods of extraction of biologically active substances. This technology gives the opportunity to concentrate the main properties of the herbal drugs of different biochemical nature in a small volume.

The aim of this study is to prove the antiulcer activity of Biofiton[®] «Healthy stomach». Antiulcer activity of the drug has been studied in a dose of 120 mg/kg (calculated according to the coefficient of species sensitivity) on the model of acute alcoholic prednisolone gastric ulcer in rats.

As a result antiulcer activity of Biofiton[®] «Healthy stomach» has been proved experimentally and made up 85.86%, and hardly yields the activity of Ranitidin comparator, antiulcer activity of which made up 91.35%. Consequently high efficacy of Biofiton[®] «Healthy stomach» makes it promising for prevention of the recurrence and in complex treatment of gastric ulcer.

EXPERIMENTAL RESEARCH OF HYPOGLYCEMIC ACTIVITY OF PLANTS EXTRACTS

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Diabetes mellitus (DM) type II is the most common and progressing endocrine disease in most countries. Adequate correction of diabetes and its complications is one of the urgent problems of modern endocrinology. Such factors as hyperglycemia and its effects: hypertension, atherosclerotic disorders, diabetic microangiopathy, retinopathy, and some others are important in the pathogenesis of diabetic complications. The use of medicinal plants in the diabetes based on the fact that a significant number of them – more than 400 – causes antidiabetic effect, and also has some other positive effects that enhance their effect in complications of diabetes. Traditionally medicinal plants are used in diabetes type II.

The aim of the research was investigation of the hypoglycemic activity of extracts of beans, dogwood leaves and lupine fruits in intact rats and in rats with a glucose load. Identification of possible hypoglycemic action of beans, dogwood leaves and lupine fruits extracts in dose 50 mg/kg compared with metformin in therapeutic dose 50 mg/kg was performed in two stages. The first phase of the research determined the hypoglycemic activity of plant extracts in intact rats, and the second stage – in rats with normal carbohydrate homeostasis under conditions of glucose load. The concentration of glucose was determined with glucosoydase method by using a set of reagents of “Filisit-diagnosis” firm.

Thick bean extract showed a more pronounced hypoglycemic activity after 6 hours after a single injection in intact animals than dogwood leaf extract and extract of lupine and was approaching to the drug comparison – metformin, which was a decrease in blood glucose levels for 10 hours. Intragastric input of glucose at a dose of 3 g/kg led to a significant increase of blood glucose at 30, 60, 90 and 180 minutes in all groups of animals, as compared with the original data, except the intact group of animals. Single-dose of thick bean extract revealed a severe hypoglycemic activity after 30 and 60 minutes than extracts: leaf dogwood and lupine fruit in comparison with the control group and with drug comparison – metformin.

Thus, the data suggest the expediency of further experimental studies of dense bean extract to create phytopreparation with hypoglycemic properties.

METAMIZOLE SODIUM CHRONORHYTHM STUDY

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Modern chronopharmacology allows using already known drugs much more effectively and helps to reduce the probability of adverse reactions' occurrence. One of the chronodependent problems is the feeling of pain.

In this research we investigated chronodependence of the feeling of pain from the time of day and chronoportrait of metamizol sodium. Pain sensitivity was assessed by the tail-flick latency period in seconds. Metamizol sodium was administered 30-40 minutes before to the specified test. During this chronoresearch it was revealed that there are 3 acrophases of minimal sensitivity to pain in the morning and afternoon. In the evening there is an increased sensitivity to painful stimulus and at night there are two acrophases when the sensitivity to pain decreases.

In the study of the metamizol's sodium effectiveness we found that its maximal analgesic effect is manifested in the form of 2 or 3 acrophases of reducing pain sensitivity. This medicine has the highest activity when it administered in the evening. Also rather high activeness of the metamizol sodium was observed at night and in the morning. The lowest activity of the metamizol sodium was observed in the afternoon.

Thus, the results of metamizol's sodium chronopharmacological research demonstrate the necessity of the development of new nonopioid analgesic regimens in order to improve its effectiveness and safety.

AN INFLUENCE OF THE NANOEMULSION OF LIPOSOMES WITH GRAPE SEED POLYPHENOLS ON THE MOTOR-EVACUATION FUNCTION OF THE INTESTINE

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Motor- evacuation disorders of the stomach and duodenum play a significant role in the pathogenesis of many diseases of the gastrointestinal tract. They can act as a leading role in the pathogenetic factor (non-ulcer dyspepsia, duodenostasis, pylorospasm etc.), and as accompanying disorders, which may increase the effects of other aggressive factors (hydrochloric acid and bile acids, reducing the protective properties of the mucous membrane). Therefore, the search for effective means of normalizing the motor-evacuation function of the gastrointestinal tract continues at the present time.

In the National University of Pharmacy, at the Department of Biological Chemistry, a new liposomal nanomedicine with grape seed polyphenols has been created. In our previous experiments was showed a high gastroprotective activity in various models of ulcerative lesions of the stomach.

Purpose. Studying an influence of the nanoemulsion of the liposomes with grape seed polyphenols (NLGSP) for motor-evacuation function of the gastrointestinal tract.

Materials and methods. The experiment was conducted on 12 white mice of both sexes weighing 18 ± 2 g, which were divided into 2 groups: Group 1 – intact control, Group 2 – animals, which were injected at a dose of the NLGSP 90 mg/kg.

Studying of an influence of the NLGSP on the motor-evacuation function of the gastrointestinal tract was performed by J. S. Stickney et al. Mice were kept for 24 hours on a starvation diet without restriction of drinking water. A dose of the NLGSP 90 mg/kg was administered to the experimental animals intragastric once. After 30 minutes, all animals were administered intragastric 0.5 ml of a contrast mass (10% suspension of activated charcoal in 1% starch paste). After 40 minutes the animals were taken out of the experiment by euthanasia.

Then the experimental and control animals was measured (in cm) absolute length of the intestine (Lia) and path (in cm) traversed by contrast mass on it (Ltc_m). The integral indicator of gastrointestinal motility, percentage of the length of the intestine was traversed contrasting weight, relative to the absolute last (Ltc_m[`]):

$$Ltc_m^`, \% = (Ltc_m \times 100\%) / Lia$$

Results. The average in the length of the intestine, contrast material covered in the intact control group reached 33.5 cm, representing 60.7% of its length. However, in animals treated with NLGSP, contrast material passed 48.9 cm intestine, which corresponds to 89.2% of its total length. As a result, it was determined that the introduction of the NLGSP a relative measure of length of the intestine, traveled by contrast material, was 28.5% more compared with that of the intact control group.

Conclusion. Analyzing the above, we can conclude that NLPVN enhances motor-evacuation function of the intestine.

NON-DRUG ARTERIAL HYPERTENSION TREATMENT FOR YOUNG PEOPLE WITH OVERWEIGHT

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Arterial hypertension (AH) treatment is an activation of organism internal reserves. The majority of patients with AH and overweight need lifestyle modification first.

The basic treatment for these patients is unloading dietary therapy. Dosed fasting has its complex effects on the patients suffering from AH. It restores self-regulation, compliance with the pumping function of the heart and level of peripheral vascular resistance, reduces cardiac output and blood pressure on the myocardium.

The purpose of the research. To study non-drug arterial hypertension treatment for young people with overweight.

Materials and methods. Patients with early stage of AH combined with overweight were prescribed a short absolute "dry fasting" for 1-3 days with subsequent limitation of taking water at 10-12 ml / kg per day, throughout the whole discharge period. Starting from the first day of fasting drug therapy was revoked.

Obtained results. At the beginning of the third day of blood pressure (BP) was reduced by 10%, and to 10.9 days in 5.5% of patients blood pressure was close to the norm for this age group already. After the course carried out, if it is necessary to prescribe drugs, the dose of antihypertensive drugs is decreased by 40.1%. It is prescribed infusions and decoctions of herbs (valerian root, motherwort herb, fruit Aronia) as maintenance therapy. It is recommended to follow a vegetarian days, hypocalorie and hyposodium diet, reducing excess weight, avoiding harmful habits, sufficient physical activity of cyclic type (walking, jogging, skiing), that in the presence of contraindications in combination with diet, 58% of patients with early stage hypertension lead to normalization of ABP level.

Summary. Non-drug treatment for patients with AH combined with a healthy lifestyle have a positive effect, since more than half of the patients had a normalization of ABP level.

EVALUATION OF CARDIOPROTECTIVE EFFECT OF DERIVATIVE OF 3,2'-SPIRO-PYRRHOL-2-OXINDOLE COMPOUND R-86

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Objectives. To examine cardioprotective effects of Derivative 3,2'-Spiro-Pyrrhol-2-Oxindole Compound R-86 on different as for genesis models of acute myocardial ischemia with a view to perspectiveness of its further in-depth study in this direction.

Materials and Methods. Examination of cardioprotective action of Derivative of 3,2'-Spiro-Pyrrhol-2-Oxindole Compound R-86 on rats has been evaluated when pharmacoprophylactic administration was used on models of adrenal cardiopathy (AC) and diathermocoagulation myocardium necrosis (DCMN) and when therapeutic administration was used in the course of a pituitrin-isadrine myocardial infarction (IM). AC was simulated by administration of 0,18 % solution of adrenal hydrotartrate in a dose of 0,05 ml/kg. DCMN was simulated by diathermocoagulation of marginal branch of the left coronary artery. Pituitrin-isadrine IM was simulated by administration within 3 days of coronarospastic agent Pituitrin (1 Unit/kg subdermal), and then β -adrenoceptor agonist isoprenalin (Isadrine), 200 mg/kg intramuscularly. Derivative of 3,2'-Spiro-Pyrrhol-2-Oxindole Compound R-86 was administered in the conditionally effective dose of 10 mg/kg of intragastric administration – such a dose provides highest implementation of its antihypoxic activity. As drug preparations for comparison Thiotriazoline (100 mg/kg), Mexidolum (100 mg/kg), Cordarone (10 mg/kg) and Corvitin (10 mg/kg) were chosen, which were injected intraperitoneal (i/p). A control pathology group got 0,9 % solution of NaCl (2 ml/kg (i/p) as a therapy. Pharmacoprophylactic administration of Compound R-86 and reference-drugs was performed every 24 hours for three days without interruption up to pathology simulation (AK or DCMN). Treatment therapy was performed for 3 days in 20 min. after Isadrine injection. Effectiveness of R-86 was evaluated in accordance with mortality dynamics and electrocardiogram changes (EKG).

Results. Results of conducted research show that Derivative of 3,2'-Spiro-Pyrrhol-2-Oxindole Compound R-86 (10 mg/kg intragastric) has cardioprotective action on models of AC, DCMN and IM during pharmacoprophylactic as well as therapeutic regimen of administration that manifested itself in possible decrease of animal mortality and de-escalation of amplitude of segment ST in comparison with animals from control pathology group. As for degree of cardioprotective effect Compound R-86 (10 mg/kg intragastric) injected preventively in conditions of AC and DCNM was as good as Cordarone, Mexidolum and Thiotriazolin, probably better than Corvitin in the course of rats' pituitrin-isadrine IM treatment.

Conclusion. Investigated Derivative of 3,2'-Spiro-Pyrrhol-2-Oxindole is a perspective biologically active substance for the further in-depth study of its cardioprotective characteristics.

FARMACOLOGY ACTION OF NEW CONNECTION DERIVATIVES 5,7-DIHYDRO- 1H- PYRROLO[2,3-D] PYRIMIDINE

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Inflammation is the local reaction of the living tissue on the damage that can occur as a disease with involving all systems of organism. The cause of the disease may be different from the action of microorganisms and the action of physical or chemical factors. Pharmacological regulation of the inflammatory process is the most actual problem of modern medicine.

The aim of our investigations was to study antiinflammatory activity of derivatives 5,7 – dihydro-1H-pyrrolo[2,3-d] pyrimidine on the model of carrageenan edema paws of rats. The model of acute carrageenan inflammation stimulate phase and causes inhibition of prostaglandin of kinin system.

The research was conducted on model of carrageenan edema paws of nonlinear white rats mass 180-200g. Compounds were investigated in dose to 5, 10 and 15 mg/kg animal mass and the reference preparation - voltaren in dose 8 mg/kg was injected 1 hour before subplantar injection of flogogen (1% solution of carrageenan in dose 0,1 ml). After 4 hours the animals were taken out the experiment and with the help of the Zaharevskii onkometr they measured the size of one foot before injection the carrageenan and after 2-4 hours after injection the carrageenan.

Antiexudative activity of investigated compounds was determined by its ability to reduce the development of edema in compare with the control, that was signify in percentege. This testified how this compound inhibits the carrageenan edema development relative to the control, where the value is taken as 100%.

In the result of the experiment was determined that connection in dose 5 mg/kg displayed the antiinflammatory activity 35,1%, 10 mg/kg – 44% and in dose 15 mg/kg - 39% which on activity is inferior the reference preparation - voltaren – 45,4%.

Thereby the connection in dose 10 mg/kg is perspective for the further research as an antiinflammatory agent.

HERB OF BUR-MARIGOLD (BIDENS TRIPARTITE) - PERSPECTIVE RAW MATERIAL FOR THE CREATION OF NEW DRUGS

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Nowadays most drugs are synthetic origin and may cause and positive pharmacological effects and side effects. Herbal medicines have fewer side effects and equal synthetic drug activity. Therefore, search for new medicines in plant materials is actually. Herb of bur-marigold (*bidens tripartite*) is interesting for investigation. Herb of bur-marigold contains tannins (5%), bitter substances, mucilages, flavonoids (more than 10 basic - luteolin, butein, butyne-7-glucoside, Auron, sulfuretin), essential oils, coumarins (umbelliferone, scopoletin, and others) amines, pigments, carotenoids, ascorbic acid (70 mg per 100 grams), vitamins and other nutrients. Infusions and decoctions of herb of bur-marigold have a diuretic, diaphoretic, choleric, inflammatory, reparative, antimicrobial, regulating of metabolism action. Experimental series of poorly studied. Shown in animal experiments that the drugs of herb of bur-marigold a series of hypotensive and sedative effect. Complex flavonoids-polysaccharide drug from herb of bur-marigold succession bile effect on exceeds flamin. The positive effect of herbs tinctures succession by 70% ethanol, with the use of an external ointment containing 2.5% of the extract of the herb of bur-marigold on the basis of a lanolin - petrolatum in patients with psoriasis.

So, the aim of this work is studying of pharmacological action of powder of the herb of bur-marigold (PHBM) in laboratory animals. Known that damage cell membranes of tissues and organs causes a disturbance of their functions and development of the disease. So, was studied membrane stabilizing effect of PHBM in doses 50 mg/kg and 150 mg/kg in method of erythrocyte hemolysis (Jager F. C.).

It was found that PHBM in both doses have membrane stabilizing effect in 35-41%% which increases with grows of the dose values. Thus membrane stabilizing activity of PHBM in dose 50 mg / kg is 35% and in dose 150 mg / kg – 41 %. It shows that the PHBM may be effective for the treatment of diseases pathogenesis of which is have damage to cell membranes (inflammatory diseases of the respiratory and GI tract, liver, kidney, hart; inflammatory, allergic and autoimmune diseases of skin, metabolic disorders and others).

So, the results show that PHBM is promising for further study in order to create a new effective and safe drugs for use in medical practice.

ANTIOXIDATIVE PROPERTIES OF EXTRACTS OF AERIAL PART OF BUPLEURUM AUREUM, HILL-GROWING SALTWORT HERB, FUMARIA SCHLEICHERI AND CYNARA SCOLYMUS IN VITRO

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In this work an oxidative state of blood serum and cytosol of rats liver has been studied in vitro through tetrachlormetane injection, and also influence of addition of herbal extracts of erial part of Bupleurum Aureum, Hill-Growing Saltwort Herb, Fumaria Schleicheri and Cynara scolymus on its rates. The data which have been obtained reveal that on condition of an oxidative stress development the herbal extracts injection in advance improves substantially oxidative state of examined objects. It was recorded, that all explored herbal extracts in vitro show antioxidative properties.

Materials and Methods. Antioxidizing properties of extracts in vitro have been studied on samples of spontaneous and ascorbate-induced Lipid peroxidation in rat liver homogenate. Numbers of extracts added to the incubative environment, have been calculated on basis of dose, that were more effective in prior researches (0,1 mg/g of liver). As comparative preparation α -tocopherol were used in dosage of 50 mg/kg, because it is a vigorous lipophilic antioxidant.

Results. According to research results in incubation of liver's homogenate in buffered solution at temperature 37°C sizable accumulation of thiobarbituric acid-reactants was shown, that indicates intensive progress of the lipid peroxidation processes. Storage of thiobarbituric acid-reactants was more evidential after ascorbate addition in incubative environment as high-powered inductor of nonenzymatic lipid peroxidation. Thus, velocity of thiobarbituric acid-reactants storage in spontaneous LP during first 20 minutes of incubation equals 0,45 nM/l per 1 minute, in ascorbate-inductive LP – 0,55 nM/l per a minute. The obtained data indicate capacity of experimental herbal extracts to block lipid peroxidation processes already for the first minutes after beginning of incubation. Evidently, it's connects with presence of polyphenoles which are part of composition of experimental herbal extracts. It is known that polyphenoles exactly are capable to couple active oxid metabolites, that are lipid peroxidation inductors at an early stages. Capacity of experimental extracts to inhibited ascorbate-inductive lipid peroxidation may be connected with coupling of Ferrum ions by poliphenoles, needed for induction of lipid peroxidation by ascorbate. On addition of extracts of Bupleurum Aureum and hill-growing Saltwort herb to incubative environment we have registered less expressed TBB-reactants comparing to trials, to which extracts of Fumaria Schleicheri and Cynara Scolymus have been added.

Conclusions. Herbal extracts of Bupleurum Aureum, hill-growing Saltwort herb, Fumaria Schleicheri and Cynara Scolymus may effectively block both, spontaneous and ascorbate-inductive activation of processes of lipid peroxidation in vitro, that is proved by their antioxidantizing activity. There was founded that extracts of Bupleurum Aureum and hill-growing Saltwort herb have the most expressed activity.

EXPERIMENTAL DEFINING OF THE RANGE OF ANTICONVULSANT ACTIONS OF PERSPECTIVE PHYTOGENIC ANTICONVULSANTS

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Epilepsy is a chronic psychic disease with complex etiology and pathogenesis. Modern possibilities of epilepsy therapy with implementing the existing anticonvulsant drugs do not make the problem less urgent. A remedy should have a complex influence on separate elements of the development of convulsive syndrome. That is why it is important to develop new anticonvulsant drugs, including the ones of herbal origin, the complex composition of which will allow to solve the problem of single-vector mechanisms of existing antiepileptic medicines.

The aim of the present study is to examine the range of anticonvulsant actions of four perspective antiepileptic drugs of herbal origin using the experimental models of seizures with different neurochemical mechanisms.

Materials and methods. As the objects of study the leaders of previous screening were chosen: dry extract of fumitory (*Fumaria schleicheri* Soy.-Willem., *Fumariaceae*) aqueous (FSDE), dry extract of basil (*Ocimum basilicum* L., *Lamiaceae*) aqueous (OBDE) and dry extracts of motherwort (*Leonurus cardiaca* L., *Lamiaceae*) aqueous (LCDEAq) and ½ alcohol (LCDEAl). The research was held on 174 random-bred male albino mice. The experimental seizure models were chosen with the aim to determine the neuromediated profile of extracts action: picrotoxin-induced, thiosemicarbazide-induced, strychnine-induced seizures and seizures induced by camphor.

Results and discussion. Pharmacological analysis suggests that the LCDEAq and the LCDEAl influence mainly on separate elements of epileptogenesis. They were effective on the models of thiosemicarbazide-induced seizures and convulsions induced by camphor. At the same time the FSDE and the OBDE have a complex influence on different pathochemical mechanisms of convulsions development: they improve the GABA- and glycinergic inhibitory processes, decrease the glutamate-induced activation, regulate the exchange of catecholamines in the brain.

Conclusions. According to the results of investigation it was established that all the chosen herbal extracts have a complex influence on the mechanisms of convulsions development. But the most efficient remedies which showed the potent activity in the conditions of all experimental models are the FSDE and the OBDE.

ROLE OF OXIDIZED MODIFIED PROTEINS IN PATHOGENESIS OF TYPE 2 DIABETES

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Type 2 diabetes mellitus (DM 2) is characterized by chronic hyperglycemia, which is accompanied by an increase in the speed of glucose auto-oxidation, followed by an increase in free radicals and oxidative stress (OS). Currently widely studied properties of the antioxidant system and lipid peroxidation (LPO), which allows to use in the treatment of patients with type 2 diabetes antioxidants. However, the problem of choosing a cell markers, which most adequately reflect the metabolic and biochemical processes in diabetes remains relevant today. Therefore, the new fundamental direction is the study of the oxidative modification of proteins (OMP) in various pathological conditions. Many researches have found a significant increase in OMP in plasma in patients with type 2 diabetes, which allows us to offer this index as a test to determine the depth of metabolic disorders in diabetes. One of the methods to evaluate the oxidative modification of protein molecules is to study the number of their carbonyl groups.

The aim of this work was to study the degree of carbonyl modification of serum proteins in experimental type 2 diabetes mellitus in rats induced by streptozotocin. Diabetes was reproduced by intravenous administration of streptozotocin in a dose of 65 mg/kg with the background of the protective action of nicotinamide. The evaluation of oxidative status of the experimental animals was performed 1 month after insulinoresistancy induction on level of MDA and on DC in serum by conventional methods, also oxidative modification of proteins were determined by Levine method in Dubinina modification.

The results showed that the level of MDA and DC in animals with pathology model was significantly higher than that of intact animals, thus confirming amplification of free radical lipid oxidation. The relationship of lipid peroxidation processes and oxidative modification of proteins in diabetic animals manifested in a significant increase in level of spontaneous oxidation of serum proteins, and less pronounced intensity induced protein degradation. The results indicate substantial activation of the total oxidative capacity in type 2 streptozotocin induced diabetes, but in the period up to 1 month of pathology adaptive capabilities of the organism in response to stimulation of protein oxidation are saved. Oxidative modification of proteins index can be used to assess the status of oxidative stress in animal models of type 2 diabetes mellitus.

CARDIOPROTECTION PROPERTY PREPARATION LATIRON IN MODEL CARDIOMYOPATHY

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One of the pathology of heart muscle is cardiomyopathy. The mechanism to form of the cardiomyopathy – activation free radical oxidation, therefore in the complex therapy to make use of antioxydants.

Investigation cardioprotective action of “Latiron” conducted in the model docsorubizine cardiomyopathy in the rats. The experimental rats will be separated into four groups by ten rats in each: 1-st group – intact control, 2-nd group – control pathology, 3-rd group animals with pathology treated with “Latiron” (40 mg/kg) , 4-th group – animals with pathology treated with preparation “Cverzetin” (5 mg/kg).

In the group of animals with control pathology changes peculiar for acute ischemic necrotic processes was of serious in myocardium. After in myocardium muscle development proliferation processes and fibrosis. At experimental animals after experiments registration of the ECG and biochemical index in the blood and homogenate myocardium muscle, what to confirm authentic increase coefficient mass heart on 37%, activation cytolysis in cardiomyocytes increase AsAT on 42% in serum.

In the ECG to mark decrease segment ST from isoline what to attest about ischemic myocardium.

Most express to brake peroxide oxygen lipids (POL) in myocardium descent under operation “Latiron” on 30%, “Cverzetin” on 28%.

At preamble investigation preparation noted increase action catalase in homogenate myocardium on 14 and 24% Cverzetine.

Analyses receive results to display, what preamble “Latiron” and “Cverzetine” recovery metabolic function myocardium in the middle on 10-14%.

Applicable “ Latiron” and “Cverzetine” increase survival animals in the middle on 50%, and mortality 10%.

“Latiron” to manifest moderate cardiothrophy action on the model docsorubizine cardiomyopathy.

SECTION № 8

**MODERN ASPECTS OF PHARMACEUTICAL MICROBIOLOGY AND
IMMUNOLOGY**

PERSPECTIVES OF VECTOR ALGEBRA THEORY IN ANALYSIS OF PROPERTIES OF ANTIBACTERIAL MEDICATIONS

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Introduction. At the present, a problem of infections diseases of human (dental, otolaryngological, dermatological, etc.) and their treatment is the issue of importance both, for Ukraine and for the world in general. But mathematical theory for quantitative description of antibacterial medications and comparison of their properties has been not described.

The aim of the thesis is to show the possibility to use vector algebra theory for quantitative description of antibacterial medications and comparison of their properties.

Materials and methods. For the purpose of screening of antimicrobial properties the following medications have been taken: “Tincture of Sophora japonica”, “Tincture of eucalyptus”, “Tincture of propolis”, “Tincture of calendula”, “Fitodent”, “Stomatofit”, “Rotokan”, “Romazulan”, “Sangviritrin”, “Chlorophyllipt” (Galichpharm), “Kamistad”, “Orasept”, “Hexoral”, “Metrogyl Denta”, “Myramistinum”, “Decasanum”, “Chlorhexidine digluconate”, “Benzalkonium chloride” and “Octenisept”.

Antimicrobial activity of medications has been determined by easily performed method of “wells”, with determination of zone diameters of microorganism growth inhibition. According to recommendations of World health organization and State Pharmacopoeia of Ukraine the following test strains of microorganisms were used for valuation of antimicrobial activity of medications: Staphylococcus aureus ATCC 25923, Escherichia coli ATCC 25922, Pseudomonas aeruginosa ATCC 27853, Proteus vulgaris ATCC 4636, Bacillus subtilis ATCC 6633, Candida albicans ATCC 885/653. Antimicrobial properties of medications have been examined in the State Institution I.I. Mechnikov Institute of Microbiology and Immunology of National Academy of Medical Sciences of Ukraine, Kharkov, under supervision of the Head of Laboratory “Biochemistry of microorganisms and nutrient media”, candidate of biological sciences, Osolodchenko T.P.

Calculation of the complex indicator of medication antimicrobial activity and its measurement error has been performed using the following formulas:

$$A = \sqrt{\left(a_1 \cdot \frac{D_1}{25}\right)^2 + \left(a_2 \cdot \frac{D_2}{25}\right)^2 + \left(a_3 \cdot \frac{D_3}{25}\right)^2 + \left(a_4 \cdot \frac{D_4}{25}\right)^2 + \left(a_5 \cdot \frac{D_5}{25}\right)^2 + \left(a_6 \cdot \frac{D_6}{25}\right)^2} \quad (1)$$

and

$$\Delta A = \sqrt{a_1 \cdot \left(\frac{\Delta D_1}{25}\right)^2 + a_2 \cdot \left(\frac{\Delta D_2}{25}\right)^2 + a_3 \cdot \left(\frac{\Delta D_3}{25}\right)^2 + a_4 \cdot \left(\frac{\Delta D_4}{25}\right)^2 + a_5 \cdot \left(\frac{\Delta D_5}{25}\right)^2 + a_6 \cdot \left(\frac{\Delta D_6}{25}\right)^2}$$

(2)

where A is a complex indicator of medication antimicrobial activity, dimensionless value, (indicator efficiency ranges: 1.0-1.5 the medication has weak antimicrobial activity; 1.5-2.5 the medication has medium antimicrobial activity; more than 2.5 the medication has strong antimicrobial activity);

$a_1, a_2, a_3, a_4, a_5, a_6$ are weighing coefficients of microorganism strain significance in the disease, in order to simplify, we have taken them as a unit, however, application data from research on prevalence degree of microorganisms in affected people can be used;

$D_1, D_2, D_3, D_4, D_5, D_6$ are zone diameters of growth inhibition of the examined microorganism strains: Staphylococcus aureus ATCC 25923, Escherichia coli ATCC 25922, Pseudomonas aeruginosa ATCC 27853, Proteus vulgaris ATCC 4636, Bacillus subtilis ATCC 6633, Candida albicans ATCC 885/653, mm;

ΔA is a measurement error of complex indicator of medication antimicrobial activity.

Results and discussion. It has been shown that among 19 medications, 7 possess upper-range value of complex antibacterial index: Chlorhexidine digluconate - 2.07; Tincture of Sophora japonica - 2.05; Chlorophyllipt (Galichfarm) - 1.99; Sangviritrin - 1.91; Decasanum - 1.84; Metrogil Denta - 1.51; and Tincture of eucalyptus - 1.50.

This method in pharmacoeconomics allows choosing optimal cost/quality ratio among the antibacterial medications.

Conclusions. This method allows evaluation of medications' antibacterial activity and opportunity to choose the most active ones, as well as compare them with each other.

It has been shown that among 19 medications, 7 possess upper-range value of complex antibacterial index: Chlorhexidine digluconate - 2.07; Tincture of Sophora japonica - 2.05; Chlorophyllipt (Galichfarm) - 1.99; Sangviritrin - 1.91; Decasanum - 1.84; Metrogil Denta - 1.51; and Tincture of eucalyptus - 1.50.

It is noted that medications of natural origin are inferior to those of synthetic origin as for their antibacterial activity, and new galenic medications possess the most antimicrobial properties.

It is noted that this method in pharmacoeconomics allows choosing optimal cost/quality ratio among the antibacterial medications.

PROSPECTIVE OF USE OF HERBAL DRUGS BY AEROBIC VAGINITIS

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Currently one of the most important medical and social problems is infectious pathology of the reproductive system in women. Significant place in the structure of this disease is taken by aerobic vaginitis, which is an independent nosological form associated with the propagation of aerobic microorganisms, mainly represented by Streptococci of Group B and E. coli. In recent years, there are more frequently met microbial associations represented by 2-5 species with equal or predominant aerobic component, which causes a more severe course of the disease and makes its treatment ineffective. Rapid and global environmental degradation, started in the middle of the XX century, and frequent adverse effects of chemotherapy, encourage a special interest in the development of herbal drugs.

The vegetable oils obtained by processing medicinal plants, find a wide application both a folk medicine and in official medicine. The experimental research of oil from Australian tea tree is expedient and the possibility of creating a new medicine on its basis is perspective since it will expand the nomenclature of the existing plant medicine.

The aim of this study was to investigate the antimicrobial activity of Australian tea tree oil and lavender essential oil.

We used the agar diffusion method according to the "Guidelines for determining the activity of antibacterial agents for the treatment of topical pyo-inflammatory infections", developed in Mechnicov Institute of Microbiology and Immunology (1991), a set of reference strains of microorganisms: S.aureus ATCC 25923, E. coli ATCC 25922, B.subtilis ATCC 6633, P. aeruginosa ATCC 28853, C. albicans ATCC 885653.

The results indicate a high level of antimicrobial activity of tea tree oil against Gram-positive and Gram-negative bacteria and fungi of the genus Candida. Zones of growth inhibition against S.aureus are 32 mm, E. coli - 50 mm, B.subtilis - 28 mm, P. aeruginosa - 26 mm, C. albicans - 50 mm. Antimicrobial activity of lavender against studied microorganisms is lower.

Thus, given that tea tree oil is well tolerated by the body and has no side effects, a wide spectrum of antibacterial, antifungal properties, tea tree oil is a promising raw material for creation of new safe and highly effective drug forms for local therapy of aerobic vaginitis.

MODERN IDEAS ABOUT THE VALUE INTESTINAL MICROFLORA

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In recent times, new data about the role of intestinal microflora in humans appear. As it is known, intestinal flora includes more than 1,000 different species of bacteria. It is clear that the intestinal microflora can be considered as an independent organ or another system of life. Everyone has their own unique, but characteristic flora, which is influenced by various factors: diet, family traditions, regional characteristics. But there are about 150 species of bacterias that form the intestinal microflora of each person.

Today the correlation of qualitative composition of the intestinal flora with obesity was proved. In addition to reducement of species diversity of intestinal microflora by obesity, characteristic for intestinal flora are the following bacteria: Firmicutes, Bacteroides, Ruminococcus, Collinsella, Eubacterium and others.

Violation of the composition and quantity of intestinal microflora may be a risk factor in the development of atherosclerosis, in the development of stenosis of liver, metabolic syndrome, diabetes type two. As a result of genetic mutations of intestinal microflora caused by association with host DNA, which leads to the synthesis of antibodies to them, allergic and autoimmune disease may develop. The link of deficit of intestinal microflora with mental illnesses - autism, schizophrenia, depression- is proved.

Despite modern new data in the study of intestinal microflora, it is still a mystery to experts. According to results of experimental and clinical studies it can be expected that in the coming days the analysis of the intestinal microflora will become the integral component in the definition of complex prognostic factors for risk assessment of many pathologies.

CONTEMPORARY MOUTHWASHES: THEIR PROPERTIES AND ANTIBACTERIAL EFFECT

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Introduction. The oral cavity is one of the most complex parts of the human body that consists of teeth, periodontal tissue, tongue and mucosa as well as secretory organelles. Thereby it harbors heterogeneous microbial community, which makes it highly prone to infectious diseases. Hundreds of bacterial species (e.g., Streptococci species as well as lactobacillus species) are involved in typical dental disease - caries. Mutans streptococci generally include Streptococcus mutans and Streptococcus sobrinus in the biofilms and produce acids as a by-product of metabolism of fermentable carbohydrates. For this reasons and more, scientific factory create some products for mouth washing "mouthwash", which have to fight against dental bacteria and harmful products of their metabolism. However, despite the wide assortment of mouthwashes, it is difficult to decide which commercial product is suitable for a particular purpose because of the variations of their antimicrobial efficacy, cytotoxicity and kinetics of the solutions. That is why it is very essential to go deep into the compounds of different mouthwashes and to understand for which purposes some of them should be used.

Aim. According to the stated above actuality of the topic, our aim was to compare some active ingredients of mouthwashes, which are sold on the consumers' market (everyday dental care), and to find out, which properties they have and which effect they may perform.

Material and methods. To compare the effect of some active ingredients of mouthwashes we have chosen two commercial products: "Colgate Plax Fresh Tea" and "Listerine Natural Green Tea". To investigate their properties and to find out their possible effects we used the following sources: literature and advertisement presented by the company-producer of a mouthwash; independent non-commercial scientific literature sources.

Results. As the active ingredient each company uses different molecule: Colgate- Cetylpyridinium chloride, Listerine - Eucalyptol, Menthol, and Thymol. So

what is the effect of this molecule on the bacteria of the mouth? The main indications are either the improvement of dental health or the prevention of infections caused by bacteria of the oral cavity in specific situations. Knowing the effect of these molecules on the bacteria and the mechanism of action can conclude the results of our comparison.

- Cetylpyridinium chloride: The polar and nonpolar regions of the molecule cause CPC to behave as a cationic surfactant with a net positive charge. CPC molecules bind to the negatively charged surface of the bacterial cell membrane. The nonpolar region of the molecule, which has similar traits to membrane phospholipids, penetrates the cell membrane of the bacteria, therefore altering it and generating an imbalance in the osmotic regulation, resulting in loss of cytoplasmic material and ultimately cell death. Its anti-gingivitis activity is also due to the neutralisation of proinflammatory bacterial toxins. CPC works by integrating these lipopolysaccharides to thereby alter their structure and neutralise them.

- Eucalyptol, Menthol, Thymol: The main ingredients in an antiseptic mouthwash like Listerine are eucalyptol, menthol, and thymol. Eucalyptol comes from naturally produced eucalyptus oil. Known for its strong and pleasant smell, it is used in sinus congestion treatments; cough suppressants and mouth wash to reduce inflammation. Menthol is derived from mint plants and is used in mouthwash for its cooling and pain-killing effect and it kill multiple kinds of bacteria, including *Staphylococcus epidermidis* and *Escherichia coli*. This effect seems to be due to menthol's ability to disturb the plasma membranes of bacteria, making them more permeable. Thymol is used in mouthwash for its antibacterial properties. The combination of these antiseptic and antibacterial ingredients kill germs on contact which in turn prevents gingivitis, calms inflammation or pain and prevents plaque buildup.

Conclusion. These two mouthwashes differ in their active molecules but the aim of their action is the same. At the same time the mechanisms of their action and their effect on bacteria are different, and these differences make each one special. But the main mechanism of their action is to disturb the plasma membrane of bacteria and to change the osmotic pressure.

RESISTANCE OF MYCOBACTERIUM TUBERCULOSIS TO MAJOR ANTI-TB DRUGS

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The course of tuberculous process, treatment and epidemiological situation of the disease is strongly dependent on the properties of the pathogen, and this is the factor as drug resistant Mycobacterium tuberculosis (MBT).

Since 90 years of worldwide landslide occurred actually increase the frequency of seizure-resistant MBT to major antimycobacterial drugs (AMBD) and clinicians began to note a decrease in the effectiveness of chemotherapy. One of the varieties is chemis resistance is multi-tresistance simultaneous resistance to a combination of "isoniazid + rifampicin" and combining it with other AMBD.

A statistical processing of bacteriological examinations of patients who were treated at the Kharkiv direct TB dystpanseri №1.

The aim of the thethis is defined study of the structure and profile of drug resistance of Mycobacterium tuberculosis to the main series of anti-TB drugs (isoniazid (H), rifampicin (R), streptomycin (S), ethambutol (E)).

The results of the analysis of the structure of Mycobacterium tuberculosis drug resistance is dominated by multi- strains (63.7 %) strains were monoresistance lowest proportion (18.8 %). The frequency of multiresistant strains was 17.5 %.

The study of the frequency and profile of multiresistant allowed to identify different strains of multidrug HR ratio of the combinations of drugs primary series (Fig. 1).

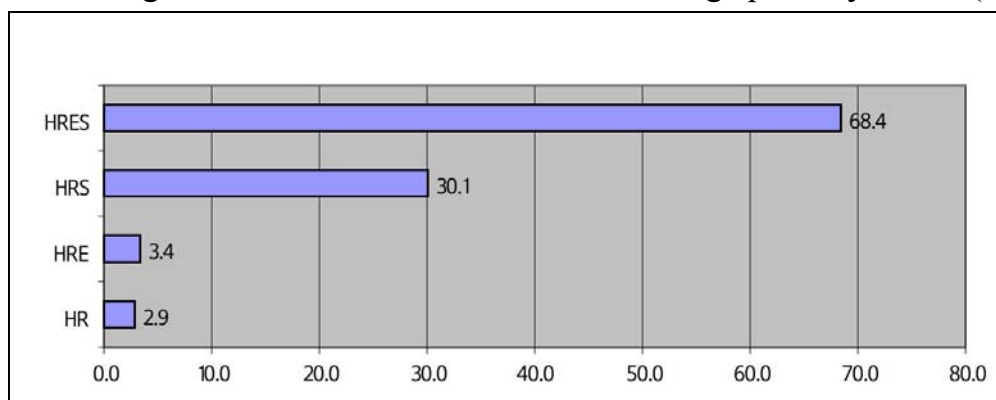


Fig. 1. Structure of multiresistant in Kharkiv region in 2013.

Conclusions. Study of the structure, frequency and profile of drug resistance enables the Office to timely adjust treatment regimens bakteriovydilyuvachiv and predict the effectiveness of their likuvannyav in a hospital. Growth multyrezysteniyh strains indicates an unfavorable redistribution in the structure of resistance.

DIFFCULTIES IN FINDING CHLAMIDIAL INFECTION IN PATIENS WITH HYPOTHYROIDISM

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Among modern medical - social problems one of the most pressing is the thyroid gland (td)pathology. This is due to the fact that the total frequency of different forms of pathology even outside the " goiter epidemic" is at least 20% of the total incidence. In goiter endemic regions in which there are about 1/3 of the human population , this figure sometimes exceeds 50% . In recent years, the ecological trouble in most countries experienced higher frequency of thyroid disease . Due to this much attention is attracted to its laboratory diagnostiks. According to the results ELISA blood test we conclude the existence of one or another disease:

- Appearance of ELISA methods makes it possible to determine the concentration of thyroid hormones and a number of high-molecular compounds that can give important information on the functioning of the thyroid, the etiology and pathogenesis of its diseases;
- Until ELISA, diagnostics of thyroid disease was based on analysis of the clinical picture ;
- Today ELISA methods are the main in the diagnostis of thyroid function abnormalities , diagnosis and control of the therapy ;
- In the arsenal of laboratory methods for diagnosis of thyroid diseases in vitro , there are 9 most common tests : determination of TSH, total and free T4, total and free T3 ThBP (" thyroid status ").

In patients with hypothyroidism from which suffers a large percentage of women , there is reduced immunity, leading to infections. There are latent infections of the genital tract, which are dominated by chlamydia and they are mutually aggravating factors of litter Pathology. Latent infections by hypothyroidism occur significantly more often than by normal thyroid function. Chlamydia - one of disease, which may be asymptomatic. Is one of the most common diseases, sexually transmitted diseases, occurs in 5-15 % of people who are sexually active. According to WHO statistics, every year the world's 100 million sick people, and the number of infected more than 1 billion people. The causative agent of the disease is Chlamydia trachomatis, which combines properties of the virus and bacteria. The dual nature and the ability to parasitize intracellularly significantly complicate diagnosis and treatment of this disease. Find infection only when the inflammatory process.

WHAT IS A MORGELLONS DISEASE: MODERN SCIENTIFIC VIEWS

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Morgellons Disease (Morgellons disease, unexplained dermopathy) is a disease of unknown etiology, first described by Mary Leitaó in 2002, who discovered it in her child. According to foreign authors, approximately 200,000 people in the world already suffer from Morgellons disease. In the U.S.A., where there is the largest number of affected by it, there are more than 12,000 patients. This disease spreads at a speed of about 1,000 victims a day. Until now, doctors can not identify if this disease is separates or if it is a set of symptoms of other diseases, it can last for years, up to 8-10 years.

The etiology of the disease is not clear. Among the authors of articles describing unexplained dermopathy, there are a few opinions . Some believe that this disease does not exist, and its clinical manifestations are hallucinations of those suffering of psychosis. The others consider it to have parasitic, infectious or fungal origin. For example, some doctors believe that this is one of the manifestations of Lyme disease, an infectious disease transmitted by ticks, there are statements that it may be caused by the bacterium *Stenotrophomonas maltophilia*. Many people make fantastic allegations of biological weapons, the impact of GMOs and nanomachines. Patients complain of tingling, itching and crawling under the skin. They see small fibers and threads sticking out of wounds, formed as a result of scratching. According to Professor Randy Vajnor, head of the research program Morgellons Research Foundation, these threads do not appear from the outside - they materialize inside the body. Doctors often say that their patients suffer from hallucinations and these symptoms are called parasitic delirium. Patients tell doctors about the strange insects that nest under their skin, some mention of worms. Specialists of the Center for Disease Control and Prevention of United States, after investigating a number of patients, found no trace of the presence of an infectious agent or parasites. They also studied fiber extracted from beneath the skin patients. Experts came to the conclusion that it is cotton or nylon. Treatment of the disease is unknown. Various drugs are used: antibiotics, de-worming drugs, psychotropic agent for the treatment of mental disorders. It is known that the parasite reacts actively to a magnetic field, which blocks and destroys it, and it should be noticed. At the moment, scientists have a task: to find out the etiology of the disease (parasitic, infectious, mental, etc.), to determine the methods of diagnosing and to find a rational treatment of the disease.

SECTION № 9

CLINICAL PHARMACY

RATIONAL DRUG THERAPY: FOR THE INDIVIDUAL AND COMBINED TREATMENT OF HYPERTENSION AND CORONARY ARTERY DISEASE

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Introduction: Coronary artery disease (CAD) is currently the leading cause of death globally, resulting in over 7 million deaths worldwide in 2012. This number has only increased at an alarming rate. Hypertension on the other hand affects 30-45% of Europeans. Although many guidelines exist on how these conditions are treated individually, little is known on how to manage patients who are concomitantly affected by both conditions.

The aim of our study was to analyze practical doctor prescriptions in patients with CAD and hypertension to optimize pharmacotherapy in mentioned clinical group.

Materials and Methods: 50 treatment histories were obtained from the therapeutic department of the scientific medical practical center of Kharkiv State Medical University, Kharkiv, Ukraine. These treatment histories were analyzed taking into account the age, concomitant illnesses and drug interactions etc.

Results: According to our results so far, it has been observed that patients who present with CAD only are more likely to be treated with a calcium channel blocker like verapamil (37% of such patients) or a beta-blocker like bisoprolol (63% of such cases) and NSAIDS are co-administered when needed. But in patients presenting with both CAD and hypertension, the physicians prefer to treat with an ACE inhibitor like enalapril (73% of cases) and in most cases together with a thiazide diuretics (52% of cases). It was also observed in all patients who were treated with ACE inhibitor the physicians were also careful not to administer NSAIDS and a hepatoprotective drug like antral was always giving.

Conclusion: With these results it appears that in combined cases of CAD and hypertension, physicians prefer to lead treatment with medications favorable for the treatment of the hypertension (which happens to be a risk factor of CAD), but concerns should also be drawn to the use of an ACEs inhibitor together with a thiazide, because this combination has been shown to reduce blood pressure very fast and this may be dangerous to the patient.

MULTIFACETED USE OF GLUCOSAMINE AND ITS COMBINATION WITH FLAVONOIDS AND NSAIDs

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There are many different diseases that threaten the human life and health. Cancer is a serious social and health problem, devastating disease with significant mortality and morbidity in both developed and developing countries. Acquired and intrinsic resistance to major classes of anticancer agents: antimetabolites, anthracyclines, taxanes and alkylating agents which are mostly pro-apoptotic present a serious challenge to management of cancer. They are also affected by the problem of drug resistance. So there is need for new anticancer agents with new mechanisms of action that are apoptosis independent.

Osteoarthritis is a chronic degenerative disease of joint characterized by progressive destruction of articular cartilage, loss of free movement and disability. The 14% of adults have osteoarthritis. The losses connected with diseases of this group increased in recent years and up to 3% of gross national income of developed countries such as USA, Canada, UK, France and Australia. Thus, the development of new highly efficient methods of treatment and prevention of osteoarthritis is a very important problem of experimental and clinical pharmacology.

These two serious illnesses can be treated with the same compounds. Among such compounds can be identified glucosamine, which in addition to being a promising drug for the correction of the toxicity of anticancer therapy. Glucosamine has nephroprotective, hepatoprotective, cardioprotective, gastroprotective, chondroprotective effects. Therefore, his combination with other drugs that are used to treat cancer and osteoarthritis can be extremely effective.

The analysis of research confirms that derivatives of glucosamine exhibit antitumor activity of hormone-dependent tumors. D-glucosamine was previously reported to show potent *in vitro* antitumor activity on a range of cancer cell lines derived from breast, pancreas and prostate cancer.

Derivatives of glucosamine at intermediate dose (250 mg/kg) had the highest inhibition ratio on tumor growth and that the inhibition ratio declined at higher dose (500 mg/kg). The antitumor activity may be due to its cytotoxic and immunomodulating properties. D-glucosamine hydrochloride at dose of 250 mg/kg could also promote obviously the T-lymphocyte proliferation induced by ConA, as well as the thymus index and spleen index.

Quercetin has also been demonstrated to display the anticarcinogenic, antiviral, antibacterial and anti-inflammatory effects. The anticarcinogenic properties of quercetin result from its significant impact on an increase in the apoptosis of mutated cells, inhibition of DNA synthesis, inhibition of cancerous cell growth, decrease and modification of cellular signal transduction pathways.

Derivatives of glucosamine improves the metabolism of cartilage. These compounds are a substrate for the synthesis of glycosaminoglycans, stimulates the synthesis of proteoglycans. Despite the high chondroprotective activity of derivatives of glucosamine it should be noted the lack of efficacy of this group on anti-inflammatory and analgesic effect, which somewhat limits the possibilities of their use in patients with osteoarthritis.

Today the most promising direction is the development of third generation chondroprotective drugs based on combinations derivatives of glucosamine with drugs of other groups (non-steroidal anti-inflammatory drugs (NSAIDs), vitamin, micronutrients, etc.). This can significantly extend the pharmacodynamics derivatives of glucosamine. The resulting combination drug influences on the several pathogenic links of destructive-dystrophic lesions of cartilage. Osteoarthritis is chronic destructive disease of the articular cartilage, which is always accompanied by pain. In order to eliminate pain is most often used NSAID as parenterally or topically in a variety of gels and ointments. Combining derivatives of glucosamine with NSAIDs will reduce pain and improve patient's quality of life.

After review of the literature suggests that the combination of glucosamine and quercetin may be more effective than the individual components thereof, and used not only as a promising toxicity correctors anticancer therapy that has been proven in our studies, but have themselves antitumor activity. This allows you to draw near to the creation of drugs – not only universal correction toxicity of anticancer therapy, and those which have themselves an antitumor effect.

For the treatment of osteoarthritis patients need long-term use of drugs with anti-inflammatory, analgesic and chondroprotective effect. The combination derivatives of glucosamine and NSAIDs can reduce pain and improve cartilage metabolism. It is very important for the treatment of osteoarthritis.

In conclusions we would like to note that the use of combinations of glucosamine with quercetin and NSAIDs can significantly increase the efficacy of treatment of cancer and osteoarthritis. Further investigation of such combinations is necessary and scientifically substantiated.

IDENTIFICATION OF RISKS TYPES THAT INFLUENCE THE QUALITY OF DATA IN CLINICAL RESEARCH

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Globalization, growth of number and complexity of clinical researches (CR) creates circumstances that make it hard to reach a high quality level because of lack of resources. In such condition it becomes especially crucial to implement a risk oriented approach in the CR control system.

The goal of our research was to study the typical risks for data control system (DCS) in CR. During the study we have used the methods of abstraction, logical analysis and structured system analysis. The first step of risks assessment is their identification where it is important to discover factors that can badly influence on some data quality and the analysis of this influence with further identification of risks for DCS in CR. As a result of a conducted analysis of national and foreign literary sources, clinical trial protocols and study designs we have pinpointed main types of risks that lead to loss of data quality in CR during their planning and organization. Thus, risks connected with the data processing and conduction of biostatistical analysis and also with clinical data control have a negative influence on a clinical data quality. As last risks we describe the following: irregular getting of informed consent; incompatibility o insertion criteria, inadequate recognition of side reactions and by-effects; false estimating of efficiency and security indicator of medicinal product ; improper randomization and use of blind design.

The analysis of the pinpointed risks types enables to properly determine prior directions in risks control for DCS in CR at the stage of its planning and to guarantee its high efficiency.

METABOLIC EFFECTS OF B2-ADRENERGIC AGONISTS

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Background. Beta-2 agonists are widely used in the treatment of asthma and chronic obstructive pulmonary disease for their effects on airway smooth muscle relaxation. They also act on skeletal muscle, although their reported ergogenic effect is controversial. Clenbuterol is popular – but banned – drug used by athletes in bodybuilding, power-related, and even endurance sports. The chemical is attractive to athletes because it appears to have an anabolic effect on human muscles, and it may also increase fat metabolism. However, the actual effects of long-term clenbuterol intake on performance, muscle power, and overall health is unclear.

Materials and methods. For this writing, we have analyzed the literature sources: Internet-articles, tutorials, articles from scientific journals, interviews with scientific figures.

Results. Clenbuterol inhibits lipoprotein lipase activity, that results in impossibility the deposition of fat in the adipose tissue. Acting on *B*-2-adrenergic receptors of the central nervous system active drug enhances the secretion of thyroid hormones. It also has a strong anti-catabolic effects, which is caused by blocking Ca-dependent proteolysis. Due to the above-mentioned mechanisms the drug has a moderate anabolic effect, which is proved in experiments on animals and has a practical use in cattle breeding to increase muscle mass in cattle. With a same aim clenbuterol used in sports medicine. Drug is banned in the sport since 1992. So as it is cumulating in adipose tissue and is releasing during stress or competition it can be revealed by anti-doping control not only before competition but for a long time after it. Popular among amatory bodybuilders who are not covered by the anti-doping control, drug causes a number of side effects, including tremors, headaches, insomnia, general anxiety, heart rhythm disturbances, hypokalemia.

Conclusions. Research results proved that Clenbuterol is not recommended for use in bodybuilding and sports in connection with a number of side effects. Despite the fact that all of them can be eliminated by ketotifen and bisoprolol (metoprolol), Clenbuterol - a drug that is primarily used in medicine for the treatment of bronchial asthma, what should not be forgotten.

ALTERNATIVE APPROACHES OF PATHOLOGY'S MODELING IN PHARMACOLOGICAL STUDIES OF MEDICINES

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Introduction of new medicines in clinical practice is impossible without preclinical studies in which are used a lot of laboratory animals. According to Council Directive of EU (86/609/EEC) of 1986, following ethical norms must be considered during holding studies on animals: reduction of number of studies, improvement of studies' severity and used species, also replacement of studies on animals that is a final goal of this Directive. Alternative of preclinical studies of medicines on animals is using of appropriate cell cultures and tissues for these goals. Modern toxicology and pharmacological laboratories use standardized cell cultures for holding screening toxicology studies, determining orientation of new biologically active substances and first evaluations of dependence "dosage - effect". But the metabolism of organism's tissue differ from one of the cell culture that prevents fully evaluate effect of medicine on all organs and systems of biological organism. Considering this, the full toxicology and pharmacological study can't be holded without using of laboratory animals.

Another alternative side of pharmacological study of new drugs is computer modeling of biochemical, pharmacokinetic and pharmacodynamic processes in human body, its organs and systems in general. Herewith, different processes of organism can be introduced with the help of number of mathematical models given with possible variations of physiological indexes. Also there can be simulated pathologies that are needed for study. The complexities of implementation of such kind of modeling pharmacological effects of medicine are wide variation of indexes under study, multifactorial effects under study and complicated correlation, interrelatedness and interaction of systems under study. Besides, verification on traditional pathology models in animals needs to be holded for conformation of their reliability and introduction into the pharmacological studies of medicines.

Especially interesting for pharmacological studies of medicines is developing and verification of kidney's mathematical model, because the most of drugs are excreting through them, so this process can be changed or broken at kidneys' diseases. Kidney anatomy and its functions are rather complicated research problem, realization of which should include several stages. Mathematical models of single processes in kidney should be created first, then they should be verified on animals and after that the model of the whole kidney can be done.

Glomerular filtration is the most important process among ones in kidneys, but it is hard to verify its pathology because of complexity of creating physiological pathology model exactly of this process. Tubular reabsorption has a lot of ways of modeling on animals exactly its pathology. In our future research it is planned to simulate tubular reabsorption and pyelonephritis as its pathology via mathematical modeling with the following their verification on animals.

VALIDATION AS IMPORTANT ASPECT OF GUARANTEEING OF QUALITY OF LABORATORY ANALYSIS

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Nowdays only a small number among hundreds of Ukrainian laboratories actually meets the requirements of ISO/IEC 17025:2005, based on the approaches to quality assurance contained in the standard ISO 9001:2000. ISO Standard ISO/IEC 17025:2006 defines a set of general requirements for the competence of laboratories to form a system of mutual confidence in the results of their work. Therefore, the immediate task is to research, develop and implement quality assurance procedures in laboratories of clinical diagnostics by means of the validation work.

The main object of evaluation are methods by which measurements are certain parameters in the laboratory, and in order to guarantee reliable and accurate analysis is a procedure of validation of laboratory methods.

In the absence of laboratory services in medical institutions of our country experience of quality control of laboratory diagnostics based on the application of the principles of a specialized laboratory medicine standard of ISO 15189-2009 «Medical Laboratories. Particular requirements for quality and competence». Specialists of national laboratories have many questions regarding the quality assurance of laboratory measurements.

The purpose of the study is to explore the aspects of quality assurance in the laboratory of clinical diagnostics of CDC of National University of Pharmacy through the validation of assessment date of hematological methods. Identify the features, approaches and requirements to assess validity (validation) of laboratory methods and key points of uncertainty.

In this work we used analytical, statistical and biological methods.

Results. In DSTU ISO/IEC 17025:2006 was given the following definition: «validation (assessment date) techniques – research and confirmation by providing objective evidence that the particular requirements for a specific target using executed». That is, the method must be appropriately rated investigated and evaluated characteristics measurement results by this method. If the estimated characteristics

meet your requirement methods, the method is considered to be validated in the laboratory, it can be used to test biological samples.

Validation of methods in the laboratory should be conducted under conditions of specificity: using calibrated working equipment which operated properly; staff involved in the validation have the necessary competence; facilities meet the requirements for monitoring environmental conditions and facilities.

Validation set of characteristics that should be determined, depending on the method, the type of product or object test/measurement, and biological test systems, which will be conducted the study. For certain techniques can be defined such validation properties: resistance to external influences (robustness), selectivity/specificity of the method, accuracy, reproducibility, repeatability (convergence), sensitivity to the effects of the parameters of the sample/the object test. Set of characteristics and methodological approaches to their definition depends on each specific technique, but the presence/absence of each characteristic must be justified in executing appropriate validated documents (validation scenarios and protocols).

A good practice is to review the information contained in the published literature that relates to the method. This allows you to evaluate the overall effectiveness of a test/calibration and to determine any possible limitations or weaknesses. The presence of links to such information helps to reinforce the validation done by the same laboratory.

Validation of the method should be conducted prior to the application of the method/test. It is important to remember that when you make any changes in the content of the method, the laboratory must evaluate it (conduct validation) and documentally impact these changes. If necessary, you need to create a new (re-) validation to check and demonstrate the compliance changes.

Conclusions. Evaluation of intralaboratory convergence and reproducibility of a number of hematological methods in the laboratory of clinical diagnostics of CDC of National University of Pharmacy showed good resistance of methods for the studied parameters; measurement accuracy is proved in laboratory throughout the range of measurements. Accordingly, the values obtained for the studied parameters can be considered accurate and reliable.

THE MODERN ASPECTS OF NEUROPROTECTION

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In those days actual problem of modern pharmacy and medicine is effective neuroprotection and invented new neuroprotective drugs.

The aim of neuroprotection is to rescue ischemic tissue and improve functional outcome by intervention on ischemic cascade. A lot of experimental trials demonstrated that neuroprotection is effective in infarction volume reduction. Unfortunately most of the effective agents in preclinical studies failed in clinical trials.

Neuroprotective agents which are most frequently used there are calcium channel blockers; glutamate antagonists; GABA agonists; antioxidants/radical scavengers; phospholipid precursor; nitric oxide signal-transduction down-regulator; leukocyte inhibitors; hemodilution; and a miscellany of other agents. Among promising ongoing efforts, therapeutic hypothermia, high-dose human albumin therapy, and hyperacute magnesium therapy are considered in detail.

One of effective neuroprotective drugs is Citicoline. Citicoline refers to the exogenously supplied form of cytidine 5-diphosphocholine (CDP-choline), a product of the rate-limiting step in the synthesis of phosphatidylcholine from choline. Orally administered citicoline is hydrolyzed in the gut to cytidine and choline, which are rapidly absorbed cross the blood-brain barrier, and can be incorporated into the phospholipid fraction of neuronal membranes. CDP-choline increases phospholipid synthesis, inhibits phospholipid degradation and free fatty acid release, increases CNS levels of norepinephrine and dopamine, and restores mitochondrial and membrane ATPase activities. While CDP-choline and its components do not directly affect phospholipase A2 (PLA2) activity in vitro, when studied in vivo citicoline attenuates ischemia-induced PLA2 stimulation and thereby diminishes the injurious consequences of phospholipid hydrolysis – namely, the generation of arachidonic acid, whose metabolism leads to formation of reactive oxygen species, lipid peroxides and toxic aldehydes. Citicoline also inhibits glutamate-induced apoptosis in cultured cerebellar granule neurons and increases glutamate uptake and expression of the membrane glutamate transporter EAAT2 in cultured astrocytes.

Future of neuroprotection is seen in concentration on the subgroup with existing penumbra, the combination of neuroprotection and thrombolysis and in prophylactic neuroprotection. The unification of the design in experimental and clinical trials is the main prerequisite for potential success in the clinical testing.

APPROUCH TO RISK ESTIMATION OF PROJECT MANAGMENT IN CLINICAL TRIALS

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Project management in clinical trials is the application of knowledge, skills, tools, and techniques to project activities in order to meet or exceed stakeholder needs and expectations from a drug development process.

An effective way to avoid expensive delays in approval timelines due to quality issues is early detection and mitigation of this risk by close monitoring and optimizing of the three parameters: quality, time, and cost

Processing the data maintained in various operational and clinical databases, against a predefined set of standards and metrics in a systemic way, is the first step in development of a rich repository of both historical and current compliance information. The step involves developing metrics to further derive base quality performance indicators (BQPI) for each parameter. With the BQPIs in place, by developing a process to continually monitor and update each parameter, a sponsor can achieve two objectives. First, it can optimize timelines or cost, while continually monitoring for changes in the quality. Second, any significant deviation from the mean (caused by an underlying change or signal) in any of the three parameters can be differentiated from background noise. The information obtained in this way can then be used to drive development cost and timeline reduction at an organizational level, while at the same time the quality of the output is intensively and efficiently monitored.

Development of accurate metrics and BQPI s for all three pillars of an operation (quality, timeline, and cost) combined with the implementation of an information management strategy such as text mining are essential elements for implementing this methodology. Combination of processes and systems that allow for early signal detection and the subsequent intervention is the true power of a data-driven quality management system. Compared to the benefit for the entire clinical organization, the investment in the technology is minimal. Selected parameters that indicate nonconformance can be obtained through all stages of product development. In combination with easy access to extensively trended information (operational BQPIs) and overview of financial BQPIs, this system provides a safeguard for sponsors to maintain an overview of the quality of their clinical operations in a cost-effective manner.

RESEARCH OF PROFESSIONAL TRAINING AMONG SPECIALISTS INVOLVED IN CLINICAL TRIAL

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Ensuring an appropriate level of professional training is an urgent problem of clinical trials. Lack of ordered training system for professionals in clinical trial (CT) in Ukraine has created a situation in which most of experts working in clinical drug development, have no specialized education - medical or pharmaceutical. To date, there was a need for assessment of CT professionals training and substantiate the importance of ensuring proper qualification of CT specialists by obtaining postgraduate specialized education.

The study aim was to evaluate comprehensively knowledge level regarding principles and standards of proper conducting of clinical research using self-assessments system among CT specialists performed various functions in clinical research. The survey was performed using specific questionnaires in which respondents were required to assess own knowledge level concerning fundamentals aspect of proper clinical study conducting. Statistical methods were used to analyze the respondents' answers.

We found that most of specialists who took part in survey need to extend their knowledge in following CT aspects: GLP; clinical data processing and statistical analysis; CT quality assurance and control; investigational medicinal product handling; responsibilities of auditor company and regulatory bodies. We determined that regardless of functions performed by specialists in CT, knowledge level concerning basic aspects of CT organization and conducting directly depends on basic education. Thus, specialists with pharmaceutical degree who had in their educational programs appropriate courses have the highest knowledge level in CT aspects. At the same time, specialists with medical degree, especially with biological degree, need not only extend their knowledge, but even to learn fundamental ideas and aspect in CT conducting.

All these findings proof the importance of implementing into Ukrainian educational system new specialty "Clinical Trials". This will enables to achieve the specialized education in CT and get sound knowledge and skills that are necessary for successful career. Also it will facilitates the assurance of high level of qualification for specialists involved in CT and proper control of its professional training within national system of higher education quality assurance and will extend the facilities of Ukrainian trial site regarding participation in international research projects.

ASSESSMENT OF ISCHEMIC HEART DISEASE TREATMENT IN DIABETES MELLITUS TYPE 2 PATIENTS

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A diabetes mellitus is one of the most common diseases in the world. According to prognosis of the World Health Organization the amount of patients with this disease will increase to approximately 366 million persons to 2030. Patients with diabetes mellitus type 2 have ischemic heart disease in 2-4 times more often than without it because of diabetes mellitus is the leading pathogenetic factor of development cardiovascular complications.

According to the Ukrainian health care protocols (Order of Ministry of Health Care Order from 03.07.2006 № 436) patients with ischemic heart disease should get therapy includes antiaggregants, nitrates, calcium channel blockers, angiotensin-converting enzyme inhibitors, β -blockers, antihypertensive agents and other.

In the prescription of antianginal drugs patients with diabetes mellitus type 2 we take into account non-selective β - blockers increase insulin resistance of peripheral tissues and lead to the development of dyslipidemia. We should prefer selective β -blockers, especially with vasodilating effect (nebivolol, carvedilol), that increase tissue insulin sensitivity. Nitrates are metabolically neutral, but tolerance to this group develops quickly, it reduces their effectiveness. In patient with diabetes mellitus we should prefer calcium channels blockers, because they do not have negative effect on the insulin sensitivity of peripheral tissues, and lipid metabolism.

Among hypolipidemic drugs most preferable for patients with a diabetes mellitus are statins, because they do not require control of peroral hypoglycemia therapy. Nicotinic acid negatively change carbohydrate metabolism, this effect is related to increasing insulin resistance. During prescription of fibrates it is necessary dosage of hypoglycemic agents carefully, because they can promote a hypoglycemic effect. Bile acid sequestrants are indicated to diabetic patients with high cholesterol and normal concentration of triglycerides in the blood, especially at concomitant kidney failure or liver insufficiency.

Patients with diabetes mellitus must take drugs for the prevention and treatment of thrombotic events because they slowly develop cardiovascular disease.

Angiotensin-converting-enzyme (ACE) inhibitors have positive effect on carbohydrate metabolism. Medicines of this group promote sensitiveness to insulin and improve mastering of glucose, which requires decline of dose of hypoglycemic agents.

Thiazide diuretics in high doses have hyperglycemic and hyperlipidemic effect; therefore for patients with a diabetes mellitus it is necessary to replace them on thiazide –like diuretics.

Cardiac glycosides are indicated in patient with chronic heart failure. In diabetes mellitus these drugs should be prescribed in ketoacidosis, accompanied by tachycardia and lower blood pressure.

EVALUATION AND IMPROVEMENT ORAL HYGIENE IN THE PATIENTS WITH MANDIBULAR FRACTURES.

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Introduction.

The problem of injuries in the maxillofacial region is one of the topical problems of dental surgery. During the last years there has been a tendency in both increasing the number of patients and the complications of these injuries. Oral health of a person with fractured jaw also affects the prognosis of the treatment. Oral hygiene, periodontal diseases, caries and its complications are the factors that influence the fracture area and worsen patients' conditions. Hygiene measures include special treatment of the patient's oral cavity performed by dedicated physicians during the process of bandaging and self-cleaning the mouth area by the patient himself. Metal dental splints, wired and nylon ligatures, lack of mandible's movement are the etiological moments that can deteriorate the process of mouth and teeth self-cleaning using saliva and solid food parts as well as becoming the place of local food particles' retardation. Within these circumstances, additional measures of oral health are crucial in order to prevent complications such as stomatitis, gingivitis and secondary development of the inflammatory process in the fracture gap. Improved treatment of the patients suffering the jaws' fractures may be achieved by early predictions, prevention of inflammatory complications and local therapy optimisations.

Purpose and objectives

The purpose of our study was to develop new means of oral hygiene that will reduce microbial contamination of dental splints, prevent the formation of soft scurf and improve oral health in general.

Materials and methods.

We have observed 20 patients with mandibular fractures who were treated in Vinnitsa City Ambulance Hospital and Vinnitsa Regional Clinical Hospital Named After N.I.Pirogov. The group consisted of patients with mandibular fractures who were treated using traditional tools and methods of oral hygiene (teeth brushing with

semirigid toothbrushes, "Blend-a-Med Complete" toothpaste and "Oral-B" mouthwash). The same methods of oral hygiene were used in the study group which were expanded with decamethoxin-containing fluoride varnish coverage of dental splints. Effectiveness of new hygiene means were measured, conducting research indices of oral health status (Fedorova-Volodkina, Silnes Loe, PMA, CPITN indices). Assessments were carried out on the first day of treatment, on the 7th and 14th days. Patient selection was performed on the bite basis - the study contained patients with direct and orthognathic bite.

Results

After analysing the comparison group of patients, it was noted a slight increase of all indices on the first day (Fedorova-Volodkina - 2.2; Silnes Loe - 1; PMA - 0,17; CPITN - 0,6). In a week upon clamping the Tihershtedt splints (7th day), oral hygiene has significantly deteriorated. The deterioration of oral health during this period is related to the jaw fracture flow period - namely, the patients have observed pain, fear and inability of handling oral treatment in the conditions of new splints' presence and impossibility of opening the mouth. At the end of the second week (14th day) upon the imposition of splints, the state of oral health has slightly improved comparing to the previous period, but the rates were significantly higher than the corresponding rates during hospitalisation (Fedorova-Volodkina - 3.52; Silnes -Loe - 1,74; PMA - 0,88; CPITN - 2,02).

At the time of admission the data of study group hasn't significantly differed from the comparison group. While on the 7th and 14th day the oral health indicators were significantly better (Fedorova-Volodkina index has received - 2.86; Silnes Loe - 1,1; PMA - 0,3; CPITN - 0.9).

Conclusions

Consequently, the use of decamethoxin-containing ftorlak coverage technology of the dental splint designs for mandible fractures reduces the oral hygiene indices. This demonstrates the feasibility of the given preparation to counteract the formation of soft scurf and inhibit occurrences of periodontal tissues' inflammatory diseases for the patients with jaw fractures.

SECTION № 10

MODERN PHARMACOTHERAPY

PHARMACOTHERAPY OF LYME DISEASE

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In recent decades, the importance of Lyme disease in the world is constantly growing due to importations birds infected ticks into new areas, as well as the increase in the number of ticks as a result of environmental change. In Ukraine, the epidemic situation remains unfavorable. According to statistics for 6 months in 2013 382 people fell ill in all 25 regions and Crimea, that 9,14 % more than the same period last year.

Lyme disease is a natural focal transmissible caused by *Borrelia Burgdorferi*. In the course of the disease distinguish three stages: the infection stage with the local development of the pathological process in the point of penetration of the pathogen as erythema migrans, the stage of dissemination of *Borrelia* in the internal organs (nervous system, heart, joints, etc.), chronic stage (late) infection, which affects the target organs - the skin, nervous system, joints and eyes. Modern pharmacotherapy of Lyme disease is aimed to eradication of the pathogen in the body. Antibiotics advise as casual pharmacotherapy. Choice of antibiotic depends on the clinical manifestations of Lyme disease. In the early manifestations of the disease as erythema migrans recommend Amoxicillin 500 mg po tid, Doxycycline 100 mg po bid, Cefuroxime axetil 500 mg po bid 10 days is sufficient, Azithromycin 500 mg po once/day for 7-10 days (less effective than other regimens). With the defeat of the nervous system in the form of Bell's palsy is prescribed Doxycycline 100 mg po bid for 14-21 days, with meningitis recommend Ceftriaxone 2 g IV once / day for 14-28 days, Penicillin G 3-4 million units IV q 4 h for 14-28 days, Doxycycline 100-200 mg po bid for 14-28 days. When cardiac manifestations recommend Ceftriaxone 2 g IV once / day for 14-21 days, Penicillin G 3-4 million units IV q 4 h for 14-21 days, Doxycycline 100 mg po bid for 14-21 days, Amoxicillin 500 mg po tid for 14-21 days. With the development of Arthritis without neurologic involvement Amoxicillin and Probenecid each at 500 mg po qid or 1 g po q 8 h for 28 days, Doxycycline 100-200 mg po bid for 28 days, Cefuroxime axetil 500 mg po bid for 28 days, Ceftriaxone 2 g IV once / day for 28 days, Penicillin G 3-4 million units IV q 4 h for 28 days. When Acrodermatitis chronica atrophicans used Amoxicillin 500 mg po tid for 14-28 days, Doxycycline 100 mg po bid for 28 days.

Thus, early antibiotic therapy can reduce the duration of the course and prevent the development of later stages of the disease.

CERIVASTATIN AS THE DRUG OF CHOICE FOR COMPLEX THERAPY OF ATHEROSCLEROSIS

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Atherosclerosis is a common chronic disease characterized by the emergence in the arteries walls of lipid infiltration lesions and proliferation of connective tissue with the formation of fibrous plaques, narrowing the vessel lumen and violating the physiological function of the affected arteries that leads to organ and general blood circulation disorder. In economically developed countries atherosclerosis is the most frequent cause of morbidity and overall mortality.

In the development and progression of atherosclerosis play the role of factors:

- modifiable (which can be removed or edited)
- not modifiable (which cannot be changed).

To modifiable factors include:

1. Style of life:

- hypodynamia,
- abuse of fat, cholesterol-rich foods, alcohol
- peculiarities of personality and behavior- stress type of character,
- smoking.

2 . Hypertension, blood pressure above 140/90mm.rt.st.

3 . Diabetes mellitus, blood glucose over fasting blood 6mmol/l.

4 . Hypercholesterolemia (high cholesterol levels).

5 . Abdominal obesity (men's waist circumference more than 88cm and women's more than 102cm).

Not modifiable factors include :

1. Age : men over 45 and women over 55 years or early menopause.
2. Male sex (atherosclerosis develops in men 10 years earlier than in women) .

Drug-free treatment involves the elimination of all risk factors for developing this disease, as well as lifestyle changes the patient. In this case, the struggle is with the risk factors that are subject to change: the fight against obesity, increase physical activity, good nutrition, minimizing food with lots of cholesterol; rejection of alcoholic beverages and tobacco, elimination of fatigue and stress.

Drug therapy for atherosclerosis involves the use of four groups of lipid (lipid lowering) medications: bile acid sequestrates, nicotinic acid, fibroses, statins. These drugs have a stabilizing effect on atherosclerotic plaque, improve endothelial function (the inner lining of blood vessels), inhibit the development of atherosclerosis, greatly reducing the severity of the impact on different lipid metabolism. Auxiliary agents are important for fish oil, essential phospholipids. They are used only in combination with statins. Statins are the best-studied group and highly lipid-lowering drugs.

Now there's a new series of statin drug cerivastatin - synthetic enantiomer of a competitive inhibitor of cholesterol synthesis. Cerivastatin selectively inhibits hydroxymethyl-glutarilcoenzim A reductase (HMG CoA reductase). This enzyme catalyzes an essential step in cholesterol synthesis - the conversion of HMG-CoA to mevalonic acid. Cerivastatin acts in liver cells. By reducing intracellular cholesterol, HMG CoA reductase activated receptors, low density lipoproteins (LDL) in the surface cells. As a result of the capture cells increases the LDL cholesterol from the bloodstream, and the total cholesterol and LDL cholesterol in the blood decreases. Cerivastatin most shows patients type IIA and IIB hyperlipidemia. In recommended doses (0.2-0.4 mg/day) reduces the level of cerivastatin OX 22.4%, LDL-C by 32.8%, triglycerides by 25.9%, 19.3% ApoB, raises HDL 6.1%. Profiles of the safety, tolerability and cerivastatin low frequency of side effects let you apply it for long-term treatment. Ability to use one every day makes it convenient for patients. This is the first statin, which has a hypolipidemic effect present in trace amounts. Subsequent studies will show how effective for the prevention of acute vascular events and reduce mortality in patients with coronary artery disease.

A REVIEW OF THE JNC 8 GUIDELINE FOR THE MANAGEMENT OF HIGH BLOOD PRESSURE IN ADULTS

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Hypertension is the most common condition seen in primary care and leads to myocardial infarction, stroke, renal failure, and death if not detected early and treated appropriately. Patients want to be assured that blood pressure (BP) treatment will reduce their disease burden, while clinicians want guidance on hypertension management using the best scientific evidence. This report takes a rigorous, evidence-based approach to recommend treatment thresholds, goals, and medications in the management of hypertension in adults. Evidence was drawn from randomized controlled trials, which represent the gold standard for determining efficacy and effectiveness. Evidence quality and recommendations were graded based on their effect on important outcomes.

The Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8) in adults was published in December 2013. Two key recommendations in the updated guidelines that differ from the JNC 7 guidelines are (1) less aggressive targeting of blood pressures (BPs) and treatment-initiation thresholds for elderly patients and for those younger than age 60 years with diabetes and kidney disease and (2) no longer recommending only thiazide-type diuretics as the initial therapy in most patients (angiotensin-converting enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs], calcium channel blockers [CCBs], or diuretics are recommended).

The JNC 8 recommendations include the following:

1. In patients aged 60 years or older, initiate therapy in those with systolic BP levels at 150 mm Hg or greater or whose diastolic BPs are at 90 mm Hg or greater; treat to below those thresholds.
2. In patients younger than 60 years as well as those older than 18 years with either chronic kidney disease (CKD) or diabetes, the BP treatment initiation and goals should be 140/90 mm Hg.
3. In nonblack hypertensive patients, begin treatment with either a thiazide-type diuretic, CCB, ACE inhibitor, or ARB.
4. In hypertensive black patients, initiate therapy with a thiazide-type diuretic or CCB.
5. Regardless of race or diabetes status, in patients 18 years or older with CKD, initial or add-on therapy should consist of an ACE inhibitor or ARB.
6. Do not use an ACE inhibitor in conjunction with an ARB in the same patient.
7. If a patient's goal BP is not achieved within 1 month of treatment, increase the dose of the initial agent or add an agent from another of the recommended drug classes; if 2-drug therapy is unsuccessful for reaching the target BP, add a third agent from the recommended drug classes.
8. In patients whose goal BP cannot be reached with 3 agents from the recommended drug classes, use agents from other drug classes and/or refer the patients to a hypertension specialist.

It is important to note that this evidence-based guideline has not redefined high BP, and the panel believes that the 140/90 mm Hg definition from JNC 7 remains reasonable. The relationship between naturally occurring BP and risk is linear down to very low BP, but the benefit of treating to these lower levels with antihypertensive drugs is not established. For all persons with hypertension, the potential benefits of a healthy diet, weight control, and regular exercise cannot be overemphasized. These lifestyle treatments have the potential to improve BP control and even reduce medication needs.

PORPHYRIA: PATHOGENETIC PHARMACOTHERAPY

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Porphyria is a group of inherited diseases caused by disorders of haem synthesis with increasing content of intermediates of porphyrins in the blood and tissues.

The place where haem is synthesized in 90% is a bone marrow, where haem becomes hemoglobin, and liver, where haem forms an antioxidant system, respiratory chain enzymes, detoxification enzymes. The last ones participate in the destruction of drugs (cytochrome p-450).

It is possible differentiate the carrier state or the latent form of the clinically obvious disease by the increased excretion of aminolevulinic acid and porphobilinogen in urine. There are two groups of porphyria: erythropoietic and hepatic. And it's depending on the preferential localization of the metabolic defect.

The acute intermittent porphyria is a form of the hepatic porphyria. Such a disease gets its name due to the fact that although the characteristic severe neurological manifestations may lead to the death. But sometimes they subside and the remission begins.

The disease is inherited in an autosomal dominant manner. Its pathogenesis involves a violation of the enzyme activity uroporphyrinogen-1-synthetase and also increased activity of delta-aminolevulinic acids which have toxic effects on the nervous cell.

Acute intermittent porphyria (APP) is the most common form of porphyria. The prevalence in European countries is about 7-12 cases per 100 000 of population.

As a rule, there is very difficult clinical form of it, which require special treatment. Therapy should be as early as possible.

There is only one pathogenetic treatment of APP. And these are medications of haem.

In acute porphyria therapists prescribe haem (normosang), aimed on aminolevulinic acid (ALA-synthetase - the first enzyme in haem biosynthesis), reducing its activity. As a result, a chain of chemical reactions is broken, and the accumulation of porphyrins is terminated.

Haem arginate (Normosang, Leiras) is administered by intravenous infusion at a dose of 3 mg (haemin) / kg of body weight one time per day. The duration of infusion is approximately 15 min. The course of treatment is 4 days. If it is necessary, it should be extended to 7 days. The solution of Normosang is preparing ex tempore. As the solvent is 0.9% sodium chloride.

Porphyria is such a hard disease. And, unfortunately, it is often poorly diagnosed. However, the timely diagnosis and treatment of acute porphyria can reduce mortality in several times, and also reduce the degree of disability of patients. The most correct solution can stop attacks of porphyria. So it is allow to save the human life.

PHARMACOTHERAPY OF NICOTINE DEPENDENCE

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Nicotine addiction is a state of craving for tobacco, which sooner or later develops in 90 % of smokers. Nicotine dependence is caused by the ability of nicotine contact c acetylcholinergic receptors in the brain. This leads to the release of adrenaline and a short-term increase of blood pressure. Nicotine indirectly increases the release of dopamine, which causes a feeling of euphoria, the tide of cheerfulness. It is known nicotine in low doses acts as a psychostimulator. Physical and psychological dependence develops when tobacco use.

For the treatment of nicotine dependence used behavioral methods (self-help, medical advice, group methods, and aversive therapy) and methods of physiological effects. Physiological methods are divided into medication (nicotine and non nicotine replacement therapy, antidepressants and anxiolytics) and non-pharmacological (reflexology, hypnosis). The aim of nicotine replacement therapy is to eliminate or decrease the maximum manifestation of withdrawal symptoms. The mechanism of action of nicotine medications is very similar to the effect of nicotine on the dopaminergic system of the brain. However, the concentration of nicotine in the blood rises more slowly than during smoking, and has lower values and prolonged action. Nicotine medications necessarily prescribed to patients who have a high degree of nicotine dependence. In the pharmaceutical market of Ukraine nicotine preparations is presented in the form of drug Nicorette chewing gum, transdermal patch and inhaler. Among the non nicotine replacement therapy prescribed varenicline (Champix), bupropion hydrochloride (Zyban), cytisine (Tabeks). Varenicline binds nicotinic receptors in the brain and, as their partial agonist; it causes the release of small amounts of dopamine, smaller than when activated by nicotine, because receptor blocked by varenicline. As a result, production of dopamine is stop and a decrease in pleasure when smoking. The mechanism of action of cytisine is close to the mechanism of action of nicotine, but with much less toxicity and greater therapeutically effect. Cytisine competitively inhibits the interaction of nicotine to the corresponding receptors, which leads to a gradual reduction and disappearance of nicotine addiction.

Thus, pharmacotherapy of nicotine addiction presented drug therapies: nicotine replacement therapy and non nicotine replacement therapy, which take into account when choosing a stage of nicotine addiction.

AGE CHANGES OF FACE. METHODS OF CORRECTION.

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The aim of our work is study the problem of skin aging and characteristic of one of the modern methods of medical treatment. The problem of physiological aging of skin is the esthetic medicine topic. The main aging changes are the follows:

- 1) Decreasing of skin density because of destruction of collagen.
- 2) Decreasing of skin humidity because of decreasing of gyaluronic acid volume.
- 3) Decreasing of flexibility because of elastin degradation.

According to the dermatoscopy it looks like: line, wrinkle and the last one is fold. Not only skin suffers from the physiological aging. In this work you can also find aging of face fat compartments, aging of facial skeleton, and aging changes of muscles (SMAS, DMAS). Moreover, we offered three stages of skin aging. There are several methods of anti-age:

- 1) Nonoperative (face resurfacing, dermabrasion, injection of neurotoxins, traditional volumizing filler, stimulators of collagen).
- 2) Surgery(operative) (Fat Autograft Muscle Injection (FAMI), face –lifting, 3D-lifting).

3D-lifting – is based on replacement of atrophic cells by implant with fixing on the periost. The effect of such procedure is more than 2 years. Now days, the most popular drug for 3D-lifting is Radiesse Volumizing Filler, Merz Aesthetics company. Composition of implant: calcium phosphate(30%), gel(70%).

Active ingredient – calcium hydroxylapatite, which is the base for fibroblasts and new collagen fibres. Implant inserts into derma, subdermal and over the periost.

Special aspect of drug usage in contrast to traditional filler is missing of antidote. Safety for use during pregnancy, in breastfeeding females or in patients under 18 years has not been established. As with all skin-injection procedures, there is a risk of infection. Patients should minimize exposure of the treatment area to extensive sun or heat exposure for approximately 24 hours after treatment or until any initial swelling and redness has resolved.

After injection, patient may experience redness, bruising, swelling or other local side effect. Most side effects or treatment resolve within a few days. More rare side effects may include swelling that longer, unevenness or firmness in the area injection.

The drug should not be injected into blood vessels. Usage of the drug in any person with active skin inflammation or infection in or near the treatment area should be deferred until the inflammatory or infectious process has been controlled.

MODERN FACILITIES OF PREVENTION ROTAVIRUS INFECTION

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According to the World Health Organization, each year worldwide rotavirus gastroenteritis is the cause of death from 1 to 3 million children. Proved that rotavirus infection in both developed and developing countries, has a share of approximately 40% of other enteric infections. That is, despite the observance of sanitary measures, reducing the morbidity is not marked. This is due to features the virus. The main mechanism of transmission of the virus - "hands - the mouth".

For rotavirus infection is necessary that the body has got only 10 - 100 virus particles. Given the physiological characteristics of children from 6 months to 2 years (knowledge of the world through the mouth, intense teething), to protect the child is almost impossible.

The rotavirus disease causes severe watery diarrhea, often with vomiting, fever, and abdominal pain. In babies and young children, it can lead to dehydration (loss of body fluids). Rotavirus is the leading cause of severe diarrhea in infants and young children worldwide. Tools specific therapies for treating rotavirus infection are absent.

Therefore, a more reasonable way to protect the child from rotavirus infection is vaccination. Vaccination of 716 million children in the world for next 20 years will save 2.4 of millions of lives. Rotarix is a vaccine given to prevent gastroenteritis caused by rotavirus. After having this vaccine, infant's natural defence system will make antibodies against the common types of rotavirus - these antibodies help to protect against rotavirus infection.

Rotarix is a monovalent the live attenuated vaccine strain G1P8 (oral suspension). The vaccine is given as an oral liquid at the same time as other routine childhood immunisations. Course of vaccination includes two doses starting from 6 weeks of age. The completion course of vaccination must take no later than 24 weeks of age. The interval between injections should be at least 4 weeks.

Lightweight implications after administration of rotavirus vaccine-children may become irritable, or they may have a temporary diarrhea or vomiting. Serious implications, possible increase in the incidence of indigestion during the first week after the first dose of rotavirus vaccine, the risk is 1 in indigestion per 100 000 infants.

Rotarix provides early, effective and long term protection against severe rotavirus gastroenteritis during the first 3 years of life in children in different regions of the world. It has been shown to protect against around 90% of the rotavirus strains.

INFLIXIMAB IN PHARMACOTHERAPY FOR PULMONARY SARCOIDOSIS

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Sarcoidosis is a system granulomatosis of unknown etiology. Morbidity in different countries varies from 0,125 to 24, 0 new cases per 100 000 of population a year and observed its steady increase.

The main pathologic substratum of sarcoidosis is sarcoid granuloma.

Considered that tumor necrosis factor alpha (TNF α) is a key cytokine that takes part in formation of sarcoid granuloma.

The primary goals in sarcoidosis treatment are suppression of inflammatory reaction, prevention of granuloma's fibrotic transformation and maintenance of patient's life quality at the proper level. Choice of treatment is determined by the process' localization, severity of inflammation and presence of extrapulmonary manifestations.

In recent years search of medicines that suppress TNF α – the key cytokine in formation of sarcoid granulomas – is considered as the most perspective.

Infliximab is a chimeric monoclonal antibody against tumor necrosis factor alpha (TNF α). It is a specific antagonist of TNF α . Clinical using of this medicine is just starting and only economically developed countries of Europe, United States and Canada have experience in its using. It is recommended for using only in countries with low level of tuberculosis distribution.

In Ukraine Infliximab is registered under the name Remicade.

Baughman R. P., Lower used Infliximab in treatment of chronic refractory to steroids and immunosuppressants sarcoidosis in dosage of 5 mg/kg once, then on 2nd, 4th and 12th weeks of treatment.

The most encouraging results of treatment of patients with pulmonary sarcoidosis and extrapulmonary manifestations that are refractory to treatment with glucocorticosteroids (GCS) and cytostatic treatment were obtained with using of Infliximab. These results are comparable with effect of glucocorticosteroids.

Skin of patients with lupus pernio is visually improved, vital capacity of patients with fibrosis increases after using Infliximab. Infliximab allows to lower the dosage of steroids and well tolerated by patients in general.

The significant deterrent factor in extension of treatment with Infliximab is very high value of treatment.

SOME ASPECTS OF MEDICAL TREATMENT OF THE DIABETIC FOOT INFECTIONS

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Diabetic foot infections (DFI) - a late complication of diabetes, which is characterized by a long period of recovery, the high probability of amputations, and therefore disability and significant economic losses. Foot ulceration is among the most significant complications of diabetes. The therapeutic management of a diabetic patient carrying a DFI is currently based on: metabolic control, debridement, (moist cures, wound dressing, local pressure off-loading, antimicrobial treatment of infections, and revascularization procedures, when indicated. In recent years, because of the improvement of preventive, diagnostic and therapeutic medical approaches it has been noticed some progress in the treatment of patients with DFI .

The purpose of the study was to investigate some aspects of the modern trends of the medical treatment of DFI, with a detailed analysis of recommendations concerning the choice of surgical dressings presented in the updated national and international standards of treatment.

The research materials: recommendations of the International Working Group on the Diabetic Foot (IWGDF), reflecting the principles of the treatment of chronic ulcerous affect of the lower limbs in patients with DFI, "Guidelines for the treatment of diabetic ulcers" and " Unify clinical protocol of primary and secondary (specialized) medical care" "Diabetes of the 2 type", Ukraine - 2012 (UKPMP).

The results of the researches: in the sources mentioned above the important part of comprehensive treatment of wound defects in patients with DFI are the surgical debridement and the appropriate choice of surgical dressings. The surgical preparation of wound bed to healing consist in continuous purification, control quantity and quality of exudate, the eliminating of bacterial imbalance. The choice of surgical dressings should be based on the account of clinical forms of diabetic foot and the stages of the wound process, as well as the contraindications to their use .

The used surgical dressings must maintain a moist environment in the wound, to control the exudate level and prevent maceration of edges (Evidence grade No1) and to be economically justified. In UKPMP it is recommended to use alginates, neutral atraumatic dressings (NAD), atraumatic dressings with antiseptics (ADA), at the granulation stage - NAD and ADA spongy/ hydropolymer dressings with collagen; at the stage of epithelialization - NAD, semipermeable membrane under the neuropathic form with ulcerous affect or osteoarthropathy (Charcot foot) at the exudation stage. For the ischemic forms diabetic foot infections after the liquidation of ischemia phenomena - APA. In the presence of ischemia to avoid the application of ointment dressings.

Conclusion: it has been analyzed the separate directions of wound defects in patients with DFI with the detailed recommendations for the selecting the dressing type accordingly to the clinical form of DFI according the materials of the national and international recommendations.

GLUCOCORTICOSTEROIDS IN PHARMACOTHERAPY FOR PULMONARY SARCOIDOSIS

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Sarcoidosis is a multisystem inflammatory disease of unknown etiology that manifests as noncaseating granulomas, predominantly in the lungs and intrathoracic lymph nodes, but it also influences the eyes, skin, nervous system and other organs, and it largely affects the young.

Every year 700 new cases of the disease are registered in Ukraine. In recent years there has been a tendency toward the increasing incidence and prevalence of sarcoidosis of the respiratory organs, which constitutes 90% of sarcoidosis in all cases. The cases of the combination of respiratory sarcoidosis with extrapulmonary manifestations have become more frequent.

According to Thoracic Society clinical practice guideline to the diagnosis and treatment of interstitial lung disease of Great Britain, Ireland, Australia and New Zealand in 2008 the new approaches to the treatment of sarcoidosis were formed. As far as the amount of spontaneous remissions is rather high, the patients with asymptomatic stage I sarcoidosis do not need the therapy.

Only the extrapulmonary disease progression or injury in vital organs is an indication for hormonal or cytostatic therapy. Oral corticosteroids are the first-line drugs for patients with progressive disease according to the chest radiographic and functional studies of the respiratory system, and the patients with several symptoms or extrapulmonary manifestations that require the proper treatment.

The treatment with prednisolone (or another equivalent dose of a glucocorticosteroid (GCS)) is prescribed in a dosage of 0.5 mg/kg/day for 4 weeks, then the dose is decreased to 5 mg/month to control the symptoms and disease progression within 6-24 months.

A high efficiency and good tolerability of methylprednisolone in comparison with other glucocorticoids can be clearly identified. Methylprednisolone is registered in Ukraine under the trade name Medrol Tabs and Metipred. The dosage ranges from 4 to 32 mg daily, in the morning. After achieving the desired therapeutic effect, the dosage can be gradually reduced by 4 mg every month. A maintenance dose may vary from 4 to 12mg of the drug once per day.

The corticosteroid therapy is a leading approach to the current treatment of sarcoidosis and, apparently, it will retain its value as long as the origin of disease does not allow the use of etiotropic drugs.

RESEARCH OF NEMATODOSISES PHARMACOTHERAPY CHARACTERISTICS

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Nematodosises are helminthosises, provoking by parasitic nematode worms Nematoda. According to World Health Organization's data, the number of people with enteric helminthosises consists 1.9 billion. In Ukraine specific gravity of helminthosises is near 90% in structure of parasitic diseases. There is information about rising of prevalence of enterobiasis, ascariasis, trichuriasis, trichiniasis, ancylostomiasis and other nematodosises in children and persons, who came from Africa's and Asia's countries.

The aim of the work was research of nematodosises pharmacotherapy characteristics to create the anthelmintic medicine. General principles of enteric helminthosises' treatment are: opportune and compulsory treatment of infested people; rational choice of anthelmintic medicine to treat specific patient; necessity of making-ready of patient depending on pharmacological characteristics of medicine; compulsory taking into account age characteristics, physical state, contra-indication during choosing dose of specific medicine; guarantee of specific dietary regimen, pathogenetically grounded and symptomatic treatment. In therapy of stable helminthes' forms it is reasonably to use the most effective and the least toxic combinations of medicines, follow principles of pharmaceutical care during chemotherapy. Anthelmintic medicines, used for nematodosises treatment, are etiotropic medicines. The mechanism of action of anthelmintic medicines (registered in Ukraine) is related to the parafunction of the neuromuscular system of round worms: pyrantel (helmintox, nemocid), piperazini adipinas, levamisoilum (decaris), flowers of tansy; operating mainly on the energy processes of helminthes: mebendazol (vermox, ahelmin-Darnitsa), albendazol (vormil, medizol-200, medizol-400, nemozol) and operating as cell poisons: tetrachlorated ethylene. So, anthelmintic medicine must satisfy such requirements: high activity, wide range of action, bad blotting capacity in a gastrointestinal tract, absence of resorptive action and damaging influence on organs and tissues of person, rapid removal from an organism, absence of cumulation.

MODERN PHARMACOTHERAPY OF ACUTE CORONARY SYNDROME

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To create an effective system of medical care for patients with acute coronary syndrome (ACS) with ST-segment elevation and implementation of reperfusion therapy in May 2013 in Ukraine was developed Unified Clinical Protocols of medical care for acute coronary syndrome. The aim of our work is to study the features of this Protocol, which are as fundamental changes in the organization of reperfusion therapy to patients with acute coronary syndrome, and familiarization with them a wide range of student-pharmacists.

ACS – a group of clinical signs and symptoms of coronary heart disease, which give rise suspected acute myocardial infarction (AMI). Pharmacotherapy ACS consists of emergency medical care and further routine treatment. Groups of drug for emergency medical care include nitrates: nitroglycerin for sublingual using; and antiplatelet agents: acetylsalicylic acid, clopidogrel. Narcotic analgesics are use as painkillers. Medication of choice from this group is morphine. As soon as possible beta-adrenoblockers are assigning. Metoprolol and propranolol reduce myocardial oxygen demand and the area of myocardial infarction. Appointment in the early hours of the next and long-term use reduces mortality. At this stage, patients with ACS recommended control and correction of blood pressure. To reduce the high pressure (BP) is preferred dopamine, and for increasing low pressure – esmolol.

Further pharmacotherapy of patients with ACS depends on electrocardiography's data. When the diagnosis of AMI without Q wave or unstable angina using anticoagulant therapy: unfractionated heparin, enoxaparin or fondaparinux. In case of the diagnosis of AMI with ST-segment elevation and failure to conduct reperfusion therapy showed thrombolytic therapy using streptokinase and tissue plasminogen activator. All patients with AMI prescribe statins: atorvastatin, rosuvastatin, and ACE inhibitors such as lisinopril and captopril. Angiotensin receptor blocker type 2: valsartan use for patients with intolerance of ACE inhibitors. For patients with heart failure aldosterone antagonists (spironolactone or eplerenone) are used.

Percutaneous coronary intervention (PCI) belongs to one of the treatments ACS. PCI is a stent implantation and allows you to mechanically stabilize the broken plaque at the site of injury. The main directions of drug therapy before PCI are: antiplatelet dual therapy (aspirin + clopidogrel), inhibitors of receptor GP IIb / IIIa (eptifibatid), direct anticoagulants (unfractionated heparin, enoxaparin, bivalirudin).

FIRST MEDICAL AID FOR POISONING OF CODEINE

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The aim of our work is study the provision of first aid for poisoning codeine. Codeine (3-methylmorphine) – is an opium alkaloid, refers to the group of narcotic analgesics, used as an antitussive drug with central action. This medication has a weak narcotic (opioid) and analgesic effects that is why it also used as a component of a number of drugs: "Pentalgin", "Nurofen Plus", "Kaffetin", "Sedalgin", "Kodterpin ", "Solpadein". Very often young people for normal condition use "favorite" medicine, not knowing that they already have a drug addiction.

In the pathogenesis of codeine poisoning leading place is occupied acute respiratory failure which occurs due to oppression effect of opioids on the respiratory center. Hypoxia, tissue acidosis and increased vascular permeability lead to pulmonary edema.

In the initial stage of poisoning there may be a stimulation of the vomiting center, appearance of tonico-clonic seizures, and disruption of the cardiovascular system. In severe poisoning (toxic dose is 0,8 g) soporous and then comatose state develops, pupils narrowed sharply and fail to respond to light, the skin reddens, increases muscle tone. Later, breathing is inhibited, up to a complete stop and death.

There are basic steps for first aid for poisoning of codeine: the injured should be laid on a flat surface and give a fixed stable position (lying on your side, knees bent) order to language not sink and vomit do not fall into the respiratory tract. Need to unbutton the collar, compressive clothes. In cases when respiratory depression is developed performance an artificial respiration. Ensure the victim calm and constantly watching him (especially in the case of deliberate overdose in suicide attempt). Do not give the injured sleep, alternate hot and cold dousing. To prevent further absorption of codeine conducted repeated lavage gastric with activated charcoal (20-30 g per 1 liter of water) independently of the time elapsed since the reception of the codeine. After gastric lavage for drug binding give inside potassium permanganate 1 teaspoon every 10 minutes for 1 hour.

If possible apply antidotal therapy: enter slow intravenous 3-5 ml of 0.5 % nalorphine hydrochloride which diluted in 20 ml of saline solution. Nalorphine hydrochloride may also administer intramuscularly or subcutaneously. If necessary, the injection is repeated with intervals of 10-15 min. Total dose should not exceed 0,04 g (8 mL of 0.5 % solution).

MODERN ASPECTS OF PHARMACOTHERAPY OF MULTIDRUG RESISTANCE TUBERCULOSIS

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Multidrug resistance tuberculosis (MDR-TB) is defined as resistance to isoniazid and rifampicin, with or without resistance to other anti-TB drugs. Irregular, incomplete, and inadequate treatment is the commonest means of acquiring drug resistant organisms. After confirmatory diagnosis of MDR-TB, patients can be treated with either standard MDR regimen or by individually tailored regimen which is based on the drug sensitivity test (DST) – the category fourth regimen. Treatment regimens should contain at least four drugs with certain effectiveness.

Category fourth regimen includes: six drugs-four bactericidal: ofloxacin (Ofx) or levofloxacin (Lfx); kanamycin; ethionamide; pyrazinamide and two bacteriostatic drugs: ethambutol; cycloserine (Cs) during 6-9 months of the intensive phase (IP) and four drugs: ofloxacin (levofloxacin), ethionamide, ethambutol, and cycloserine during the 18 months of the continuation phase (CP). PAS is included in the regimen as a substitute if any drug among ofloxacin (Ofx) or levofloxacin (Lfx); kanamycin; ethionamide; pyrazinamide is not tolerated or any drug among two bacteriostatic drugs is not tolerated. Do not use drugs for which there is a possibility of cross resistance. Preferably the standardized regimen as recommended in the national DOTS-Plus guidelines should be used: 6 or 9 kanamycin, ofloxacin, ethionamide, cycloserine, pyrazinamide, ethambutol/18 ofloxacin, ethionamide, cycloserine, ethambutol.

New alternative pharmacotherapy for MDR TB includes some other drugs with initial promising results: β -Lactam antibiotics and β -lactamase inhibitors, linezolid, phenothiazines, antimalarial agents, tuberactinomycin, aminophenazines and others.

Currently available drugs are not sufficiently effective in treating MDR TB. Modern treatment of MDR TB demands working out of new drugs.

EFFICIENCY OF THERAPY IN NEUROMETABOLIC FOR PATIENTS BY ISCHEMIC STROKE

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The most common diseases are vascular of the brain in Ukraine. The last 10 years the prevalence has increased 1.5 times, over 3 million patients with this pathology were registered. The most severe form of cerebrovascular diseases are brain strokes. Annually 100 to 110 thousand inhabitants of the country for the first time ill cerebral stroke. In the structure of stroke, ischemic disorders of cerebral circulation occupy a leading position, because they are much more common than hemorrhagic. Due to stroke about 45 thousand inhabitants die every year of the country, which is by 100 thousand of population is 92.2. This figure is almost 2 times higher than in developed European countries. Therefore, the problem of prevention and effective treatment of stroke is one of the most actual medico social problems around the world and in Ukraine firstly.

The purpose of this research was to evaluate the effectiveness of the application of cytoflavin as metabolic neuroprotector in treatment of patients with acute ischemic stroke in the acute period.

Materials and methods. Under our supervision there were 57 patients with hemispheric ischemic stroke in the three-week period from the beginning of the disorder treated cytoflavin on basic therapy. The anamnesis of diseases were considered, analyzed the medical records of pre-hospital and hospital stages, the results of objective inspection: data somatic and neurological status, the results of the EEG.

The results of the research. During treatment, patients receiving cytoflavin (to the 21st day of treatment), there was observed positive dynamics of focal neurological symptoms. There was a significant decrease in the number of patients with the most severe forms of nervous system (aphotic disorder, dysarthria, hemihypesthesia) group therapy with cytoflavin, in comparison with group of the patients received basic therapy.

Introduction of cytoflavin patients with acute ischemic stroke caused pronounced shifts in the bioelectrical activity of the brain.

Conclusions: received results allow to conclude that the use of cytoflavin intensive therapy of acute disorders of cerebral circulation improves quality of treatment of patients due to influence on pathogenetic parts of the pathological process.

MODERN PHARMACOTHERAPY OF PSORIASIS

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On today's time of about 4 % of the population suffer from dermatological diseases such as psoriasis. Clinical manifestations of psoriasis are often located on visible parts of the body, causing psycho-emotional stress, depression patient that exacerbates the disease. Environmental, genetic, and immunologic factors are important in the development of psoriasis. About 30 % of patients are at risk of developing severe forms of dermatosis, psoriatic arthritis, leading to disability.

Nowadays, the actual problem is the selection of an effective method of treatment of this dermatosis. Modern pharmacotherapy psoriasis includes an external therapy, systemic therapy and phototherapy (PUVA has an antiproliferative effect and also helps to normalize keratinocyte differentiation). For the external therapy used of emollients; keratolytic agents (Salicylic acid) are used to remove scale, to smooth the skin, and to treat hyperkeratosis; ointments, creams, lotions containing glucocorticoids (Triamcinolone acetonide, Betamethasone); preparations containing activated zinc pyrithione, ointments containing synthetic analogs of vitamin D₃ (Psorcutan, Divonecs) allowing vehicles - ointments containing tar, naphthalene. Systemic therapy based on the use of antimetabolites (Methotrexate), calcineurin inhibitors (Cyclosporine), synthetic retinoids (Acitretin), glucocorticoids (Dexamethasone). Breakthrough in the treatment of psoriasis was development of pathogenetic part immunobiological therapy, mechanism of action which is aimed at the selective inhibition of specific markers of immune inflammation in the skin. In the treatment of psoriasis recommended tumor necrosis factor inhibitors (Infliximab), selective immunosuppressants (Efalizumab). New possibilities in the treatment of psoriasis drug Ustekinumab (Stelara). This is a fully human monoclonal antibody, overwhelming both the initial and key stage of the disease pathogenesis. Ustekinumab indicated for the treatment of adults (18 years or older) with moderate-to-severe plaque psoriasis. According to the literature Ustekinumab has optimum safety and efficacy profile, clinical improvement (reduction of erythema, infiltration and desquamation) 75 % have almost 80% of patients, the drug was well tolerated, convenient outpatient treatment (subcutaneous injection of 1 time per quarter, four times per year), a side effect is not amplified with time and at the level of placebo.

Modern pharmacotherapy of psoriasis with new immunobiological preparations, in particular ustekinumab, provides control over the course of psoriasis.

PHARMACOTHERAPY OF IRRITABLE BOWEL SYNDROME

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At present the problem of irritable bowel syndrome (IBS) is very crucial in Ukraine and worldwide. About 15-20 % of the world population suffers from IBS, which commonly diagnosed in young, working-age persons. There are factors contributing to the development of IBS: stress, irregular food intake, genetic predisposition, transferred intestinal infections .

IBS is a disorder of motor and secretory functions of the intestine without structural changes in the body, developing as a result of the interaction of psychosocial factors and physiology of the digestive tract through the axis of the "brain – intestines". There are main clinical symptoms of IBS (according to Rome criteria III, 2006): increased frequency of bowel movements more than 3 times a day or reducing the frequency of bowel movement at least 3 times a week, not a normal stool, straining during bowel movements, feeling of incomplete emptying of bowel, mucus during defecation, feeling of fullness, bloating in the abdomen.

Therapeutic tactics in patients with IBS should be individualized, flexible, and with the obligatory account of psychosomatic status of patient. Such an approach to treatment of IBS would reduce the clinical manifestations of the disease and improve the quality of life of patients. The most important stage of treatment is the use of psychotherapy, including hypnosis, "abdominal" option autogenous training, behavioral therapy techniques. Psychotropic medications used as pharmacotherapy: amitriptyline, desipramine, nortriptyline. Selective serotonin reuptake inhibitors: fluoxetine, sertraline, paroxetine. Anxiolytic medications from nonbenzodiazepine series: etifoxine hydrochloride; from benzodiazepine series: diazepam, clonazepam, gidazepam . In pharmacotherapy also used: antispasmodics (anticholinergics – platifillin, butilskopalamin, otilonia bromide, pinaveria bromide; selective sodium channel blockers – mebeverin, ditsikloverin); myotropic antispasmodics (drotaverin, papaverine). Antidiarrheal agents prescribe for pharmacotherapy of IBS with the prevalence of diarrhea (loperamide, alosetron, cilansetron, ondansetron, tropisetron), probiotics (prema, enterol250, bifiform). Laxatives (lactulose, macrogol 4000, mukofalk, psyllium, prokinetics (metoclopramide, domperidone) and 5NH₄-agonists (tegaserod) are used when constipation is a predominant clinical sings of the IBS.

Criteria of treatment effectiveness are cessation of symptoms, pain relief, normalization of stool and laboratory indicators, and improvement of health without significant positive dynamics of objective data.

«HELIOPLANTUM®» INNOVATION IN THE ASTHMA TREATMENT

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Bronchial asthma (BA) treatment relevance increases every year, as on the background of morbidity increase the existing arsenal of pharmacological agents and strategies of orthodox medicine has only symptomatic orientation and do not imply a complete cure. The aim of our study was to investigate the effectiveness of the «Helioplantum®» method in the treatment of patients with BA, which provides adjustment and synchronization (under age and genetic rules) of natural biochemical processes at all levels, leading to a systemic self-healing of organism. 72 patients with BA were selected for investigation. 37 were allergic, 26 had infection dependence, 5 had professional and 2 aspirin form of BA among them.

To exclude the risk of asthma attacks and to provide the quality of life, the treatment using «Helioplantum®» method always started on the background of the prior therapy (according to the traditional protocol). As the normalization of state the dose and frequency of the orthodox drugs were reduced until their complete abolition.

Treatment using «Helioplantum®» methodology was ranged from 6 to 10 months. The adjustment of dose of individualized regulatory content was performed by an electronic testing. Effectiveness of the therapy was evaluated by reducing of the frequency and duration of asthma attacks, improvement of the general state of the patient (personal complex of symptoms dynamics), and if necessary, confirmed by the classical laboratory methods (spirometry, pikfluometry, biochemical analyzes of blood and sputum, computed tomography, etc.). Clinical observations have shown high efficiency and promising application of «Helioplantum®» in BA therapy of various etiologies and advance of disease. This was reflected in the gradual decrease in the frequency and severity of asthma attacks, relief of BA complex of symptoms until their complete disappearance in all 72 patients.

A five-year monitoring of patients after treatment using «Helioplantum®» system showed absence of breathlessness attacks and associated complex of symptoms of BA, suggesting the possibility of its complete cure. Systematic monitoring of possible side effects or recrudescence of asthma related pathologies drew our attention to the fact that in some cases, in parallel with the treatment of asthma, we observed the elimination of related chronic diseases such as hypertension, psoriasis, migraine, type 2 diabetes, polycystic, bazilomy, sepsis, etc. This confirms that the treatment using «Helioplantum®» system significantly increases the protective and restorative capabilities of the body and opens new perspectives in the treatment of classically incurable diseases.

MODERN PHARMACOTHERAPY OF ACNE

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Acne (acne vulgaris) is chronic multifactorial disease polymorphic hair follicles and sebaceous glands caused by Gram-positive rods *Propionibacterium acne* (*P. acne*). May occur years and lead to the formation of stable cosmetic and scarring. It is believed that 85% of people anyway faced with acne.

Rational pharmacotherapy of acne is determined pathogenetic factors and focuses on reducing the production of sebum, the normalization process of keratinization in the hair follicle, the suppression of the microflora, reducing inflammation. For mild severity (presence of open and closed comedones and papulopustular less than 10 elements) prescribe topical therapy. Recommend azelaic acid (20 % cream, 15 % cream) which has anti-inflammatory and antimicrobial activity, zinc hyaluronate (gel solution) that has an antiseptic effect and stimulates the proliferation and regeneration of cells, benzoylperoxide (gel 2.5%, 5% , 10%), which improves tissue oxygenation inhibits sebum production, has an antimicrobial a bacteriostatic effect on *P. acnes*. Erythromycin and zinc complex with anti-inflammatory and antimicrobial activity also use. In the presence of comedones recommend means normalizing keratinization processes – topical retinoids (tretinoin, isotretinoin, adapalene). At moderate severity (presence of multiple papulopustular elements comedones, acne single infiltrative) with topical therapy administered systemic pharmacotherapy. Systemic retinoids – isotretinoin is recommended. This medications normalizes the terminal differentiation of cells, inhibits the proliferation of the epithelium of the sebaceous glands and reduces the production of sebum easier; antibacterial agents from the group of tetracyclines (tetracycline, doxycycline, minocycline), lincosamides (clindamycin), macrolides (erythromycin). Women with acne recommend the use of anti-androgen drugs – Diane-35. In severe acne severity (presence of infiltrative, cystic acne, papulopustular with a tendency to form scars) are the drugs of choice for systemic use of retinoids (isotretinoin). Also antibacterials for systemic use (doxycycline or minocycline), local therapy (adapalene, tretinoin , clindamycin, benzoyl peroxide etc.).

Thus, the modern pharmacotherapy acne represented by a combination of external and systemic medications, which are taken into account when assigning data etiopathogenic, clinical forms of acne severity of the disease, psychosomatic status of the patient.

THE FEASIBILITY OF USING MICROBIOLOGICAL ANALYZER VITEK 2 COMPACT.

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Adequacy of antimicrobial therapy plays a crucial role in recovery of patients with infections, the success of the therapy in many respects depends on quality of the microbiological analysis. Now in microbiological laboratories the distinct aspiration to automation of the researches, mentioning and a stage of determination of sensitivity to antimicrobial drugs is noted.

Currently, the increasingly popularity of automatic analyzers, among which a special place is occupied by microbiological analyzer Vitek 2 Compact, produced by the company Bio Merieux is the recognized leader in production of bacteriological analyzers for clinical, biological and industrial laboratories.

Automatic microbiological VITEK 2 Compact is intended for carrying out identification and determination of sensitivity of microorganisms to antibiotics and represents a considerable step forward concerning increase of convenience of using, reliability and universality in comparison with the previous analyzers of firm.

Advantages of VITEK 2 Compact before similar systems:

- Productivity is up to 60 cultures a day, single loading of 30 tests.
- Possibility of continuous additional charge of test units without technical breaks. Reading the test of cards happens each 15 minutes, the result of the analysis is available in 2-4 hours. Identification of mushrooms in 18 hours.
- It isn't required additions of additional reagents and/or indicators (neither for identification, nor for sensitivity). The improved Advanced Colorimetric TM technology, allowing to use bigger number of lengths of light waves, wider range of substrate, so to define bigger quantity of species of microorganisms and their strains with very high precision. The optimum quantity of substrates for card everyone the test reduces risk of inexact reading of results.
- Full automation of process thanks to barcoding system the test of cards. Everyone shaped the code bears information on a party code, an expiration date, a code of a product and unique identification number (or accession number). Cartridges for the test of cards also have shaped a code for prevention of mistakes at registration.

Automatic sealing of test unit for an exception of spill of bacterial suspension and personnel contact during the work and utilization.

EFFECT OF A NEW COMBINED OINTMENT WITH DIHYDROQUERCETIN, COENZYME Q10 AND LICORICE EXTRACT ON BURN WOUND HEALING IN RATS

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Objectives. To study the effect of a topical ointment with dihydroquercetin, coenzyme Q10 and licorice extract (LCD) on healing of burn wound in rats. And to compare the efficacy of rutin and dihydroquercetin in the composition of the ointment.

Materials and methods. Partial thickness burn wounds were reproduced on 20 albino rats, weighting 260-300 g under ketamine (100 mg/kg) anesthesia by pouring hot molten wax at 80°C into pattern of 4 cm² placed on the animals' side. Rats were divided into four groups of 5 animals each: 1st - control group, 2nd – LCD ointment group, 3rd – methyluracil ointment group (reference-drug), 4th – LCR ointment group (treated with ointment containing rutin, coenzyme Q10 and licorice extract). The formulations were applied topically once daily. Evaluation was done by measuring wound contraction and recording the period of epithelization.

Results and discussion. Our study revealed that topical application of LCD and LCR ointments decreased healing time by 6.8 and 4.4 days, respectively compared to the control group ($p \leq 0.05$). Crust rejection in LCD ointment group started from the day 9 and the mean epithelization period was 14.8 days, which is 31.5% less compared to the control group ($p \leq 0.05$) and 28.1% less compared to methyluracil ointment group ($p \leq 0.05$). Epithelization period in LCR group was 17.2 days and was significantly lower than in control group (<20.4%, $p \leq 0.05$) and compared to the reference-drug (<16.5%, $p \leq 0.05$). However, no significant differences between LCD and LCR ointment groups were found. Assessment of wound contraction percentage have shown that on the day 5 burn area decreased by 63.5% and on the day 15 – by 98.2% in LCD treated group, which exceeded control group by 20.9% and by 19.95%, respectively. In LCR ointment group percentage of wound contraction was on the day 5 – 44.6% and on the day 15 – 94%, which exceeded control group by 10.55% and 9.2%, respectively.

Conclusion. The present study shows a significant improvement in burn wound contraction in rats treated by LCD ointment. It also showed improved healing in LCR ointment group. Based on these we propose that ointment LCD could significantly enrich the assortment of topical medications available for the treatment of burns and its prohealing property can be explored further by future studies.

SECTION № 11

PHARMACOECONOMIC RESEARCH OF MEDICINES

PHARMACOEPIDEMIOLOGICAL RESEARCH OF CONSUMPTION OF FIXED COMBINATIONS OF ANTIHYPERTENSIVE DRUGS IN UKRAINE

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Arterial hypertension (AH) is a serious problem for the people of different countries and is one of the major risk factors for stroke, myocardial infarction, heart and renal failure, ischemic heart disease. According to official statistics in Ukraine there are more than 12 million patients with hypertension, about 32.2 % of the adult population. Recently there has been a steady increase in the prevalence of hypertension is increasing. The basic strategy of AH pharmacotherapy - achievement target blood pressure. The situation of AH control in Ukraine is extremely unfavorable. Despite the large number of antihypertensive drugs (AHD), the target blood pressure is achieved in a tiny part of patients. Monotherapy is effective less than in the 50% of patients and about 60% of patients need of treatment by more than one drug, that considerably reduces patient compliance. According to it, the role of fixed combinations (FC) in antihypertensive therapy, that allows the following advantages: reducing the cost of treatment, simplification of the treatment regimen, improves patients' adherence to therapy, is important.

The purpose of the study - to evaluate the place of AHD FC in antihypertensive therapy in Ukraine by estimating the volume of consumption in DDDs/1000 inhabitants/day. In the common structure of all AHD, the consumption of FC is 25%, that is less, than the proportion of patients requiring combination therapy. This suggests, that a significant number of patients treated with combinations of free AHD, that may lead to a decrease in their compliance. Among leaders of consumption are the FC of ACE inhibitors with diuretics or calcium channel blockers (CCB) (12.4 DDDs/1000 inhabitants/day), representing 17% of the total consumption of all AHD and 29.9% of the total consumption of ACE inhibitors. It was found, that consumption of FC of BRA and beta-blockers with diuretics and CCB is respectively 3% and 4% in the overall structure of AHD consumption, 44.5% and 23% of the consumption of the certain groups of AHD.

Thus, the pharmacoepidemiological study of consumption AHD showed, that one fourth of the treated patients with hypertension in Ukraine uses FC of later generations. These results confirm, the use of evidence-based medicine approaches in medical practice, provided by the introduction of the formulary system and clinical treatment protocols in the health care system of Ukraine.

PHARMACOEPIDEMIOLOGICAL ANALYSIS OF STATINS CONSUMPTION IN UKRAINE

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Leading causes of death in all industrialized countries, as well as in Ukraine, are cardiovascular diseases (CVD). Hypercholesterinemia is an important progression risk factor of CVD. The main drugs for hypercholesterinemia care and reduction of risks of cardiovascular complications nowadays are statins.

The purpose of this study is the analysis of dynamics of statins consumption in Ukraine during the last five years (2008-2012 years).

Methods and materials. The ATC/DDD-methods and data about sales of drugs of the reference retrieval system "Pharma drugs" of the Morion Company in the period of 2008-2012 years were used.

Results. The market of statins in Ukraine was analyzed at the first stage of research. It was determined, that according to the State pharma drugs register there are 7 INNs of statins, that are presented in the total number of 186 drugs. The given data proves, that the statins are widely represented at the pharmaceutical market of Ukraine. Atorvastatin, simvastatin and lovastatin are represented by both foreign and home producers. Depending on the producer the prices are vary greatly. This means, that pharmaceutical market gives a real opportunity to use of statins in a wide clinical practice. Dynamic analysis of statins usage showed, that during the last 5 years usage of statins in Ukraine was raised on 2.5 times and made in DDDs/1000/day respectively: 1.17 (2008); 1.32 (2009); 2.04 (2010); 2.64 (2011); 3.42 (2012). The results of the analysis of the general statins usage show, that approximately only 0.26% of population of Ukraine, mainly 0.12 mln. of people, take every day one DDD of any statin. Taking into consideration, that more that 12 mln. patients with arterial hypertention were registered in Ukraine in 2012, it becomes clear, that the usage of lipid-lowering drugs in our country at a level of population still remains extraordinarily low and inadequate as to the morbidity level of the population.

Conclusions: Pharmaceutical market of Ukraine gives real opportunities for usage of statins in the wide clinical practice for patients with high cardiovascular risks. The general volume of statins usage during the last five years was raised in more than 2 times, but it still remains extraordinarily low and does not correspond to the CVD morbidity level of the population.

EVALUATION OF KNOWLEDGE OF THE NUPEMLOYEES AS OF THE MAIN RULES OF ANTIBIOTICSAPPLICATION

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The goal of the research is statistical assessment of knowledge of patients as of the rules of rational application of antibacterial preparations.

Materials and methods of the research. An anonymous questionnaire survey of employees of the National University of Pharmacy has been carried out, 371 respondents have participated. The respondents are mainly females – 77.4%, 25-50 years old – 45.7%, university-educated – over 97.5% (362 respondents): pharmacists – 59.7%, engineers – 9.1%, economists – 9.1%, doctors – 6.9%, clinical pharmacists – 4.5%, chemists – 4.4%, biologists – 3.9% and laboratory technicians – 2.5% respondents. Research methods: statistical, sociological, method of computer data processing and analytical method.

Research results. The research has shown that respondents with medicinal or pharmaceutical education reach 71% of the total number of respondents with university education (257 persons), 68.5% of which take antibiotics on doctor's prescriptions, 3.5% - on the recommendation of a pharmacist in a drug store, and 25.3% prescribe antibiotics themselves (65 respondents). At this, 33.1% of respondents consider a pharmacist allowing patients to buy antibiotics on the first demand, without a prescription, being right, 22.5% of respondents are at a loss to answer this question and 44% of respondents consider selling of anti-bacterial preparations, which are in "prescribed" list, over the counter being wrong. Those respondents, who prefer self-treatment: 23.1% use antibiotics for curing of acute respiratory diseases, 21.5% stop taking antibiotics when the disease symptoms disappear and the patient subjective state gets better, while all the respondents say, that they are aware that non-control antibiotics application and their wrong application results in formation of resistive microbial strains, infectious matters.

Conclusion: Despite the fact, that most respondents are persons with university education, and area of their professional activity is related to health protection, the results of the analysis have shown that most respondents take antibiotics not considering the basic rules of rational application of antimicrobial preparations, which fastens development of resistive microbial strains. As we know, antibiotics resistance increases the cost of patient adjunctive treatment. A longer course of the disease and more complex schemes increase cost of patient treatment, as well as financial loss of individual families and society in whole. Experts consider that the total load of antibiotic resistance equals about 1.5 billion euro in countries of European Union each year.

PHARMACOECONOMIC ANALYSIS OF THE STANDARD THE TREATMENT AND CARE OF PEOPLE WITH HYPERTENSION

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High blood pressure (hypertension) is a serious condition that can lead to coronary heart disease, heart failure, stroke, kidney failure, and other health problems. In Ukraine there are clinical guidelines and standard for the treatment and care of people with hypertension.

The purpose of the study is the determination of the range of the cost of pharmacotherapy of hypertension stage II according to the national standard of care.

Materials: standard for the treatment and care of people with hypertension, State Formulary of Ukraine. Methods: pharmacoeconomic methods of the total cost of illness and cost-minimization analysis.

Results. There are 5 pharmacological groups in the national standard of pharmacotherapy of hypertension: β -blockers, thiazide diuretics, ACE inhibitors, angiotensin receptor II inhibitors, calcium antagonists. According to the State Formulary there are 9 INN β -blockers (71 trade name – 21 of them are drug domestically produced and imported 50 drugs), 2 INN thiazide diuretics (19 trade name – 4 of them domestic and 15 imported drugs), 10 INN ACE inhibitors (71 trade name – 15 of them domestic and 56 imported drugs), 7 INN angiotensin receptor II inhibitors (42 trade name – 6 of them domestic and 36 imported drugs), 5 INN calcium antagonists (50 trade name – 14 of them domestic and 36 imported drugs).

Cost of monotherapy within one year depends on the chosen drug. Lowest cost of treatment lowest cost of treatment the case using: β -blocker Atenolol-Astrafarm ("Astrafarm", Ukraine); ACE inhibitor Enalapril ("Lubnyfarm", Ukraine); ARB Kasark ("Kievmedpreparat", Ukraine); a calcium channel blocker Amlodipine-Astrafarm ("Astrafarm", Ukraine); thiazides Hydrochlorothiazide ("Borschagovsky CPP", Ukraine). The most expensive cost of treatment: β -blocker Nebival ("Kiev Vitamin Plant", Ukraine); ACE inhibitor Captopril ("Kievmedpreparat", Ukraine), ARB Kasark ("Kievmedpreparat", Ukraine); a calcium channel blocker Felodip («TEVA» Czech Republic); thiazides Hydrochlorothiazide ("Chinoi", Hungary).

Conclusions: Ukrainian pharmaceutical market provides real opportunities for choice of antihypertensive drugs for patients with a variety of economic opportunities. Depending on the choice of drugs difference in treatment price is nine times.

SECTION № 12

MANAGEMENT AND MARKETING IN PHARMACY

POSITION PSYHOTROPIC ANTIDEPRESSANTS ON PHARMACEUTICAL MARKET OF KAZAKHSTAN

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Relevance of the topic. in the total burden of disease in the Republic of Kazakhstan a special place occupy mental illness and their percentage is growing every year, today corresponds 1,9%. Relevance of marketing research pharmaceutical market of psychotropic antidepressants is in constant growth in the Republic of Kazakhstan some socially significant diseases including mental. Especially, frequently reported persistent neurotic disorders and psychosomatic pathology.

Goal research: an analysis of psychotropic antidepressants in the pharmaceutical market of the Republic of Kazakhstan (RK)

Research methods: content analysis, factorial cluster analysis. Analysis of the official scientific literature, qualitative and quantitative market research.

Results and conclusions: found that the share of the pharmaceutical market of the Republic of Kazakhstan for the 2013 year (turnover on public procurement) psychotropic antidepressants compose 0.01%. Moreover, psychotropic antidepressants include 23 trade names of drugs, exclusively foreign production in the absence of domestic medicines. Preferable dosage forms are tablets - 58.8, capsules - 41.2%. Conclusion: pharmaceutical market revealed a very low proportion and limited range of antidepressants in the structure of general assortment of drugs Republic of Kazakhstan. National production of the studied drugs not mastered.

MARKETING RESEARCH OF DRUGS CHOLERETIC ACTION

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Literary sources indicate that among hyper-endemic diseases disease of the biliary system is one of the leading and well represented in all age groups.

There is an increase in the number of patients with cholelithiasis utilities, the increase in prevalence in 10 years is 97.5% according to the Center for Health Statistics of the Ministry of Health of Ukraine, Primary cause of the disease is the image and the human condition and the environment, genetic predisposition and operation of healthcare facilities.

The most common treatment of gallstone disease is associated with hospitalization and high cost. Each year, the world is made of more than 2.5 million transactions in the biliary tract.

One of the alternative methods of treatment involves the use of drugs that are natural and synthetic drugs.

Nowadays herbal medicines are gaining popularity. Made from herbal medicinal herbs have a wide range of therapeutic action of gradual, slow development of therapeutic effect , high bioavailability, patients can be used for a long time. Their action is not only aimed directly at treating disease, but also to protect and strengthen the organism as a whole.

The aim of our work is to conduct market research drugs choleretic action.

Market research of pharmaceutical market drugs choleretic action were conducted.

It was shown that the majority of range choleretic drugs is formed by foreign producers, they accounted for 62% and 38% domestic take.

The countries importing drugs of the research group were installed .

Proved that among the drugs choleretic action, a tablet is the most common dosage form, their share is 55%.

Prevalence manufacture of tablets due to a number of well-known advantages over other dosage forms: ease of use and storage, dosing accuracy, the ability to combine incompatible physical and chemical properties and therapeutic effect of drugs, portability, etc.

The results of the marketing analysis allowed to prove the feasibility of establishing a combined medicinal products based on vegetable raw materials with a wide range of therapeutic actions that have a high performance, quality and availability to the general public.

TIME MANAGEMENT

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The purpose of this paper is to study the problems of time management. Time management is the act or process of planning and exercising conscious control over the amount of time spent on specific activities, especially to increase effectiveness, efficiency or productivity.

Time management may be aided by a range of skills, tools, and techniques used to manage time when accomplishing specific tasks, projects, and goals complying with a due date. Initially, time management referred to just business or work activities, but eventually the term broadened to include personal activities as well. A time management system is a designed combination of processes, tools, techniques, and methods. Time management is usually a necessity in any project development as it determines the project completion time and scope.

The major themes arising from the literature on time management include the following:

- Creating an environment conducive to effectiveness
- Setting of priorities
- Carrying out activity around those priorities
- The related process of reduction of time spent on non-priorities

Time management has been considered to be a subset of different concepts such as:

- Project management. Time Management can be considered to be a project management subset and is more commonly known as project planning and project scheduling. Time Management has also been identified as one of the core functions identified in project management.

- Attention management: Attention Management relates to the management of cognitive resources, and in particular the time that humans allocate their mind (and organize the minds of their employees) to conduct some activities.

- Personal knowledge management.

Manage your free time

Time management helps you make better use not only working time, but the stay. In particular , it is recommended not to take work home , to organize life so that it takes a minimum of time , carefully planned in advance and free time to follow these plans, in particular the regular practice of emotional (theaters , concerts, exhibitions , etc.) and physical (sport fitness) switch . In American companies if an ordinary employee remains on the job longer than that found in his employment contract, this fact may cause dismissal, since it indicates that the employee does not have time to do their tasks during their working hours. Used for active recreation not only the weekend, but at least one evening a week of the day, as well as used as a mini- holiday long weekends and holidays. In business travel plan free time (from several hours to two days) for sightseeing . Vacation set the rules of using the phone, email, Internet , etc. and stick to them .

I think that time management is very important in every person's life, because this section of the management makes life easier. If you will apply knowledge of time management in practice, then you will have a lot of free time, which you can use for the benefit of themselves.

PARAPHARMACEUTICAL PRODUCTS IN GOODS ASSORTMENT IN THE PHARMACY ORGANIZATIONS OF THE REPUBLIC OF KAZAKHSTAN (RK)

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Along the development of open layout of goods in the pharmacy organizations the notable widening of goods assortment takes place, moreover often at the expense of increase of assortment of parapharmaceutical products, which volume today at the pharmacies is up to 60%. Absence of a legal base of principles of forming of pharmacies assortment in many cases leads to presence in the pharmacies of the RK goods nonrelevant for pharmacy organizations.

Aim of the work is: definition, classification, studying of legislative-normative regulations and tendencies of the development of the parapharmaceutical products within the pharmacy organizations of the RK.

Object and materials of the research: the assortment of parapharmaceutical products of the pharmacy organizations in Almaty along the materials of their information databases. Method of continuous sampling, content-analysis, graphical analysis have been used in the work.

As a result of the work the main factors and tendencies of development of the parapharmaceutical products assortment have been revealed, the legislative regulations of these products turnover in the CIS countries and USA have been analyzed; experimentally the solid share of parapharmaceutical products in the pharmacies assortment has been proved – it is more than 50%.

Conclusions:

1. Parapharmaceutical products – is important and integral part of the pharmacies assortment.
2. It is necessary to provide the legislative defining and regulation of parapharmaceutical products turnover in the RK.
3. Considering the current tendencies of development of parapharmaceutical products assortment in the pharmacy organizations in the RK, we should forecast the further increase of its sale volumes.
4. Increase of parapharmaceutical products assortment will provide an increase of competitiveness of pharmacies, growth of their profit and cost-effectiveness.

HISTORY OF MANAGEMENT THOUGHT

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Purpose of this article is to study the history of management thought. People have been shaping and reshaping organizations for many centuries. Looking back through world history, we can trace the stories of people working together in formal organizations such as the Greek and Roman armies, the Roman Catholic Church, the East India Company, and the Hudson Bay Company. People have also long been writing about how to make organizations efficient and effective, since long before terms such as "management" came into common usage. Prominent and instructive example is the writings left for us by Niccolo Machiavelli. Although the adjective 'Machiavellian' is often used to describe cunning opportunists Machiavelli was a great believer in the virtues of a republic. This is evident in Discourses, a book Machiavelli wrote in 1531 while he lived in the early Italian republic of Florence. The principles he set forth can be adapted to apply to the management of organizations today.

- An organization is more stable if members have the right to express their differences and solve their conflicts within it.
- A weak manager can follow a strong one, but not another weak one.
- A manager seeking to change an established organization "should retain at least a shadow of the ancient customs."

Scientific Management theory arose in part from the need to increase productivity. In the United States especially, skilled labor was in short supply at the beginning of the twentieth century. The only way to expand productivity was to raise the efficiency of workers. Therefore, Frederick W. Taylor, Henry L. Gantt, and Frank and Lillian Gilbreth devised the body of principles known as scientific management theory.

Frederick W. Taylor (1856-1915) rested his philosophy on four basic principles:

- The development of a true science of management, so that the best method for performing each task could be determined.

- The scientific selection of workers, so that each worker would be given responsibility for the task for which he or she was best suited.

- The scientific education and development of the worker.

- Intimate, friendly cooperation between management and labor.

Taylor contended that the success of these principles required "a complete mental revolution" on the part of management and labor. Rather than quarrel over profits, both sides should try to increase production, he believed, profits would rise to such an extent that labor and management would no longer have to fight over them. In short, Taylor believed that management and labor had a common interest in increasing productivity.

Scientific management was concerned with increasing the productivity of the shop and the individual worker. Classical organization theory grew out of the need to find guidelines for managing such complex organizations as factories.

German sociologist Max Weber (1864-1920) developed a theory of bureaucratic management that stressed the need for a strictly defined hierarchy governed by clearly defined regulations and lines of authority. He considered the ideal organization to be a bureaucracy whose activities and objectives were rationally thought out and whose divisions of labor were explicitly spelled out. Weber also believed that technical competence should be emphasized and that performance evaluations should be made entirely on the basis of merit.

Although bureaucracy has been successful for many companies, in the competitive global market of the 1990s organizations such as General Electric and Xerox have become "bureaucracy busters," throwing away the organization chart and replacing it with ever-changing constellations of teams, projects, and alliances with the goal of unleashing employee creativity.

POSTMARKETING RESEARCH IN PHARMACY

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Postmarketing surveillance (also post market surveillance) is the practice of monitoring the safety of a pharmaceutical drug or medical device after it has been released on the market and is an important part of the science of pharmacovigilance. Since drugs are approved on the basis of clinical trials, which involve relatively small numbers of people who have been selected for this purpose - meaning that they normally do not have other medical conditions which may exist in the general population - postmarketing surveillance can further refine, or confirm or deny, the safety of a drug after it is used in the general population by large numbers of people who have a wide variety of medical conditions.

Postmarketing surveillance uses a number of approaches to monitor the safety of licensed drugs, including spontaneous reporting databases, prescription event monitoring, electronic health records, patient registries and record linkage between health databases.

Postmarketing research conducted to support the use of the medicine and begin by marketing or medical departments of pharmaceutical companies. More often they are following types of studies:

- comparative studies of company product and main medicines competitors;
- comparative analysis of dosage forms and dosage;
- research of effects of the drug on quality of life (QoL);
- analysis of the interaction with concomitant treatments;
- additional pharmacovigilance data on broader populations and longer duration exposure;
- product uptake and public perception “Real-life” practices for treatment of disease;
- health information and education;
- hypothesis generation and publication support.

These studies are not required to obtain the approval by licensing authorities. But doctors, pharmacists and other staff providing health services, pay much attention to the results of postmarketing research during the appointment of the drug to the patient. Postmarketing research can provide unique and valuable data for a wide range of stakeholders, including regulatory agencies, sponsors, and payers, physicians, and their patients.

CONFLICT ON PHARMACY BUSINESSES

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The presented work is a part of a study conducted during the process of working on the course paper *Conflict Management in pharmaceutical companies*, which aims to identify ways to prevent the emergence and development of the conflict situations in the systems of pharmaceutical companies: worker – worker, patient – pharmacist.

A typical feature of any company is the presence of the numerous and diverse conflicts. Therefore, the study of nature, causes, mechanisms of conflicts in the society, and the development of the ways of their prevention and solvation have a great theoretical and practical significance. Thus, the conflict is the ratio between the social interaction's subjects, which are characterized by the presence of the opposite motives (needs, interests, goals, ideals), or judgments (attitudes, evaluations, opinions).

The backbone of any organization is the people (staff). The set of conditions in which there is collective, can cause both increased efficiency and various conflict situations that lead to its decline, and even its collapse. It is therefore necessary to properly control all these processes, whose task should be the prevention of unwanted, negative conflict, and providing constructive. Managing conflict is perhaps the most important function of any manager.

Considering the problem of the dealing with conflict situations, the native conflict management relies on the theoretical foundation, which was laid in the science of management by the American scientist Elton Mayo in the doctrine of human relations. The behavior of people is determined not only by the rational impulses but also by the irrational ones, causing it to be difficult to predict. These moments of spontaneity increase in the terms of emotional tension and stresses, which are associated with conflicts, and makes the task of solving them extremely difficult by using scientific methods.

To conduct the study, a questionnaire survey method of all levels employees and visitors of the pharmaceutical institution was used. We interviewed 100 people of which half men and half women, they are all different ages and occupations.

During the conduction of the study the following data were yielded:

- women enter into conflicts by 75% more than men, this applies to both visitors of the pharmacy and its employees;
- the majority (64%) conflicts only on the fundamental for them issues (a higher prices, lack of the medication in the pharmacy, unappropriate service), and only 2% of the respondents said that they will not turn to the pharmacy institution after the conflict;
- 19 % of employees do not participate in disputes within the team, 69 % are trying to remain neutral and do not specifically support any of the conflicting parties, and 12 % are actively involved;
- 64% of the respondents stated that they will propose changes, 21% are willing to take in their hands, and only 15% will be afraid to intervene because of the possible job losses, while 61 % of respondents said that they are ready to criticize his superiors openly.

In the proses of making the research there were found the data that is necessary to pay attention to by the management of pharmaceutical institution for the normalization of the work (incompetence of pharmacists, moral standards, work ethic etc.) and the prevention of the conflict situations, that can make a bad affect on the image of the institution as well as its work. Possible good manager have to carry out such surveys among their employees and visitors. It will help to identify all deficiencies, identify the causes of discontent employees, spend measures to improve quality, to attract new personnel and investments; because workers in a good mood means quality work, satisfied visitors and in what way it is advertising, which will increase the popularity of your organization. It is necessary to carry out measures for the promotion, encouragement of both workers and customers, to create favorable conditions for the encouragement of the buyers.

MARKETING ACTIVITY OF ONLINE STORES

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Internet firmly entered our lives as a very handy tool readily available to receive and transmit information. The scope of use of Internet is constantly growing. The idea of creating a virtual store with real products has appeared a long time ago, but only now online shopping became very popular. This can be explained not only by the great popularity of Internet, but also changing, ever-increasing pace of modern life, when there is simply no time to visit regular shop familiar for most of us.

Online shopping today is a website that contains product descriptions, pictures and price where the buyer can to make purchases using the computer. Due to the popularization of online stores, there are some difficulties with the choice of the site, where you can make a purchase.

The purpose of our research is to study and make comparative analysis of marketing activities of online stores.

Recently there has been strong growth in the number of online stores and their sales volumes. To date, the system UPC EcommerceConnect includes 919 online stores, whereas a year ago there were 443 ones. Average monthly turnover of traders connected to the UPC also increased. Now online shopping earn 80 % a month more than last year. Number of purchases in Ukraine made online by cardholders is 68% more than last year.

On the basis of investigation by Opinion Software Media research company InMind the top 5 online retailers Ukraine has been identified (Table 1).

Table 1

Top 5 online stores in Ukraine

№	Online Store	Business Referrals
1	2	3
1	rozetka.com.ua	online shop of household, computers, mobile devices, software, goods for tourism, fishing, hunting
2	aukro.ua	online auction of European level. You can buy or sell almost any thing for very different prices from the cheapest to the otherworldly
3	bookclub.ua	online store, which occupies a leading position in the market for distance selling of books and media products in Ukraine

1	2	3
4	mobilluck.com.ua	online store selling household appliances, mobile devices, personal computers, notebooks, photo, video, audio, sports, recreation, etc.
5	eldorado.com.ua	online store of largest retail chain selling home appliances and electronics: computers, photo and video phones, gifts

We have conducted a comparative analysis of the marketing aspects of activity of the leading online retailers of household appliances, computer hardware, mobile, photo, video, audio, goods for sports, recreation. Analysis has been conducted for online shopping "Rozetka" and "Mobillak" actively operating on the Ukrainian market, particularly in Kharkiv and familiar to consumers (Table 2).

Table 2

Comparative analysis of the marketing aspects of online retailers

Criteria	«Mobillak»	«Rozetka»
A wide assortment	5	4
Level of service	4	4
Delivery in Ukraine	5	5
Discount system	5	0
The price level	4	4
Providing loan products	3	4
Image of the store	4	4
Advertising of the store	3	5
Total	33	30

Thus, we can conclude that e-commerce market in Ukraine is growing. To achieve the objective of further growth of the potential customers number it is necessary to use marketing activities in advertising, on television, in magazines and other media sources. According to the research of thought customers we offer to leaders of online stores to consider enabling payment at the goods issue departments through terminals.

Managers of the company ought to consider the possibility of monitoring various criteria, such as the number of visitors, number of calls and number of orders. Another approach of the conversion increasing is to know as much as possible about customers which visit stores. The importance of data collecting is very high, as to fill CRM system with this data and put it to work.

THE INVESTIGATION OF INFORMATION TECHNOLOGY INFLUENCE ON PROCESS OF MODERN STUDENT STUDYING IN TERMS OF NUPh

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The aim of this work is to investigate information technology influence on process of modern student studying in terms of NUPh.

It is impossible to imagine our modern life without computer technology using (CT), mobile connection and access to Internet network, especially during process of modern student studying.

One of the main tasks of higher pharmaceutical school modernization is to create the distance courses (DC) or electronic educational courses (EEC). Peculiarity of EEC is that – it is intended to independent and systematic mastering of educational material by students under teacher's guidance.

Methods of investigation. Field investigations have been used in this work. Questioning has been carried out.

Results of investigation. The questioning of 2-5 year students of NUPh has been carried out. All questioned students (100%) use CT in everyday life and can't imagine their living without Internet. The majority of questioned students use Internet very often (75%). However, 65% of questioned students use CT with the aim of communication, 35% – for studying. Modern students use Internet mostly for communication in social networks: V Kontakte, Odnoklassniki, Facebook, Instagramme, Viber, Twitter, spending from 1 to 3 hours a day (50%). For preparing to classes, Internet is used by 30% of questioned students. 75% of students use books, 50% – use notes of lectures, 37% – use electronic books. Now electronic lectures are wide spread among students. 55% of questioned students use them. Electronic archives of University's library are used by only 5% of questioned students during preparing for classes. 62% of students heard about EEC, but not all of them used it due to many reasons. Among them: not all students have access to Internet network, it is enough to use only textbook or lectures' notes during preparing for classes. At that students of junior grades (especially 2-year students) know more about EEC and mostly use such elements of EEC as: information material, video courses and test tasks. Consequently, modern student has a wide choice of sources, which includes EEC during preparing for studying.

COST-EFFECTIVENESS BASED PHARMACOECONOMIC ANALYSIS IN A BRONCHOALVEOLITIS THERAPY

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Pneumonia is one of the major health and social problems in our country and around the world because of its substantial prevalence and high mortality. Pneumonia treatment is carried out in accordance with the national protocol, according to which the following drugs are prescribed: antibiotics, expectorants, antipyretics, and sometimes, antihistamines.

Bronchoalveolitis treatment requires as early as possible antibiotics prescribing, taking into account clinical, X-ray and microbiological data; suitable combination of different groups drugs is required. In the treatment of a pneumonia penicillins, cephalosporins, fluoroquinolones are traditionally used by courses 10-14 days at least.

The objective of the study was to conduct a comparative pharmacoeconomic evaluation of three drug regimens of bronchoalveolitis treatment with antibiotics of different groups: penicillin, cephalosporin and fluoroquinolone groups.

The method of the research was "cost-effectiveness" based pharmacoeconomic analysis.

The objects of the research included 109 patient medical records of Almaty clinical hospital No.21 (period of study – 2011-2012 years).

The results of the study were as follows.

A comparative "cost-effectiveness" pharmacoeconomic evaluation of three drug regimens of bronchoalveolitis treatment with antibiotics of different groups (penicillin, cephalosporin, fluoroquinolone) was performed.

According to the "cost-effectiveness" analysis bronchoalveolitis pharmacotherapy with cephalosporin antibiotics was the most effective compared with a group of penicillin and fluoroquinolone and it had a lower cost, which allows to consider these drugs more cost effective in the treatment of bronchoalveolitis.

Analysis of treatment costs allows to plan medical institution finances in the future.

ANALYSIS OF ANTIHELMINTIC BIOLOGICALLY ACTIVE ADDITIVES ON THE PHARMACEUTICAL MARKETS OF ROW OF THE CIS COUNTRIES

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Aim of the research. The conduction of comparative analysis of the assortment of antihelmintic (AH) biologically active additives (BAA), which have been registered in the Republic of Kazakhstan (RK), Russian Federation (RF), Ukraine, Uzbekistan.

Materials and methods of the research. Data of the State register of BAA of the RK, RF, Ukraine, Uzbekistan; statistical data of the leading consulting firm of the RK “Vi-ORTiS” on the volume of retail sales for 2010-2013 along the pharmaceutical companies and countries-manufacturers, which import AH BAA onto the territory of the RK, and also data of the center of medical-pharmaceutical information. The methods of statistical analysis, comparative analysis and meta-analysis of the data have been used in the current work.

Results of the research. It was found out that 11 AH BAA had been registered on the territory of the RK, in the RF – 6, Ukraine – 14, Uzbekistan – 6. AH BAA are released in 5 dosage forms (DF). A row of trade names of AH BAA in the RK are manufactured simultaneously in 5 types of DF. The biggest share in the total nomenclature has been taken by herbs (46%) and tablets (18%). AH BAA are imported onto the pharmaceutical market of the RK by 3 firms-manufacturers: CJSC Evalar (Russia), SC PlantExtrakt SRL (Romania), Biomardon-Pharma (Uzbekistan). The share of their own AH BAA in the studied countries is relatively high: it is 100% in the RF, 67% - in Uzbekistan, 57% - in Ukraine. The share of domestic manufacturers is 64%. The share of CIS countries at the domestic market of AH BAA for the studied period in US dollars has a tendency to decrease from 13.05% in total in 2010 till 11.01% in 2013 year; in packages from 18.37% till 14.26% correspondingly.

Conclusions. It is considered as a rational to conduct the marketing analysis of preferences, forming the optimal assortment for the most complete satisfaction of the consumers’ needs in the studied BAA, and also developing of new biologically active additives of the nature origin.

SECTION № 13

SOCIO-ECONOMIC RESEARCH IN PHARMACY

THE ANALYSIS OF COMPETITIVENESS OF UKRAINIAN PHARMACEUTICAL MANUFACTURERS

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Despite the rapid growth of the Ukrainian pharmaceutical market, consumers of drugs have doubts about the quality of domestic drugs as compared with their imported analogues. Imported drugs hold the lead in the sales volumes of pharmaceutical products in money terms, but every year their share is reduced. At the same time from 2011 the plant "Farmak" holds primacy on volume sale of medicinal products in money terms. It was able to outrun foreign manufacturers, such as "Berlin-Chemie" (Germany), "Takeda" (Japan), and "Sanofi" (France).

Considering a sufficient number of world manufacturers in the Ukrainian pharmaceutical market and their influence on formation preferences consumers as well as in order to determine potential domestic producers we evaluated the competitiveness of industrial pharmaceutical enterprises in Ukraine.

The objects of study were Public Joint Stock Company "Farmak", Private Joint Stock Company "Pharmaceutical company "Darnitsa" and the corporation "Arterium", consisting of Public Joint Stock Company "Kievmedpreparat" and Public Joint Stock Company "Galychpharm". During the analysis we used the data on financial activity of these companies.

Evaluation of the competitiveness of the enterprise was carried out us with using one of the most common matrix methods – methods scores, the implementation of which envisages several stages.

The first stage of the analysis was the formation of performance indicators for separate components the enterprise: marketing, production, financial and staff potentials, and its calculated (Table 1).

The next stage of the research involves ranking of performance indicators for the impact on one or another criterion exactly for evaluating competitiveness of enterprises (Table 2).

Among presented indicators we selected maximum value, what equated to 10 points. During the next stage we conducted the calculation of scores that obtained by firms for specific performance indicators by comparing their actual values with the best in this total. The establishment generalizing scoring of competitiveness was the final stage during which were found the weighted scores for each indicator (Table 3).

Table 1

The results of calculation performance indicators of competitiveness of pharmaceutical manufacturing enterprises

№	Indicators	Values indicators (K _{ij})			K _{maxi}	B _{maxi}	Points of performance indicators (B _{ij})		
		«Farmak»	«Arterium»	«Darnitsa»			«Farmak»	«Arterium»	«Darnitsa»
Marketing potential									
1	Ratio trade items	1.191	0.877	0.852	1.191	10	10	7.36	4.98
2	Reversibility of stocks	7.204	6.084	5.368	7.204	10	10	8.45	7.45
3	Return on sales. %	56.47	37.82	51.28	56.47	10	10	6.7	9.08
Production potential									
4	Capital productivity	1.949	5.895	2.419	5.895	10	3.31	10	4.10
5	Growth rate of receipts	1.155	1.160	1.268	1.268	10	9.11	9.15	10
6	Return on realization. %	22.08	13.93	10.57	22.08	10	10	6.31	4.79
Financial potential									
7	Return on equity. %	24.85	6.32	13.86	24.85	10	10	2.54	5.58
8	Coefficient of autonomy	0.674	0.319	0.650	0.674	10	10	4.73	9.64
9	Absolute liquidity ratio	0.088	0.013	0.57	0.57	10	1.54	0.23	10
Staff potential									
10	Labour productivity	0.971	0.716	1.181	1.181	10	8.22	6.06	10

11	Coefficient of stability	0.939	0.891	0.967	0.967	10	9.71	9.21	10
12	Growth rate of wages	1.19	1.21	1.094	1.21	10	9.83	10	9.04

Table 2

The degree of influence of individual components of the potential companies on their level of competitiveness

The factors competitiveness	Importance of factors
1. Marketing potential	0.2
2. Production potential	0.4
3. Financial potential	0.3
4. Staff potential	0.1

Table 3

The results of calculation of the integral indicator of competitiveness of enterprises

№	Indicators	Importance (k_i)	K_{maxi}	B_{maxi}	Points of performance indicators (B_{ij})			Weighted scores $B_{ij} \times k_i$		
					«Farmak»	«Arterium»	«Darnitsa»	«Farmak»	«Arterium»	«Darnitsa»
Marketing potential										
1	Ratio trade items	0.2	1.191	10	10	7.36	4.98	2	1.47	0.99
2	Reversibility of stocks	0.2	7.204	10	10	8.45	7.45	2	1.69	1.49
3	Return on sales. %	0.2	56.47	10	10	6.7	9.08	2	1.34	1.82
Total marketing potential								6	3.73	2.68
Production potential										
4	Capital productivity	0.4	5.895	10	3.31	10	4.10	1.32	4	1.64
5	Growth rate of receipts	0.4	1.268	10	9.11	9.15	10	3.64	3.66	4
6	Return on realization. %	0.4	22.08	10	10	6.31	4.79	4	2.52	1.92
Total production potential								8.96	10.17	7.56
Financial potential										
7	Return on equity. %	0.3	24.85	10	10	2.54	5.58	3	0.76	1.67
8	Coefficient of autonomy	0.3	0.674	10	10	4.73	9.64	3	1.42	2.89
9	Absolute liquidity ratio	0.3	0.57	10	1.54	0.23	10	0.46	0.07	3
Total financial potential								6.46	2.25	7.56
Staff potential										
10	Labour productivity	0.1	1.181	10	8.22	6.06	10	0.82	0.61	1
11	Coefficient of stability	0.1	0.967	10	9.71	9.21	10	0.97	0.92	1
12	Growth rate of wages	0.1	1.21	10	9.83	10	9.04	0.98	1	0.9
Total staff potential								2.77	2.53	2.9
Integrated indicator of competitiveness								24.19	18.68	20.7

According to the calculation results, "Farmak" has the highest integrated indicator of competitiveness – 24.19

So as a result of conducted research we establish that the most competitive manufacturer of medical products in Ukraine is plant "Farmak" by the sum of all indicators. It has a high position in the construction of the marketing and staff potential, and the lag on some indicators may indicate about the risks that associated with development of the plant, improvement material and technical base, the desire to be a leader in the domestic market, expanding its presence abroad.

STAFF AUDIT

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Abstract. The article considers the nature of the audit staff, and why there is a human resources audit . State personnel policy to date and prospects for future development.

Keywords : audit, staff personnel.

Ukraine's transition to a market economy has put a number of fundamentally new challenges , the most important of them - the most efficient use of staff organizations. The deep crisis of modern Ukrainian economy is largely determined by the low efficiency of economic organizations. Financial difficulties, most domestic enterprises are the result of low efficiency of management of organizations in general , the essence of which is HR . However, the deteriorating economic situation usually causes a decrease in attention to the problems of personnel management, which ultimately leads to further deterioration in the financial condition due to a fall in labor efficiency at all levels of operation. Update Personnel Policy , the formation of a new concept of HRM in modern terms is significant potential for raising the competitiveness of enterprises and the factors necessary for their effective development. In this situation, the practical use of tools The research objective of the system of personnel management in the form of audit staff is very important.

The aim of this work - evaluation of the effectiveness and productivity of staff as one of the most important factors ensuring profitability of the organization.

Organizational and human resources audit - is the assessment of the structural and human resources of its objectives and development strategy for the preparation and adoption of promising strategic decisions.

HR , conducting personnel audits should be clear about what processes and how effectively conducted in an organization. Key personnel processes, audit areas shown in the following diagram:

Human resource planning : Assessment of available manpower, professional potential collective goals, conditions and prospects of the organization, future staffing needs .

Recruitment , Personnel Reserve : Information on staffing needs . Determining the methods, techniques , sources and principles of recruitment. Evaluations of the program evaluating the selection procedure . The change in the dynamics of human resources and the possibility of its effective use.

Develop incentive systems : Analysis of the structure of wages, the share of basic and premium rates , the availability of circuits , differential payments in accordance with efficiency. Analysis of the average market rates and payment principles.

Adaptation Management: Analysis and description of the operating procedures of adaptation , assessment of their effectiveness. Analysis of the coefficient of turnover.

Training and staff development : analysis of the objectives and learning. Analysis of information on staff development, training effectiveness assessment system , changing the motivation to work.

Evaluation of work : Evaluation of existing procedures for certification , the frequency of the Conference, results and future decisions. Implementation of innovative methods in the Evaluation System of the company.

Since personnel policies are derived from the general development strategy , the justification of its choice depends on how efficiently were conducted market research now possible implementation of its products and its competitiveness. Therefore, the overall plan of personnel policy should be adjusted according to the changes that are made. In evaluating personnel policies should take into account the possibility of integrated effects when the final result of higher than the sum of individual results. Evaluation of personnel policies for compliance with the conditions , consisting of the company staff , perceived collective rather quiet.

CIRCULATION PROBLEMS OF DIETARY SUPPLEMENTS AT THE UKRAINIAN MARKET

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Among the key measures of the state identified in the Concept of the State Policy of Ukraine it is rather important to implement measures to preserve the health of the population and capacity to work, extension of the duration and quality of life of citizens. The state of sanitation and human performance are affected by many environmental factors, including nutrition, the level of physical and nervous loads and stress, the speed of information exchange, etc. One of the measures to reduce the negative effects of the environment is the use of nutritious food, as well as designing and constructing food products that are not only safe for human, but also of those protecting the genetic structures of a harmful influence. These products are referred to as functional purpose products, food and biologically active additives (dietary supplements). They have a positive effect on the corresponding body functions; thus, providing for their regular consumption reduces the risk of chronic diseases.

According to the literature about 70 % of the EU countries and the United States take dietary supplements. Less than 10 % of the population of Ukraine regularly consume special foods, although the statistics in our country is not practically conducted. It should be noted that according to modern research the use of dietary supplements for native citizens is more important than for the population of developed countries. Sales of dietary supplements in pharmacies and other pharmacy institutions of Ukraine are not prohibited under paragraph 1.3. of the Order of the Ministry of Public Health of 23.07.96 No. 222, i.e. it has been stated that the dietary supplements can be sold through pharmacies, branch pharmacies and so on.

The aim of our study was to identify the problems of circulation of dietary supplements at the pharmaceutical market of Ukraine taking into account the legal framework that regulates the circulation of special food.

In the course of these studies we have also outlined the range of regulations governing the circulation of dietary supplements in Ukraine, namely the Ministry of Public Health of 30.06.94 No. 117 "On the Procedure for prescribing and dispensing

medicines and medical products from pharmacies", Ministry of Public Health of 23.07.96 No. 222 "On approval of sanitary rules and regulations on the use of dietary supplements", Resolution of 26.07.06 No. 1023 "On implementation of Article 28 of the Law of Ukraine" on the safety and quality of food", a number of specifications, specifications for the manufacture of certain dietary supplements and others.

As a result of the analysis of these legal acts the "nontransparency" and the low availability of information concerning safety and optimal dosage when using some prohibited substances have been determined. For example, Hepatoclin contains an alcoholic extract of *Convallaria majalis*, which is a potent plant raw material and cannot be used by the consumer without regard to the individual state of the cardiovascular system and mandatory professional advice. Another concern is the fact that dietary supplements can be purchased via online shops, supermarkets, distributors, and use them as you wish. We believe that this problem can be solved by creating an appropriate legal framework for the use of dietary supplements.

Many researchers, including scientists working under the supervision of prof. Nemchenko A.S. and prof. Mnushko Z.M., have shown that most of the consumers have a responsible attitude towards the use of dietary supplements, consult with doctors or pharmacists how to take them and about the consequences of their action and possible complications, explaining that they trust to these healthcare professionals. However, because of the lack of complete information dietary supplements purchased over the counter can be regarded by the consumer as drugs that do not have a sufficient level of evidence.

Thus, it can be stated that pharmacies themselves are one of the basic tools of quality control of dietary supplements on their way to consumers. Therefore, one of the main areas to regulate the dietary supplements circulation is to have a clear definition of the status of dietary supplements and to set the rules of providing information about them to the consumer, creating protocols of this group dispensing, advertising, giving the information on the package leaflet of the product.

THE PROBLEM OF THE MEDICINE PRICING IN LEBANON

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Lebanon is a country with relatively uncontrolled drug price regulations. High drug cost, difficult economic situations and low income pushed the patients to find other alternatives to the elevated medicine prices. Government and Health care associations must solve such problems and provide affordable therapeutic solutions to overcome the rising cost of health care and drugs. Lebanon is also known for its very limited drug manufacturing and most drugs are imported mainly from European countries, USA and some Arab Countries. Besides, imported drugs prices are very high in terms of international pricing and the elevated prices are therefor due to shipment fees and taxes imposed by the government on the imported drugs.

Another misconception, is that patients believe that high cost drugs are more effective and direct their drug purchase to the expensive drug. Those who can't afford elevated costs shift to "*Fraud Drugs*" for the reason that it's cheaper and affordable. By comparing the genuine drug's price in Lebanon with the Fraud drug's price, a patient can recognize that the same drug will cost him double, triple and sometimes 5 times the price of the same drug in his home country. Therefore, the patient with low or middle income decides to cut costs and to get the cheapest choice. "*Fraud Drugs*" are usually outsourced from neighboring countries.

As a result of such actions, another problem rise in the neighboring countries where the drug demands exceeds the drug availability. Getting medicines from neighboring countries do not solve the problem of "The Drug Accessibility". A huge number of patients do not have connections with neighboring countries and stay obliged to either buy high cost available drugs in Lebanon, remain with incomplete treatment or sometimes with absence of treatment.

To resolve all those issues, several solutions must be found to provide Good HealthCare Quality for "Drug Consumers" and reasonable profit to "Drug Manufacturers".

Ethically, Manufacturer's profit should never come first. It's the patient's health that should be a priority.

In Developed countries around the world, big manufacturers are asked to produce effective medicine along with an optimum price for the patient.

In such countries, Government support the manufacturer by decreasing the tax or by reducing the import fees of the drug's raw material.

Nowadays, Drug Manufacturer's around the world are spending enormous amount of money and time to produce, test and release a new drug. Once the drug is licensed, ready to be launched and to be sold to end users, Manufacturers sell this drug with high cost and in bulk quantities to wholesalers, intermediaries and pharmacists and exert on them push force to sell the product in a short period of time. All of this is in the aim of covering their loss and expenses during the years of research and testing.

To help the manufacturer and cease him from increasing the cost of the licensed drug, the government should facilitate and fasten the release of the drug license and patents and reduce all the expenses of the drug between the two different phases of development and licensing.

On the other hand, government also should supports patients by decreasing the price of the drug in private pharmacies, provides a wide majority of medicines in the governmental hospitals with low prices and it also must facilitate the paper work needed from patients to get their medicines from governmental hospitals and doctors.

Moreover, "WHO" (World Health Organization) and several different associations are often releasing and publishing various recommendations to follow. Such recommendations are documented, available and easy to apply. These recommendation help to decrease the cost of the drug leading to decrease its public price.

RESEARCHES OF NATIONAL LISTS OF ESSENTIAL MEDICINES IN UKRAINE AND TURKMENISTAN.

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The health care and pharmacy systems in over the world have significant differences in strategic intentions and objectives, buildings, mechanisms and methods of state influence. Most of countries implement the Concept of Essential Medicines today. It was proposed by specialists of the World Health Organization. The intention is equal access for population to medical and pharmaceutical care through the introduction of drugs and medical devices included in the National List. These drugs have conclusive advantage in pharmacotherapeutic action, safety, quality and others. So we researched conformity of National Lists in Ukraine and Turkmenistan with the List of World Health Organization.

The analysis showed that List of WHO consists of 456 INN, National List of Ukraine consists of 541 INN and 374 INN consists in Turkmenistan's List. It should be noted that the list of OLZ WHO is divided into basic and additional . Basically a list of those medicines listed are recommended for the treatment of the most common pathologies. An additional list of drugs submitted for priority treatment of diseases that require specialized diagnostic or supervisory equipment , and / or specialized medical care and/or training. National lists of Ukraine and Turkmenistan Consequently , it was found that the draft list of Ukraine consists of primary and secondary meeting the requirements of the WHO and Turkmenistan - only basic, they contradict. Analysis were conducted by anatomical Therapeutic Chemical (ATC). They showed that anatomical group J (antibiotics for systemic use) has the maximum number of items in the Ukraine's and Turkmen's Lists. It has for 19,6% and 15,7% of the total drugs in Lists. The second position was taken by the group A (digestive system and metabolism). It contains for 9,06% and 14,25% respectively. The group G (the urogenital system and sex hormones) contains the least amount of items in the Ukrainian List. It has for 3,88% of the total drugs. The group H (hormone's drugs, except sex and insulin) has for 1,69% of the total drugs in the Turkmen's List. Solid medicaments dominate. The data indicate that National List of Ukraine partially complies with the requirements of the WHO unlike Turkmen's. A significant drawback of these Lists they don't update every 3 years. It indicates the use of outdated medicines and their compliance to modern methods of treatment. Selection of medicines in both countries are broadly consistent with the WHO's requirements.

POTENTIAL COMPETITIVE ENTERPRISE

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Relevance of the chosen research topic is that many companies can not effectively use their available resources and establish a profitable activity for themselves due to the lack of high-quality, competitive products and a lack of strategic thinking. The experience of recent years has shown that not all domestic enterprises eligible to conduct effective competition. Even the availability of competitive products do not allow many of them to realize these benefits due to lack of practice using whole set of measures [1]. It should be pointed and destabilizing external factors surrounding the Ukrainian producers: an inefficient tax system, unfavorable investment climate, inadequate legislation and others. [2].

The purpose of competitive potential - discover the possibilities of the company. In focus is the question: "What special ability is firm," "In some areas it is not competent enough?".

Competitiveness potential to include virtually all areas of business: management, production, research, finance, marketing and so on. [3]. The most appropriate way to gather information about the potential of the firm is a systematic review of all of these areas. The source of quantitative indicators can serve as internal documents. Evaluation of quality characteristics can be carried out by experts [4].

Competitiveness potential of the company - a comprehensive comparative characteristics that reflect the level of aggregate indicators for assessing the prevalence of business opportunities that determine its success in the marketplace over time in relation to a set of similar parameters enterprises competing.

Competitiveness potential of the company has several features such as:

1) competitiveness is not inherent quality of the company (ie its inner , natural quality). It can be discovered and appreciated only in the presence of competitors (actual or potential).

2) it is a relative concept , that is, it has a different level on different competitors.

3) competitive potential of the company is determined by the productivity involved in the use of production resources.

4) the level of competitive potential of the company depends on the competitiveness of its components (mainly products), as well as the overall competitiveness of the industry and the country.

Depending on the focus on management functions:

1 level. For businesses characteristically consider the organization of management personnel as intrinsically neutral element potential. The role of the head is reduced to the output without worrying about the problems of competitiveness and customer satisfaction.

2 level. Companies are trying to make a production capacity element "external neutral." This means that the potential of the company must fully comply with the standards set forth its main competitors.

3 level. Managers of enterprises understand their own advantages in the competitive market somewhat differently than their main rivals, and try not to adhere to manufacturing standards that have been established in the industry.

4 level. Success in the competition is not so much a function of the production as a function of management and to the quality, effectiveness, management, production. These businesses provide its leading position in the market for a long time [5].

It can be concluded that the management of competitive potential of the company - a meaningful impact on the factors and conditions that shape it. Therefore, the analysis and prediction of the impact of both positive and negative factors must realize in the original defined competitive advantages, which include the use of the new features of the market environment and micro-enterprises, and minimizing risks.

MARKET ANALYSIS OF DRUGS USED FOR THE TREATMENT OF CEREBRAL PALSY

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More than 14 thousand people of all ages suffer from cerebral palsy (CP) in Ukraine nowadays. The most important consequences of this disease are disability and reduction of life expectancy of patients. That's why the improvements of pharmaceutical help in terms of improving of its accessibility and adequacy are important medical and social problems.

In view of the above, the purpose of the study was to analyze the domestic market of drugs (LP) used for the treatment of cerebral palsy. We used the marketing and statistical research methods and the methods of scientific analysis, in particular, comparison, grouping, summarizing data.

According to the state social standards of medical care for patients with cerebral palsy, we have found that the main groups of drugs used for the treatment of cerebral palsy is anxiolytics, muscle relaxants, cardiogenic, antiparkinsonian, m- and n-cholinomimetics, nootropic, antihypoxants, vasodilators, anticholinergic agents, α - blockers. According to the research of the pharmaceutical market of Ukraine for the period of 2011-2013, 32 trade names of drugs of ten groups were registered. Among these drugs 11 drugs are produced in Ukraine by the 6 companies and 21 drugs are produced in other countries by 19 manufacturers. In percentage, it is 34% and 66% respectively. The results of the study of the countries - manufacturers show that the number of firms and the drugs they propose are represented widely geographically. For example, drugs for the treatment of cerebral palsy are imported to Ukraine from 12 countries. The main importing countries are Poland and Austria, supplying 13% and 9% respectively of the total number of drugs for the treatment of cerebral palsy. Ireland, Hungary, USA and Germany export to Ukraine 2 drugs each that is 25%, France, Switzerland, Latvia, Slovenia, Spain, Italy- export 1 drugs each, it's 19%, respectively. Among domestic manufacturers the leading position occupies FC (Pharmaceutical Company "Zdorovyie" ("Health") (5 products) and JSC "Farmak" (2 pills), representing 16% and 6% of registered drugs for the treatment of cerebral palsy, respectively.

Based on the above, it can be argued that the Ukrainian pharmaceutical market drugs for the treatment of cerebral palsy is characterized by significant dependence on imports and requires diversification of domestic production of drugs to enhance performance availability of drugs for patients with socially significant diseases, which include cerebral palsy.

THE INVESTIGATION OF MAIN DIRECTIONS OF IMPROVEMENT PRESCRIPTION MEDICINES IN UKRAINE

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Today one of the most pressing problems in the issue of improving the efficiency of both medical and pharmaceutical sectors of Healthcare of Ukraine is unregulated prescription drugs (medicines). According to a survey of the literature and conducted applied research found that the said issue has the following negative phenomena as extremely low financing medicine and pharmacy, lack of effective direction for the development agenda of free and preferential delivery of drugs, mechanism of compensation of the cost of drugs and a number of other factors have a negative impact on the modern condition of health care. Therefore, one of the most urgent reform tendencies of modern medicine and pharmacy should be to identify the main areas of improvement of prescription drugs in Ukraine.

The results of a survey among 132 pharmacists and pharmaceutists from different regions of Ukraine allowed to highlight the main problems of prescription circulation disorders and factors. It was found that the majority of respondents - 55.3% (73 experts) believe that the current recipe is not fulfilling its purpose and does not meet the social, medical, economic and legal functions. The majority of respondents - 83.3% (110 professionals) believe that prescription must guarantee the safe and efficient provision of pharmaceutical care to the population.

When asked about the causes of the problem of prescription drugs respondents were as follows: 33.33% - 44 experts believe a violation of prescription issue of the lack of control over occupational physicians, 2.27% - 3 experts see this lack of control over the professional activities of their colleagues, and the vast majority of respondents - 64.6% (85 experts) recognize this complex problem throughout the health care system of Ukraine.

The results of the studies consider rational the following main areas of improvement of prescription drugs in Ukraine, such as: improvement of both material and technical basis of the national health system, active integration into the national health system of modern information technology, improving standards of medical and pharmaceutical activity. Thus, the basic directions of perfection of prescription drugs allow, in our opinion, first of all solve the problem of prescription drugs trafficking, and generally contribute to the removal of national health systems to a new level of effective functioning.

APPROACHES OF PROVIDING WITH MEDICINES OF PATIENTS WITH PSORIASIS

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Numerous researches, which are devoted to a problem of treatment of psoriasis, do not define the perfect scheme of treatment of pathology, even considering a variety of medicinal preparations that are present in the pharmaceutical market. First of all this fact is explained by set of factors which influence disease emergence, and also problems in system of rendering the medical and pharmaceutical care the patient and lack of the coordinated system of normative and legal regulation of providing patients with medicinal preparations.

Definition of the main approaches to provision of medicines of patients by a psoriasis taking into account ground levels of rendering the medical and pharmaceutical care to the population became the purpose of our research. At research, methods of the comparative, logical and marketing analysis were used.

According to the marketing analysis of the range of medicinal preparations carried out by us which are recommended for complex treatment of a psoriasis, it is established that the range is characterized as rather wide and is presented by preparations of different producers and release forms. However preparations of the previous generations prevail among preparations of a domestic production.

By results of the analysis of regulating lists of medicinal preparations which regulate rendering the medical and pharmaceutical care by a sick psoriasis, it is established that in the main of them, in particular in the treatment Protocol, preparations under concrete trade names are registered instead of the indication of group of medicinal preparations of complex therapy. According to the analysis of the V release of the state form of medicinal preparations, preparations with the proved effectiveness and safety for treatment of psoriasis antimetabolites, immunosuppressant, corticosteroids and the combined dermatologic preparations the majority from which are not specified in the treatment Protocol are defined.

Considering the list of unresolved questions stated above at all levels rendering the medical and pharmaceutical care, we offered model of-level formation of approaches to optimization of providing patients by a psoriasis taking into account ground levels of rendering the medical and pharmaceutical care to the population, in particular state, regional and level of the consumer.

Thus, the main approaches to optimization of provision of medicines of patients by psoriasis consist in exercise of a complex of actions at each level of regulation and are characterized by legible definition of existing problems and a definition of concrete ways of their overcoming.

RESEARCHES OF RELEVANCE A PROBLEM OF UNTIMELY IDENTIFICATION OF PSORIASIS

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Psoriasis is the chronic disease which specific weight makes from 7 to 10% and among hospital patients with skin diseases to 20-25% in the general structure of incidence of skin.

As it is known that lack of the timely qualified medical care can lead to development of heavy forms of psoriasis and even an invalidization of the patient, definition of the period of duration of a disease with which patients for the first time ask for medical assistance became the purpose of our research.

We carried out the retrospective analysis of medical records of inpatients in number of 767, were passing treatment in the Kharkov regional skin and venereologic clinic №1 in 2011-2013 and it was established that 22.2% of patients asked for medical assistance in treatment-and-prophylactic establishment for the first time.

The special attention is deserved by that fact that the majority of patients for years weren't treated, or self-medicated, including 35 patients (21.8%) for the first time addressed to the doctor after 1-2 years of sufferings, 34 patients (21.1%) – after 3-10 years of a disease, 6 patients (3.7%) – after 11-30 years of a disease, also 22 patients (13.6%) noted that they were ill some years, and 5 patients (3.1%) – they were ill a lot of years and only 59 patients (36.7%) suffered a dermatosis till 1 year (among them 17 patients (10.6%) the first manifestations of psoriasis proceeded till 1 month).

Considering that more than 40% of patients for the first time address to the doctor after 3-30 years of life with psoriasis and, respectively, aren't registered in official bases, debatable there is a question of reliability of official statistical data of Ministry of Health on prevalence of psoriasis in Ukraine (for today more than 1 million population of Ukraine are sick with psoriasis though, according to official statistics, their less than 100 thousand).

The obtained data testify to extreme relevance of psoriasis which remains a significant problem of medical and social character, despite a significant amount of medicines and treatment methods. In our opinion, for the purpose of identification and rational pharmacotherapy of patients, first of all, it is necessary to carry out systematic monitoring of incidence a dermatosis at the state and territorial levels.

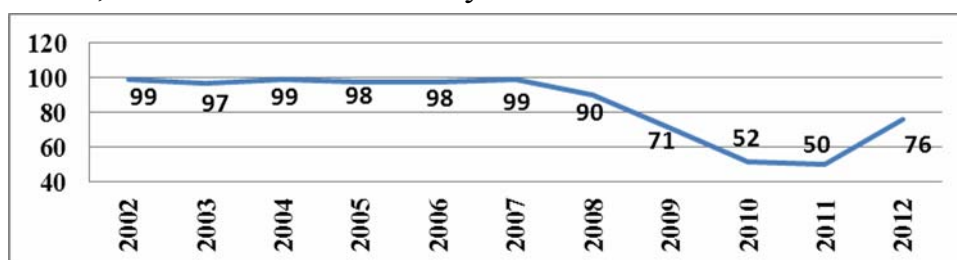
THE ANALYSIS OF THE CHILDREN IMMUNIZATION BY DTP VACCINE IN UKRAINE

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According to WHO estimates the implementation of of immunization can prevent up to 2 - 3 million deaths per year, but, unfortunately, infectious diseases are still a major cause of mortality in the world. According to the Global Vaccine Action Plan, which was adopted on the May 26, 2012 at the 65th session of the World Health Assembly, immunization is recognized the most effective preventive measure in health care and immunization level by 2020 has to reach 90%. National immunization programs and active in different countries calendars of preventive vaccinations contribute to implement these plan.

In view of the above, the aim of our study was to analyze the level of children immunization by adsorbed vaccine against diphtheria, pertussis and tetanus (DPT) in Ukraine.

According to WHO recommendations, the level of DPT vaccine immunization should be 95%. Analyzing statistical data about children vaccination in Ukraine for the period 2002-2012, it can be concluded that in recent years there has been decline of immunization. Thus, during 2002-2007, it remained almost the same and amounted an average of 99%, what is ideal. However, in 2009, the immunization level decreased to 71% and reached a minimum in 2011, accounting for 50%, which is highly negative trend. In 2012 this indicator increased to 76%, which still remains very low (Pic. 1). The specified situation may be associated with an active campaign against vaccination, which was conducted by the media at this time.



Pic. 1. The level of the children immunization by DTP vaccine in Ukraine.

Thus, the present level of immunization in Ukraine is unsatisfactory. We think, that one way to solve this problem is to return public confidence to the vaccination by active government support in the health education among the population in order to disseminate knowledge about the immunization.

RESEARCH OF ORGANIZATIONAL STRUCTURE OF PROVIDING MEDICATION AND WARES OF MEDICAL SETTING SYSTEM OF TROOPS IN UKRAINE

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With the purpose of maintainance and strengthening of health of servicemen, grant them of necessary medical and pharmaceutical help, treatment and proceeding in a capacity and military efficiency, after diseases and traumas the system of measures, which submits medical service of Military Forces of Ukraine in accordance with a current legislation, operates in Ukraine. The compensation of money for the grant of medical and pharmaceutical help servicemen is carried out due to the estimate of Military Ministry of Ukraine (MMU).

Basic operative units in the system of the pharmaceutical providing are military medical clinical centers (Centers). Six centers that are inferior MMU and are the organs of medical service management in Military Forces of Ukraine function in Ukraine. In a peace-time the pharmaceutical providing of soldiery parts is carried out according to the territorial principle by Centers and medical parts or establishments. Planning and providing medications and wares of the medical setting (WMS) of Centers and soldiery parts is carried out by the health protection Department of Military Ministry (HPDMM). Centers determine a requirement in medicines and WMS, carry out decentralizing their purveyance and distributing between soldiery parts, proceed in supplies. Except for it, Centers carry out control over an accounting, storage of pharmaceutical and medical commodities and readiness, to the use after their setting. the annual plans of medicine and WMS supply are developed by HPDMM. The purchase of commodities for addition and proceeding the supplies of Centers is carried out in a size of three months necessity.

According to the territorial principle reports-requests about a presence and necessity of medicines and WMS are given to Centers, and the Centers are given by the generalized reports-requests in HPDMM. Providing of troops with medicines and WMS is carrying out from the pharmacies of soldiery parts and pharmacy compositions. The basic setting of soldiery pharmacies consists in making and sales of medicines and WMS, which are needed for treatment of patients and realization of prophylactic measures.

Organizational principles of construction of effective model of supply of medicines and WMS of Military Forces of Ukraine require the permanent revision in the conditions of active development of the system of the pharmaceutical providing of the population.

COST OF TREATMENT OF PATIENTS WITH ISCHEMIC STROKE IN UKRAINE

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Today there is an acute problem of patient quality and accessible health care as in the world as in Ukraine. First of all, it is related to the intensive development of science, which is characterized by the appearance of new medical technologies, including new diagnostic methods and therapy, while the economic resources of the health sector remain limited. So, among the major issues that require urgent solutions at all levels of health care systems leading place belongs to the problem of financing the most common nosology and medical technologies. In connection with this special attention is paid the rational use of available health resources recently. One of the tools contributing to the decision-making in health care is pharmacoeconomic analysis, including analysis "cost of illness".

According to the above mentioned, the aim of our study was to conduct economic evaluation of direct medical costs for patients with ischemic stroke.

Cost analysis was performed by using systematic, logical, statistical, pharmacoeconomic ("cost of illness") and normative-cost methods.

The first stage of the analysis of direct costs for treatment of ischemic stroke was to evaluate the cost of the use of laboratory and instrumental methods of diagnosis of the disease. Within the analysis of the cost of hospitalization of patients also were taken into account the cost of specialists' consultations (Figure 1).

In order to calculate the direct medical costs related to hospital health care, we used "The unified clinical protocol of health care for patients with ischemic stroke" No 602, approved by the Ministry of Health of Ukraine dated 03.08.2012, which includes a variety of medical and laboratory diagnostic procedures, their number and frequency of use, and price-list on donation of paid health care services dated 01.03.2012 of the Railways Central Hospital.

The costs of medical procedures were defined by us as follows:

$$Cost_S = \sum Price_S \times P_S \times n_S \quad (1)$$

where $Cost_S$ - the cost of medical procedures, UAH;

$Price_S$ - the price of medical procedures, UAH;

P_S - the frequency of assignment of medical procedures;

n_S - the number of units of medical procedure.

Distribution of the costs for the main therapeutic measures related to in-

hospital treatment of patients with stroke is presented in Figure 1.

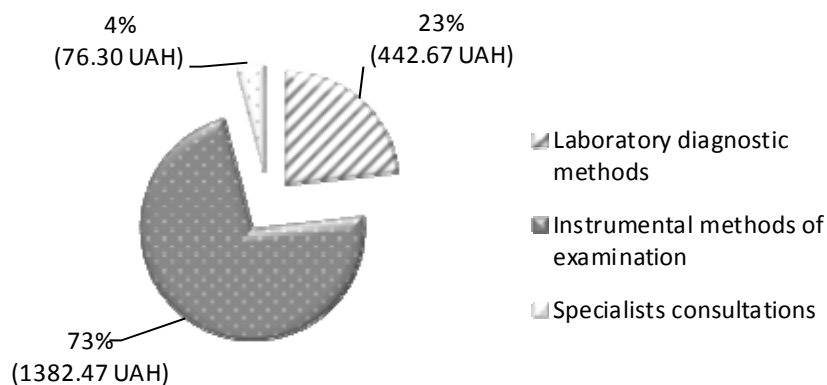


Figure 1. Distribution of the costs for to in-hospital treatment of patients with stroke

The analysis showed that the cost of medical procedures provided to one patient with ischemic stroke, taking into account the multiplicity and frequency of their appointment is 1 901.44 UAH.

According to the methodology of the study, the analysis of the direct costs for treatment of stroke also included drug expenses. Calculating the cost for pharmacotherapy for individual medicines were calculated by using the actual data on their cost of production and form of issue and the multiplicity of admission, course dose and frequency of prescribing obtained by the results of a retrospective analysis of 581 hospital cards, by the formulas:

$$C_{PHT} = \sum Price_M \times P_M \times D_M \quad (2)$$

$$Cost_{PHT} = \frac{C_{PHT}}{581} \quad (3)$$

where C_{PHT} - the cost of pharmacotherapy, UAH;

$Price_M$ - price per unit of drug's active ingredient, UAH;

P_M - the frequency of drug's prescription;

D_M - drug's course dose, mg/ml/Unit;

581 – number of analyzed hospital cards of patients with stroke.

Thus, the results of calculations determined that the cost for a patient's drug treatment was 2 057.56 UAH.

The next stage of the study was the calculation of the direct in-hospital cost per patient with an ischemic stroke, which was carried out by summing up the cost of diagnostic, specialists' consultations and drug costs.

Thus, the results of pharmaco-economic analysis found that in-hospital cost for a patient's with ischemic stroke treatment was 3 959 UAH.

SOCIAL AND EPIDEMIOLOGICAL INDEXES RESEARCH AMONG ELDERLY POPULATION IN UKRAINE DUE TO GLAUCOMA AT THE NATIONAL AND REGIONAL LEVELS

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In modern conditions of global population aging, the issue of elderly people provision with medications raises seriously. Therefore, the study of medical and demographic characteristics, health state and trends of this part of population appear to be of great importance within the healthcare development prognosis forming.

Taking into account the significant prevalence of glaucoma among the elderly population of Ukraine, the purpose of our research was a comparative analysis of the morbidity and disease prevalence.

The Medical Statistics of Healthcare of Ukraine data presented in the annual reports of public health from 2009 to 2012 were used as the methodological basis of the research. During this study we used retrospective, statistical, epidemiological, systematic, comparative and graphical analysis methods.

The glaucoma morbidity dynamics among elderly population in Ukraine has undulating nature (Figure 1). Thus, there is a positive trend in the 3 years dynamics (2009-2011) towards a gradual reduction of morbidity – from 165.3 in 2009 to 158.5 in 2011 per 100 thousand people. But in 2012, the number of patients with newly diagnosed glaucoma began to increase.

The analysis of the glaucoma morbidity in different regions of Ukraine showed that higher levels of this disease are observed in the population of Kharkov and Vinnitsa regions. The lowest rates of glaucoma morbidity were observed in Transcarpathian, Ternopil and Odessa regions.

Comparing the overall glaucoma prevalence among the elderly population of Ukraine the rapid growth of the stated index should be noted (Figure 2). Thus, the number of patients with glaucoma increased from 1688.8 in 2009 to 1764.8 in 2012 per 100 thousand people. It was established that over the past four years glaucoma prevalence increased in all the regions of Ukraine, and had the highest rates in Kyiv,

Sebastopol and Chernihiv regions. The lowest prevalence rates were established in the Transcarpathian region.

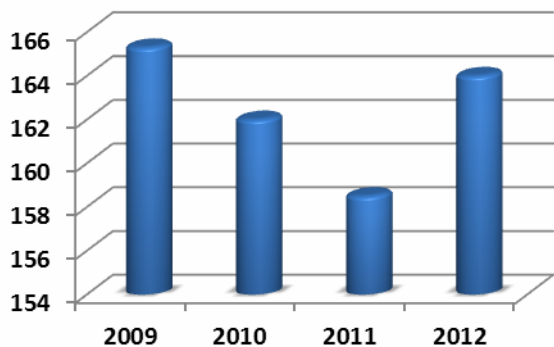


Fig. 1. Glaucoma morbidity dynamics in 2009-2012 (per 100 thousand of population)

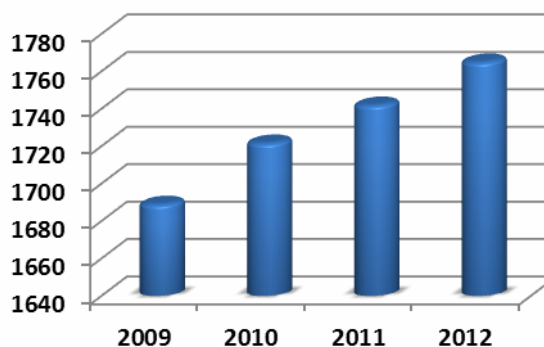


Fig. 2. Glaucoma prevalence dynamics in 2009-2012 (per 100 thousand of population)

Thus, as for the morbidity rates, it was found that during the 2009-2011 these indexes had a positive downward trend, but in 2012 took place their impressive growth by 4.5% compared to 2009, which concerns doctors and pharmacists.

The health state analysis of this part of the population demonstrates the necessity to apply an integrated approach to improve the elderly population health, the main directions of which, in our opinion, are:

- increasing the educational level about disease prevention;
- carrying out annual medical examinations for pensioners in local clinics;
- modern diagnosis methods introduction and improvement of material and technical base of medical institutions;
- health care accessibility and quality improvement;
- doctors and junior specialists in gerontology and geriatrics training;
- improvement of the health care legal and regulatory framework for elderly people;
- implementation of the measures aimed at healthy lifestyles promoting.

RELEVANCE OF IMPLEMENTATION OF LOGISTIC INSTRUMENTS IN FOREIGN ECONOMIC ACTIVITY OF PHARMACEUTICAL COMPANIES

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The purpose of this study is justification of organizational, legal, economic aspects of logistic process in foreign economic activity (FEA) of pharmaceutical organizations.

Materials and methods. Analytical methods and analysis of the systems were in-process used.

Results. Necessary condition for the development of the national economy, the deepening of cooperation with foreign countries, creating a favorable environment for investment are the proper administration of foreign trade. Management of foreign economic activity of the pharmaceutical company covers all its areas of activity associated with the movement of resources, goods, services and labor across national borders. Logistics can significantly reduce the time lag between the receipt of raw materials, semi-finished and finished product delivery to customers, helps to significantly reduce inventory and transportation costs, speeds up the process of obtaining information increases the level of service. Consequently, logistics FEA in pharmacy should be viewed as a system whose purpose is to deliver drugs in a given place, in the right quantity and range, as much as possible prepared for consumption at the lowest possible cost with maximum level of information support for the movement of material flows. Logistics FEA used pharmaceutical companies if it exports of manufactured products, imported raw materials, produces in-bulk. It is proved that the priority of logistics FEA pharmaceutical companies is to optimize the movement of material, financial and information flows beyond the enterprise and outside the country, while ensuring an adequate level of quality.

Conclusions. Implementation of the proposed methods based on the use of logistic approach to optimizing traffic flows pharmaceutical companies that go out of the country, will improve the level of competitiveness in international markets.

THE ESSENCE AND SIGNIFICANCE OF PERSONNEL DEVELOPMENT OF THE PHARMACEUTICAL ENTERPRISES

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The article considers the nature, tasks and methods of personnel management, the pharmaceutical enterprises.

The problem formulation. Sufficient availability of personnel with the necessary knowledge and skills, rational use, high levels of productivity are of great importance for the domestic pharmaceutical companies in relation to the increase of sales volumes of drugs and increasing production efficiency. In particular, from supply of pharmaceutical company staff and its efficient application depend on the volume and timeliness of performance of all works, the degree of use of the equipment and as a result the volume of drugs production, their quality, cost, profits, and other economic indicators.

Analysis of the last researches and publications. Study of certain aspects of working with personnel and its management in the pharmaceutical companies are described in the works of such domestic and foreign authors, as Hops FI, Yaremchuk, Lysak Century, Shchekin, GV, Yanovsky A.M., I. Komarov, Ouchi Century, Posilkina A.V., Bratishka US, Mnushko Z.N., Tolochko V.M., Kotka A.A. and others, But in modern literature did not reflect on the research of the disadvantages and advantages of a modern instruments of personnel management, the issues of formation of effective system of personnel development on the pharmaceutical enterprises. Also a little investigated problems of adaptation of foreign experience in the sphere of control of personnel development on the Ukrainian pharmaceutical enterprises.

The aim of the study is to examine the peculiarities of personnel management in pharmacy in the introduction of quality management, the understanding of which will help managers of pharmaceutical companies to develop an effective system of

personnel development with consideration of the specifics of the pharmaceutical enterprises.

The main material. The most important element of economic development is human resources; their qualifications, education, training, motivation activities. There is an undeniable dependence of the competitiveness of the pharmaceutical and food & optical enterprises, the quality of the personnel of the pharmaceutical company. Personnel development is one of the most important components of General increase of efficient production. In economically unstable periods problems of personnel development was not sufficient attention, but in the period of crisis development of personnel is one of the conditions of preservation of existing rates of economic growth. To achieve high efficiency of use of personnel only if it has the necessary knowledge, skills and purposefulness of activity. Education and training of personnel as a component of its development should be a continuous and correspond to modern requirements of international standards. It should be noted that in the conditions of economic instability personnel requirements increase, and the employees must realize

The conclusions. The staff is the main link of all processes in the pharmaceutical company. Whatever the latest technology, innovative ideas, they will never be effective, to bring the maximum benefit without high-efficiency work, proper training and qualification of personnel. The management of personnel development is a complex process, because people in different degrees endowed with intellect, the ability to think and learn and development. Sustainable development of staff is a necessary condition for the functioning of any pharmaceutical enterprises, especially in conditions of the modern changes in the requirements for professional knowledge on the background of the management of quality and orientation of the industry on an innovative model of development.

RESEARCH OF THE DISTRIBUTION OF DRUGS IN UKRAINE AND THE EUROPEAN UNION

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Introduction. The need to determine the main directions and priorities of the pharmaceutical healthcare of Ukraine caused by the real political and socio-economic processes. Priority areas of national pharmacy is to create appropriate conditions for improving the quality of treatment and medicines (drugs) in Ukraine. Requirements to ensure the quality of drugs is to create a system of quality management of the entire cycle of circulation of drugs by implementing standards of good practice GLP, GCP, GMP, GDP, GPP. Good Distribution rules and conditions of storage of drugs in wholesale sales (distribution) for participants in the pharmaceutical market. Accession of Ukraine to the Pharmaceutical Inspection PIC / S (Pharmaceutical Inspection Cooperation Scheme) also requires harmonization of Ukrainian legislation to European standards, including the requirements of GDP in 2013

Materials and methods. Study materials as opposed guide to Good Practice distribution of drugs for human EU («Guidelines of 5 November 2013 on Good Distribution Practice of Medicinal Products for human use (2013 / C 343/01)»), which sets out the principles and rules (requirements) to the wholesale sale of drugs in Europe and the new edition of GDP Ukraine 2014. (Guidelines "Drugs. proper practice of distribution. CT-N 42-1.0:2014 Health Ministry " (Ministry of Health of Ukraine of 05.02.2014 № 100), which was designed to update and harmonize in accordance with the regulations of the EU «Guidelines of 7 March 2013 on Good Distribution Practice of Medicinal Products for Human Use (2013 / C 68/01) " . was used in the study and comparative analysis method for organizing and summarizing data of good practice.

Results. Practice proper distribution under license terms of Ukraine - a set of guidelines and rules for the wholesale drugs (procurement, storage, supply or export of drugs, except for drugs supply to the final consumer), which ensures compliance

with the quality at all stages of the trade. Distribution chooses by manufacturer to cooperate one or more suppliers of their products. One feature of Ukrainian pharmaceutical market is the variety of distribution models. Between the Ukrainian pharmaceutical manufacturers and consumers, there are three types of distribution channels: *domestic manufacturers - retailers*, *domestic manufacturer - wholesaler company (affiliate products) / distributor - retailers*, *domestic producer - independent wholesale companies / distributors - retailers*. At the same time, in Europe there are six kinds of distribution models: *manufacturer - distributor - Pharmacy - patient*; *Manufacturer - Distributor - Pharmacy - patient* (DTP (Direct verily Pharmacy)); *manufacturer - distributor - Pharmacy - patient* (DD (Direct Distribution)); *producer - distributor chosen - Pharmacy - patient* (RWA (Resticted Wholesaler Availability)); *producer - selected distributor - hospital pharmacy - patient* (FFS hospital distribution). Foreign companies practically not sell drugs directly through retailers and therefore can not use distribution model *maker - Pharmacy - patient*. Other models are different from distribution model *domestic manufacturers - retailers* on method of supply medicines to pharmacies.

Conclusions Researches have shown that Ukraine should pay attention to and consider introducing models supply of drugs available in the EU, allowing pharmaceutical companies producing ensure compliance with appropriate standards for the storage, delivery, dispensing drugs and export of pharmaceutical products and to develop other services to patients in collaboration with pharmaceutical pharmacy staff.

DIRECTIONS OF IMPROVEMENT IN ACTIVITIES OF FINANCE

DEPARTMENT OF ENTERPRISE

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The aim of the work is to study of the best national and international experience of organizational support of finance departments of companies for improving the organization of financial activities of pharmaceutical companies.

Materials & methods. It was used analytical, statistical and economic-mathematical methods.

Results. Financial resources as an important factor of efficient function of the enterprise play an important role in the management of production, distribution and services. Finance departments have to provide the required amount of financial resources for the processes of production and sales, to determine the direction of their most efficient use, monitor the status of financial discipline in all departments of the company and others. Finance department is an independent division that performs certain functions in system management of enterprise. Financial relations in the company requiring the implementation of certain organizational forms. It has expressed in the formation of a variety of specialized units at the management structure. Exploring the practice of foreign companies (USA, Japan) shows that finance departments of these countries are very reputable and determine the financial policies of firms.

In a market-based economy the role of finance departments significantly has increased. It was established that the activities of such services of pharmaceutical enterprises of Ukraine does not fully meet the requirements of today, they did not have enough qualified financial management, so problems of cash resources, accounts receivable, inventory and so on are current problems.

On the problem of the efficient functioning of finance departments at the company are working scientists, as Yu.V. Petlenko (investigated the effect of factors on the rational organization of the financial management, in particular such as a

feature of industrial activity, the nature and scope of activities, compliance with applicable regulatory and legal acts on organization of the financial management and allocation of duties between employees at different levels); O. Komaha (was developing criteria for evaluating the effectiveness of the financial structures of firms); O. Pryhodko (defined attributes efficiency of financial policy enterprises), V.P. Kodatska (studied the characteristics of financial work of Kharkiv enterprises); O.O. Tereschenko (explored the advantages and disadvantages of different organizational structures of financial services).

Hromovyk B.P., Posylkina O.V., Tolochko V.M., Musienko N.M. have investigated ways of improvement in financial activities of pharmaceutical companies.

Conclusions. It is necessary to determine which functions should perform finance departments of enterprise in the current economic conditions and which units will come of it for the successful formation of the financial structure of the company. It is necessary to develop and approve documents regulating the activities of the service and its subdivisions, including finance department regulations and its subdivisions, the job descriptions of employees of finance department, standards, operating procedures, and so on. The coordination and approval of these documents are removed many issues related to the number of employees, the organization of their jobs, their requirements for training, payroll, etc.

AN ANALYSIS OF MICROECONOMIC LEVEL OF PHARMACEUTICAL INDUSTRY IS FOR OPENING OF PHARMACY

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Main objectives of the national medicinal policy are: availability of medicines, their quality and rational application.

The analysis of literary, statistical data, standard and legal documents showed that for today in Ukraine availability of the population to the main medicines both physical and economic doesn't conform to national requirements.

Therefore the purpose of our researches was:

To carry out the analysis of conditions of a microeconomic level of pharmaceutical branch for opening drugstore.

To implement this goal the following tasks delivery were defined:

- to analyze and generalize data of literature on the basic principles of the organization of medicines provision in microeconomics system;

- to carry out the analysis of license conditions of implementation of the economic activity connected with retail sales of medicines in the territory of Ukraine;

- to carry out a choice of a location of a drugstore and the analysis of possible conditions for goal implementation;

- to carry out questioning of pharmacists in Kharkov for the purpose of definition of expenses articles which future drugstore in accordance to will have license conditions of pharmaceutical activity in Ukraine;

- to carry out the analysis of the calculated main indicators of trade and financial activity of future drugstore in order to forecast the point of profitability.

The objects of research were healthcare institutions of Ukraine in Kharkov which provide the population, necessary medicines and products of medical appointment.

The subject of research was a process of opening of pharmaceutical enterprise in order to improve the availability of providing the qualitative pharmaceutical help for the population.

One of the criteria which influences on the availability of medicines is the number of inhabitants served by one pharmaceutical establishment. An average figures show flat across Ukraine 2193 persons served by one pharmaceutical institution.

Then we continued the calculation of average sales of one pharmaceutical institution during the year which we need for definition of the main indicators of trade and financial activity and definition of a point of profitability became the following stage of our researches. For Ukraine this average value is nearly 1 million 730 thousands UAH a year.

Hi order increase in an indicator of commodity sale turnover of the future drugstore we carried out questioning of customers. In the questionnaire a number of questions which defined factors influencing increase in this indicator were set. The analysis of questioning showed that different factors influences on commodity

turnover of a drugstore: qualification of the personnel, the drugstore location, the range of the drugstore, the open presentation for parapharmaceutical goods, opportunity to get primary medical advice and the help (to measure pressure, level of blood sugar, etc.).

Carrying out questioning of 20 drugstores of Kharkov for the purpose of definition of their primary and monthly articles of expenses was the following stage of our researches. So for one pharmaceutical institution that will work in accordance with general practice on tax accounting with apartment purchase were the expenses 624 thousand 500 UAH. The sum of average monthly expenses on one pharmaceutical institution will make 22 thousand 120 UAH.

The analysis of the profitability was carried out at constant level of trading imposing and the sums of expenses showed that drugstore opening with profitability in 1,3% isn't perspective. Because the net profit will make about 880 UAH, and primary expenses counted by us make earlier 642,5 thousand UAH. It means that primary expenses will be blocked more than in 60 years. With profitability in 5% in 13 years, from 6-8% respectively in 10,5 and 7 years, but the point of an extremum is the best of all with profitability in 13% will come in 3 years.

The following stage of our researches carried out calculations of the same indicators, but for pharmaceutical institutions with the simplified tax system (the 2nd group: to 10 workers with commodity turnover to 1 million UAH). For this group of businessmen average monthly expenses could be from 10 to 22 thousand 900 UAH. In our questioned group they made approximately from 15 thousand to 18 thousand UAH.

The analysis of the calculations of profitability that we have carried out and a profitability point for a pharmaceutical institution which works at a uniform tax showed that the net profit will make nearly 4800 UAH, and primary expenses will decrease to 635 thousand UAH. It means that primary expenses will return in 11 years, and profitability will make 6%-7%.

As a results of research we come to the conclusions:

1 . The analysis of number of pharmaceutical institutions and the population in Ukraine showed that 2160 persons are served by one pharmaceutical institution.

2 . The results of calculations of average sales of one pharmaceutical institution that it makes 1729,1 thousand UAH In Ukraine a year.

3 . The analysis of results of questioning of 20 drugstores of Kharkov showed that average prime expenses counting on one pharmaceutical institution make 624500 UAH. Average monthly expenses counting on one pharmaceutical institution which works in accordance with general tax practice, make 22120 UAH, and on the simplified system from 16 to 18 thousand UAH.

4 . The analysis of the calculations of a point of profitability carried out by us showed that with profitability in 13% the point of an extremum will come in 3 years, and for pharmaceutical institution which works at a uniform tax and income in day doesn't exceed on the average 3300 UAH primary expenses will be blocked in 11 years, and profitability will make 6%-7%.

SECTION № 14

**QUALITY CONTROL IN THE PHARMACEUTICAL AND
HEALTHCARE INDUSTRY**

QUALITY ASSURANCE REVIEW FOR ROSIGLITAZONE

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One of the major health problems is diabetes, with a high percentage of people around the world having this disease and many companies are producing new drugs for the treatment or management of this disease.

Rosiglitazone is an antidiabetic drug in the thiazolidinedione class of drugs. It works as an insulin sensitizer, by binding to the PPAR receptors in fat cells and making the cells more responsive to insulin. It is marketed by the pharmaceutical company GlaxoSmithKline (GSK) as a stand-alone drug or for use in combination with metformin or with glimepiride. First released in 1999, annual sales peaked at approximately \$2.5-billion in 2006; however, following a meta-analysis published in the New England Journal of Medicine in 2007 that linked the drug's use to an increased risk of heart attack, sales plummeted to just \$9.5-million in 2012. The drug's patent expired in 2012.

Despite rosiglitazone's effectiveness at decreasing blood sugar in type 2 diabetes mellitus, its use decreased dramatically as studies showed apparent associations with increased risks of heart attacks and death. Adverse effects alleged to be caused by rosiglitazone were the subject of over 13,000 lawsuits against GSK; as of July 2010, GSK had agreed to settlements on more than 11,500 of these suits.

Some reviewers recommended rosiglitazone be taken off the market, but an FDA panel disagreed, and it remains available in the U.S. From November 2011 until November 2013, the federal government did not allow Avandia to be sold without a prescription from a certified doctor; moreover, patients were required to be informed of the risks associated with its use, and the drug had to be purchased by mail order through specified pharmacies. In November 2013, the FDA lifted its earlier restrictions on rosiglitazone after reviewing the results of the RECORD clinical trial (a six-year, randomized control trial), which failed to show any of the previously-suggested cardiac risks associated with the drug.

In Europe, the European Medicines Agency (EMA) recommended in September 2010 that the drug be suspended from the European market. However, patients currently taking rosiglitazone are advised to discuss alternative options during their next physician appointment. In New Zealand, rosiglitazone was withdrawn from the market in April 2011. It was banned in India in 2010.

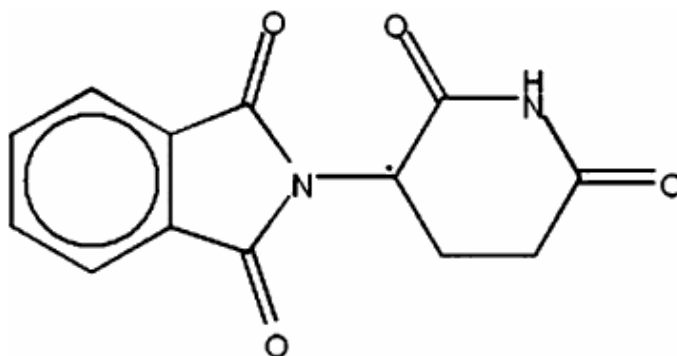
QUALITY ASSURANCE REVIEW FOR THALIDOMIDE

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Quality assurance in pharmacy is one of the major tasks nowadays. Health of the population becomes very important and directly depends on the drugs we consume. Thalidomide was a widely used drug in the late 1950s and early 1960s for the treatment of nausea in pregnant women. It became apparent in the 1960s that thalidomide treatment resulted in severe birth defects in thousands of children. Though the use of thalidomide was banned in most countries at that time, thalidomide proved to be a useful treatment for leprosy and later, multiple myeloma. In rural areas of the world that lack extensive medical surveillance initiatives, thalidomide treatment of pregnant women with leprosy has continued to cause malformations. Research on thalidomide mechanisms of action is leading to a better understanding of molecular targets. With an improved understanding of these molecular targets, safer drugs may be designed.



Note: • = asymmetric carbon atom

The thalidomide tragedy marked a turning point in toxicity testing, as it prompted United States and international regulatory agencies to develop systematic toxicity testing protocols; the use of thalidomide as a tool in developmental biology led to important discoveries in the biochemical pathways of limb development. In celebration of the Society of Toxicology's 50th Anniversary, which coincides with the 50th anniversary of the withdrawal of thalidomide from the market, it is appropriate to revisit the lessons learned from the thalidomide tragedy of the 1960s.

QUALITY ASSURANCE REVIEW FOR DOMPERIDONE

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Domperidone (trade names Motilium, Motillium, Motinorm Costi, Nomit and Molax) is a peripheral, specific blocker of dopamine receptors.

The uses or indications of domperidone vary between nations. For instance, in Italy it is used in the treatment of gastroesophageal reflux disease and in Canada, the drug is indicated in upper gastrointestinal motility disorders and to prevent gastrointestinal symptoms associated with the use of dopamine agonist antiparkinsonian agents. In some nations, including Australia domperidone is as a therapy for mothers who are having difficulty breastfeeding with uncertain result. In the United States, domperidone is not approved for this or any other use. In response to reports that women may be using an unapproved drug, domperidone, to increase milk production (lactation), the Food and Drug Administration (FDA) is warning breastfeeding women not to use this product because of safety concerns.

Moreover, according to the publication's hypothesis, the number of sudden deaths connected to domperidone could have been between 25 and 120 in 2012 in France. In 2011, the risk of sudden death was flagged up by the French Medicines Agency (Agence Nationale de Sécurité du Médicament et des Produits de Santé, ANSM) and the primary firm who market the product in France. The ANSM also warned against the unauthorised use of Motilium to ease breastfeeding. According to the periodical, which used medical insurance data, approximately seven per cent of adults, which translates to about three million people, received a prescription for the medicine in France in 2012. It is estimated that 23 million people in France received at least one prescription for domperidone between 2003 and 2013. In March 2013, a review of all domperidone-containing medicines was launched by the EMA at the request of Belgium. The Belgian Medicines Agency raised concerns over the safety of the medicine for patients with heart problems. Domperidone-containing medicines could be purchased over-the-counter in Belgium until the end of 2013, when a new law came into action, making it available only with a prescription. The EMA has started a full review on the effects of domperidone, evaluating its benefit-to-risk ratio. The conclusion to the review is expected to be published in March of this year.

DESIGNING OF MODULAR-COMPETITIVE MODEL FOR SPECIALIST IN ASSURANCE AND QUALITY MANAGEMENT FOR THE PHARMACEUTICAL INDUSTRY

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The problem of acute shortage of personnel, competent in matters of quality assurance (QA) and quality management (QM) for industrial pharmaceutical sector, proved us by analyzing the needs of the modern job market, based on data of monitoring the situation in Ukrainian industrial pharmaceutical companies (IPC), which discussed in several previous publications.

Order to determine functional responsibilities of specialist for QA and QM in pharmacy we analyzed the job regulations and qualifying characteristics of employees of departments of assurance and management quality in leading Ukrainian IPC. To form the list of key competencies analyzed national and international experience of training for QA and QM at the European Organization for Quality and the Ukrainian Association for Quality, and considered the spectrum of basic of knowledge and skills of professionals in the example of Germany and the United States as leaders in developing relevant personnel training. Based on an analysis of the main reasons for lack of effectiveness of quality management systems (QMS) in IPC (Pharmaceutical Quality Systems) we had formulated a set of typical competencies and disciplines for specialist QA and QM in pharmacy, proposed for consideration the leadership of a number of leading national IPC in the form of questionnaires. Based on obtained data were ranked disciplines of professional and practical training and professional competencies.

Results of evaluation the degree of significance of competence demonstrates that clearly necessary for future specialists is competence «planning participation in internal audits (self-inspections)», «working with process model PSQ», «working with documentation PSQ», «planning process indexes of effectiveness PSQ», «management of non-conformities and development of corrective and preventive actions». Most important for the formation of special-professional skills disciplines were identified «Audits QMS», «Regulatory support», «Good manufacturing practice (GMP)», «Good distribution practices (GDP)», «Statistical process management», «The approaches, methods and means QM», «Standardization and certification of pharmacy products», «QM of production processes», «Designing of QMS».

Based on the questionnaire we will develop standards for higher education for the specialties «Quality Assurance in Pharmacy» (bachelor) and «Quality Management in Pharmacy» (MSc).

COMPARATIVE ANALYSIS OF PROCESS VALIDATION BY THE EXAMPLE OF PHARMACEUTICAL COMPANIES AND ORGANIZATIONS OF FOOD INDUSTRY

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The aim of this paper is a comparative analysis of the validation process in different industries. Objects of research: the pharmaceutical and food industries. The subject is the validation process in an industrial company. When consideration of this issue were used analytical methods. All results obtained from analysis of the regulatory farmework of these industries and some enterprise documents.

The shot results present in the summary table below:

Pharmaceutical Company	Food business
Standards used by the companies are:	
1. GMP (principal for the pharmaceutical enterprise); 2. ISO 9001	1. ISO 22000 (HACCP) (principal for the food enterprise); 2. ISO 9001.
The presence of a special department	
Usually there is a special department of validation	No special department and performs staff work part-time with the main responsibilities
The need for validation process	
The validation activities are regulatory requirement	Standards established by the company does not necessarily require validation of processes
Stages of the process of validation in pharmaceutical and food industries do not different	
Documentation, which is made during the validation in pharmaceutical and food industry is not different, but the look of each document is not regulated and determined by the management of each company	

Significant difference during the validation of the pharmaceutical enterprise standards are regulations for its implementation, in contrast to the enterprises of the food products.

However, to ensure the products quality, the strategic goal of the food industry is the development of detailed implementation methods of the validation process, the development of the necessary documentation and ensuring proper control over the execution of validation activities. For this can be successfully applied the experience of many Ukrainian pharmaceutical companies.

REALIZATION OF PROCESS APPROACH PRINCIPLE DURING THE IMPLEMENTATION OF QUALITY MANAGEMENT SYSTEM AT THE NATIONAL UNIVERSITY OF PHARMACY

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As education is one of the main factors in the economic and social development of a country, quality in the area of higher education is a need of increasing significance. The present management systems of universities still utilize the traditional principles and are deficient of any element of modern management. The management of universities is being based on principles of “common law” that in the most cases don’t correlate with actual requirements of dynamically developed society. In many cases there are not clearly defined responsibilities and authorities. The management systems are without desired level of transparency and formalization. Currently the universities are situated at competitive environment. It is the principal reason why they have to identify as the organizations providing the services that satisfy their customers. To lead and operate an organization successfully, it is necessary to manage it in a systematic and visible manner.

The implementation of quality management system (QMS), as inherent part of university management, is the way how to reach this aim. That’s why The National University of Pharmacy decided to implement QMS into university management. The decision was supported by existence of ISO 9001 registration. The ISO 9001 certificate is outstanding supporting material. It is the evidence that proclaims the university is properly managed, the needs of their customers are identified and the environment to satisfy them is established. One of the important parts in QMS is the implementation of process approach (PA). PA is a way of organizing and managing, helps to achieve planned goals and objectives, allows the organization to focus on improving process effectiveness and efficiency, facilitates consistent performance and contributes to lower costs. The main steps of implementation of PA are:

- Determine processes needed;
- Determine sequence and interaction of processes;
- Determine criteria needed to keep operation and control of process;
- Ensure the availability of resources and information needed to support operation and monitoring of processes;
- Implement action to achieve planned results and continual improvement.

So we identified all processes and described them. There are 3 main processes, 6 management processes and 11 auxiliary processes have been defined (Table 1). Thereafter were determined interactions between processes with help of graphic and text tools. This model would be the basis for the regulation of all QMS processes.

Table 1

Offered Processes of QMS of the University

Main processes	Management processes	Auxiliary processes
Educational activity	Planning of QMS	Interactions with suppliers
Scientific and Research	Development and designing of services	Personnel maintenance
Socio-cultural activity	Resource management	Management of the infrastructure and work environment
	Analysis of QMS by top management	Publishing activity
	Marketing research	IT, library and information provision
	Public awareness and interactions with consumers	Logistical support
		Financial provision
		International activity
		Documentation management
		Educational and methodological support
		Providing safety and labor protection

Therefore we suggest making their description using such documents:

- Quality manual (includes the scope of the QMS, including details of, and justification for, any exclusions, the documented procedures established for the QMS and a description of the interaction between the QMS processes);
- Documented procedures for carrying out processes (describe the conditions and the execution order of each process according to the PDCA Cycle);
- Standard Operating Procedures (SOP's), duty regulations, regulations for divisions (describe some operations or activities under the QMS processes);
- Records (protocols, journals and other instruments of registration).

So, an effective implementation of the PA would start by laying out how we select, manage and improve the most critical processes that impact our customers and internal management objectives. This would include assigning responsibility to certain individuals or teams to take charge of our key processes. Teams work well when processes cut across the organizational structure. Then, these process owners will monitor and improve these processes on an ongoing basis taking full responsibility for their performance.

SECTION № 15

INFORMATION TECHNOLOGIES IN PHARMACY AND MEDICINE

SOLUTION OF THE EQUATION AND CHARTING IN MATHEMATICAL PACKAGE SCILAB

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There are many programs that can calculate various mathematical operations. One of these programs is Scilab .This package of applied mathematics program, representing a powerful open environment for engineering and scientific calculations. Scilab contains a variety of mathematical functions.The system is available for solutions of equationsand graph plotting. Scilab has distinctive features that give their advantages. It's free and small size.

This paper discusses various methods for solving equations and systems, as well as the creation and editing of graphs of functions.The methods for finding the roots of polynomials of different degrees, methods for solving linear and nonlinear equations, transcendental equations, graphical solution of various equations.

Besides the solution of equations considered methods for solving systems of linear algebraic equations.Discusses how making: Cramer method, Gauss, linsolve, matrix. The theorem of existence and uniqueness of solutions of systems of linear algebraic equations used. The system is available a variety of tools to build and edit: 2D and 3D graphs. Different methods of constructing and editing two-dimensional and three-dimensional graphs of functions.

As a result, we can conclude that Scilab provides great opportunities for creating and editing graphics and surfaces, solving linear and nonlinear equations and systems. Although Scilab is a free product compared to Matcad, Matlab and Matematika, its computational capabilities quite correspond to the potential of computer systems professional level.

ARTIFICIAL GROWING ORGANS IN THE HUMAN BODY AND OUTSIDE THE BODY

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Problem of growing of organs is actual now because many diseases, including life-threatening person associated with in the activity of a particular organ. Not in all cases, these disorders can be corrected by conventional surgical or pharmacological effects. There are a number of alternative ways of how to restore the function of patients in case of serious injury: stimulation of regenerative processes in the body, replenishing organ functions using devices not of biological origin, the use of donor organs, growing bodies.

In this paper we reviewed and analyzed the latest methods and technologies of artificial cultivation from more than 40 online sources. Also are shown the results obtained using bioinformatics technologies developed by Petrov A.N. Organs may be grown artificially in the human body, and outside the body. In some cases it is possible to grow your body cells of the person to whom he is going to be implanted. A recently developed technique PKI (induced pluripotent stem cells) allows reprogramming adult stem cells so that they could get from any body.

A number of methods has been developed for growing biological organs, for example, by means of special devices that operate on the principle of 3D printer. Instead of ink cartridges are filled with suspensions of various types of stem cells. The computer calculates the structure of the body and sets the print mode.

A review of Internet sources shows that there are already significant advances in the use of cultivation for the treatment of not only simple tissues such as skin and bone, but also quite complex organs such as the bladder, or trachea. Technology growing more complex organs currently experimented on animals. Scientists predict the development and implementation of cultivation techniques of complex organs - a matter of time and it is likely that in the future will be perfected technique so that the cultivation of complex organs will be widely used in medicine, replacing the most common method now transplantation from donors.

METHODS FOR INVESTIGATING THE PROPERTIES OF WATER

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Water is a chemical compound that performs an essential function in the life of all living things. Although a single molecular formula, it is characterized by different properties. There are various methods of investigation of the water properties: micro photographic, photometric, gravimetric, spectrometry, a method for studying the surface tension, the water influence on the micro flora, the study of the permittivity and others. For water treatment and disinfection various methods of physical effects on water systems are applied. Isotopic composition, magnetic influence, effect of elektroplasma charges, ultrasonic cavitation.

Well known that water has a memory of different energy impacts. Information properties of water have been taken into account, which are no less important than its molecular composition. In this paper we consider various methods to control the information properties of water. Spectral method (nuclear magnetic resonance - NMR), proton magnetic resonance (PMR), spectrophotometric method, microphotometric method, the gas discharge visualization method, electrically-magnetic properties controlling method of water. With these methods have been investigated various properties of water. Different qualities of water demonstrated its unique properties and showed different characteristics.

These studies demonstrated the need to examine not only the chemical and physical but also informational properties of water. Polluted water has disrupted structure, as if randomly generated structure. Recent advances in the study of information properties of water is that researchers have shown that water respond to various influences, and is indeed a living system.

THE STUDY OF DYNAMIC MODEL OF THE COMPETITION BETWEEN TWO ENTERPRISES

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A lot of literary works are dedicated to the mathematical modeling of the competition processes. For our project we have chosen the model of population's interaction by V. Volterra which was used to develop the dynamic model of competition in the work [1].

As for example consider two companies, which produce the interchangeable commodities of the same quality, and which are at the same market sphere. In this case, the single price is set for the whole market, which is determined by the balance of gross demand and supply. Therefore, within a model, competitive battle is conducted with the help of marketing methods: the opponents can influence each other only by changing the parameters of their manufacturing.

The changing of the vending capacity of the competitive companies, within the time, is presented by the nonlinear system of differential equations:

$$\begin{aligned}\frac{dq_1(t)}{dt} &= a_1 q_1(t) [N - (q_1(t) + q_2(t))] - b_1 q_1(t) q_2(t); \\ \frac{dq_2(t)}{dt} &= a_2 q_2(t) [N - (q_1(t) + q_2(t))] - b_2 q_2(t) q_1(t),\end{aligned}$$

within initial conditions: $q_1(0) = q_{01}$, $q_2(0) = q_{02}$. The vending capacity of the first and the second company is denoted as: $q_1(t)$, $q_2(t)$, N - the capacity of the marketing pending segment, a_1 , a_2 , b_1 , b_2 - positive coefficients, which determine the degree of influence of various factors on changing the market capacity of the first and the second companies.

The numerical solution of this problem was obtained with the help of Scilab system. The final dependencies of the changes at the market demonstrate the mortification of one company, depending on the initial parameters of the system. The productive analysis of the differential equation system shows, that the stationary condition, when $b_1, b_2 > 0$ and the two companies' vending is more than zero, and is unstable.

Conclusion. The given model reflects the real tendencies of the development of this situation, except for long-lasting co-existence of the companies.

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DEVELOPMENT OF THE PROFILE-FORMING BASE STANDARTS FOR THE COMPLEX ASSESMENT QUALITY AND SAFETY OF THE MANUFACTURING EXECUTION SYSTEM (MES) OF PHARMACEUTICAL ENTERPRISE

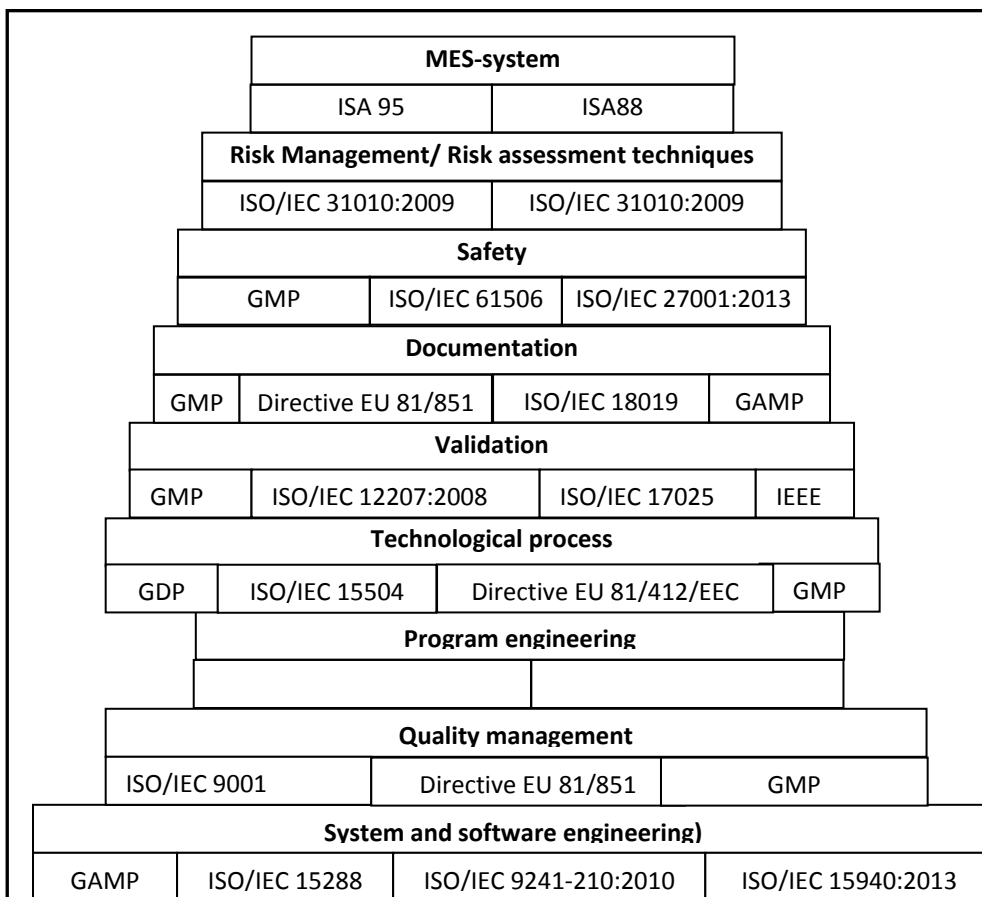
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Using MES-systems becomes increasingly hot topic in pharmaceutical manufacturing environments. This is due primarily to the fact that quality assurance of medical products and drugs is critical from the standpoint of patients safety.

For the creation safety model of the MES-system of pharmaceutical enterprise is necessary to conduct profiling (analysis) normative base. Profile-forming base should be include the normative documents and standards, which affect the technological process of the manufacturing drugs (pic.1).



Pic.1. The profile-forming base

A represented profile-forming base standard allows a comprehensive assessment of MES-system of pharmaceutical enterprise. This is will enable build the model of safety and quality of MES-system of pharmaceutical enterprise and select the standards, which link with usability.

REALIZATION OF SIMPLE MATHEMATICAL MODEL OF INFECTIOUS DISEASE WITH THE HELP OF SPREADSHEETS

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Aspects of an organism's defense against viral and bacterial infections and the reaction of immune system to infection are the main problems in practical immunology. In addition to anti-viral and antibacterial defense, the immune system plays a decisive role in tissue incompatibility reactions, antitumor immunity, autoimmune diseases, and allergies.

Understanding of regularities in immune response provides the researchers and clinicians new powerful tools for the stimulation of the immune system in order to increase its efficiency in the struggle against antigen invasion. In this connection the development of mathematical models of immune response to an antigen irritant seems to be the only right tactics to understand these regularities.

The simple mathematical model of infectious disease was constructed on the basis of an equilibrium relation for each component that participates in an immune response. There are three main components: antigen, antibody, and plasma cell that produced antibodies. During disease the degree of damage of an organ subjected to antigen attack is of great significance, since it leads to lowering of the immune system's activity. This phenomenon must be taken into account in mathematical models.

The basic acting factors of an infectious disease are as follows: 1) concentration of pathogenic multiplying antigens, $V(t)$; 2) concentration of antibodies, $F(t)$; 3) concentration of plasma cells, $C(t)$; 4) relative characteristic of affected organ, $m(t)$. Thus, the simple mathematical model of infectious disease is represented as the following system of nonlinear differential equations:

$$\left\{ \begin{array}{l} \frac{dV}{dt} = (\beta - \gamma F)V \\ \frac{dC}{dt} = \xi(m)\alpha V(t - \tau)F(t - \tau) - \mu_c(C - C^*) \\ \frac{dF}{dt} = \rho C - (\mu_f + \eta\gamma V)F \\ \frac{dm}{dt} = \sigma V - \mu_m m \end{array} \right.$$

This system of equations describes the dynamics of pathologic infection development during immune response.

Realization of simple mathematical model of infectious disease with the help of spreadsheets allows to compute the main parameters of disease and to represent graphically the different forms of disease (subclinical, chronic or acute forms).

ANALYSIS OF VARIABLE OF HEARTY RHYTHM

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The hearth system executes an important role in an organism, which is necessary for normal functioning. Diagnostics of functioning of the system is one of above all places in medicine.

One of new methods of study of the state of the hearth is mathematical analysis of cardiointervalgram. I studies the change of rhythm of heart as reaction of organism on external influence. This method is characterized by simplicity of registration of signals, which can be cardiograms or other signals, caused by operation of heart are signals of registration of pulse, graphic arts of change of pressure of blood in time.

The traditionally measured middle frequency of result of numerous influences on the vehicle of circulation of blood. The different states of organism can correspond to the same frequency of pulse. Research of variations of rhythm can give necessary information the explored object. The dynamics of indexes of in many cases passes ahead the changes of laboratory information. In the sequence of intervals there is information about processes, not only in a heart but also in the different links of the control system of organism: nervous interlacements, ductless glands, nerve-centres of brain.

Measuring of period of must be conducted during the interval of time from a few minutes to a few days. The slow changes of rhythm show up at such time of analysis – with a period from a few seconds to a few days.

In medicine methods are developed also the diagnosticians, based on the analysis of spectrum of electrocardiograms, electroencephalograms and other signals at the inspection of man.

By these methods the analysis of two ten-minutes rows of information was conducted about the rhythm of man, when an organism was at peace and at after loading. On the basis of the measured some generalized parameters were calculated - frequency of reductions, coefficient of variation, level, index of tension, is built and analysed histogram of distributing of values of periods of pulse. On the basis of spectral analysis, distributing of spectral closeness of signals is found between, low and very low high-frequencies and the such generalized parameters of the state of organism: index of centralization, index of activating of nerve-centres characterizing the state of organism.

SECTION № 16

COMMODITY SCIENCE

THE PRESENT IN MEDICAL PRODUCTS BARCODING

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The main feature of the production and distribution of medicinal products in the pharmaceutical industry is their extremely wide range. Therefore, it is difficult to imagine organization of a modern pharmacy activity without bar-coding technology. First steps to develop barcode in the form they look now have been made in 1948. International non-profit and non-governmental organization - the EAN Association, established in 1977 is engaged in assigning of bar codes.

Coding of goods is assignment of symbols in the form of digital, alphanumeric and bar code for products with identification purposes.

Classification of goods - ordered on the basis of certain characteristics of the goods distribution by grade and smaller subsections, independent of one another, or which are in a logical order and subordination.

Currently, there are two main ways of encoding information in the bar code. Linear bar codes are probably the most famous of all the automatic identification technologies. Currently EAN / UPC barcodes underlie global diversified communications system. Historically, in trade, including the distribution of medicinal products, the most widely used code is EAN / UPC.

New growing trend in the world of bar codes is two-dimensional codes. Two-dimensional are called symbologies designed to encode large amounts of information. Decoding of the code is performed in two dimensions (horizontal and vertical).

In Ukraine, barcoding of goods by subjects of entrepreneurial activity is performed on the basis of the CMU Decree № 574 (1996), the Order of ME and VEIU № 255 from 20.08.2002. (with subsequent amendments). According to the Decree of Cabinet of Ministers № 574 items are marked with EAN barcode. Since 2007 in Ukraine goods barcoding is done by the Association «GS1 - Ukraine", which is the rights holder of reorganized Article Numbering Association of Ukraine (EAN - Ukraine).

Today, a common thing for a pharmacist at drug dispensing is to bring its package to the barcode scanner and to get information about the name, manufacturer, quantity of goods, which is available at the moment in the pharmacy and the corresponding price on the terminal screen, and also gives the possibility to obtain information about the volume of sales of goods, for the current and specified period of time. It is this "popularity" that calls for the promotion of barcoding in pharmacy.

STABILITY STUDIES OF DENTAL GEL "ROTRYN-DENT" IN ALUMINIUM TUBES

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At present there is a problem of expanding the range and choice of packaging that meets the current requirements of the pharmaceutical market for storage of soft medicinal forms. Therefore, topical is to provide proper storage of a medicinal form with minimum costs when choosing an inexpensive and safe packaging.

Aluminum tube is an economic package, which is most commonly used for drugs in dental gel form. All internal volume of the tube is filled with drug at packaging. In fact, the volume of the tube is equal to the volume of the packed product and it ensures tightness during prolonged storage.

Aluminum tubes are resistant to fats, moisture resistant, serve as barrier for oxygen and UV radiation. Ease in applying for a consumer is that opening a tube, he uses as much gel as he needs. The rest of the product remains protected inside the tube without contact with air. Another property that significantly affects the quality of the gel is the absence of suction effect after tube compression.

As it is known in the aluminum tube there is no so-called "shape memory", i.e. after compression the tube its walls deform and do not return to the original shape. While in plastic laminate tube it happens just the opposite. At the same time plastic tube sucks back, first air, which leads to the oxidation of content, and secondly squeezed and not completely used partly contaminated part of drug. It may be concluded that the most useful properties of aluminum tubes remain hidden from end users.

Choosing an aluminum tube for a given dosage form among other types of containers, we have noticed a number of benefits for consumers, namely that an aluminum tube does not affect the quality of the developed dental gel, it is easy to use and has lightproof properties and absence of absorbing effect.

So as containers for developed dental drug we have used, aluminum tubes with metal membrane with a long nose, bushonnes and inner varnish coating of type Paclac 11-15-000.

The study of the stability of the gel was performed on five series for over 30 months by analyzing studied samples every 6 months by the following parameters:

organoleptic and physical-chemical properties (appearance, color, odor, pH, thermal and colloidal stability), average weight of the packaging contents. Methods of selected indicators study and their characteristics are governed by SPU and other regulations.

Also performed identification and quantification of active substances (main components of phytosolution "Rotokan" and triclosan) and preservative by HPLC. Shelf-life of the gel was determined at two temperatures, namely (8-15) °C (cool place) and at (15-25) °C (room temperature).

The results of the pilot stability study of series of dental gel under different storage conditions for the above indicators were satisfactory, namely gel had homogeneous mass without impurities, yellowish- brown in color with a pleasant taste and odor that met the standard of developed gel, pH was within 5,00-7,00.

To determine the behavior of the gel at temperature and storage conditions deviations studied colloidal and thermal stability. Studies have confirmed that colloidal and thermal stability of the dental gel for two years remained unchanged.

Identification of active substances and excipients, which are part of the gel, has been confirmed during controlling shelf life. It was established that during the expected shelf life the quantitative content of the active substances and preservative in the gel remained within acceptable limits.

The mass of the contents of the tube was also stable during the observation period and amounted to $30,2 \pm 0,5$, ie gel did not dry out.

In developing dental gel additionally studied the structural and mechanical properties. According to the research were plotted full rheograms of flow of the developed gel samples (6, 12, 18, 24, 27 months) and concluded that the gel in the test interval did not change its rheological properties and was stable.

Also carried out tests of the dental gel on the microbiological purity by SPU 1 ed. (Section 2.6.12, 2, 6, 13) by the following criteria: absence of bacteria family Enterobacteriaceae, *P. aeruginosa*, *S.aureus* in 1 g of the drug, the total number of viable nonpathogenic microorganisms (not > 100 aerobic bacteria and fungi in total). The results have shown that the total number of bacteria in 1 g of the drug did not exceed 15, fungi 20.

Proceeding from this it has been found that concentration of preservative taken had provided microbiological purity of dental gel during storage at room temperature. The results of the drug stability study of the other four series studied were identical.

STUDY OF BREASTFEEDING PRODUCTS RANGE

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Nowadays, unfortunately, artificial feeding significantly prevails over natural. Statistics show that in the third month after birth only every third woman continues to breastfeed. They face challenges that seem insurmountable (lack of breast milk or, on the contrary, its stagnation, cracked nipples) and refuse breastfeeding in favor of artificial mixtures. However, modern feeding accessories allow solving these problems and help women to continue breast feeding. Among these accessories there are breast pumps (devices for expressing breast milk).

The aim of this work was to investigate the range of products such as breast pumps, their safety and harmlessness.

All manufacturing companies, have two main types - an electrical, working from the network or battery (more popular) and a mechanical, which can be actuated by force of arms or legs. They have their own peculiarities and are made of safe materials: polypropylene or polyethersulfone, which are characteristic of harmlessness and inability to react chemically with breast milk. But the main feature is the absence in the composition of bisphenol A (a chemical compound, used in production of consumer goods of polycarbonate), which is known for its ability to cumulate and carcinogenic effect on the body. Polycarbonate plastic is a colorless, shatterproof material, which is often contained in water bottles, food containers, toys, containers for breast milk produced by some companies.

These products on the market of Ukraine meet international standards (ISO).

Thus, when a woman is faced with certain problems that lead her to purchase a breast pump, the first thing she decides for herself is the use of what kind will be more comfortable for her. Indeed, because of circumstances, not all women can use both hands to milk, or simply do not have enough physical strength. Next, a woman's choice falls on less important points, such as: accessories (depending on the company-manufacturer there can be pads for milk collecting, nipple conditioners, silicone nipple protectors, sterile bags for milk collection, insulating bags, and additional containers for milk), the possibility of complete disassembly and the ability to be sterilized, bottles adaptation of other vendors, the color of the product. If a breast pump is electric, important aspects are noiselessness, the ability to work on the battery and number of regulated speeds (intensity). Also very important in medical technology is aesthetics of design. Products must be not only functional, but also attractive in appearance. Because in the design of a product appearance plays one of leading roles.

ANALYSIS OF RANGE OF CHILDREN'S PRODUCTS IN THE FORM OF SOOTHER IN THE PHARMACEUTICAL MARKET

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In the first half of the XX century, when special attention has been paid to neatness and good manners soothers have been treated inappropriately, as both unhygienic and unpleasant habit. But in the last few years the attitude to soothers has become favorable again, as they help at delayed gases and prevent sucking fingers.

It was found that newborns who were given soothers subsequently rarely suck fingers. On the other hand, many children are accustomed to soothers, still need it till 1-2 years, and sometimes - even up to 3 years.

Ancient soothers were a piece of animal skin. Pacifier appeared in modern form around 1900, when it first was patented in the U.S. as a "baby comforter".

The range of children's soothers currently has increased significantly. For example, pacifier - a soother without holes attached to a plastic disc that is not allowing a child to involve the entire pacifier in her mouth.

Currently, there are many new baby soothers: pacifiers of firm Chicco (soft natural pacifiers in the form of cherry, anatomic shape, fluorescent, "drop" soother, orthodontic, etc.) Avent firm pacifiers (different soothers for bottles, conventional pacifiers, orthodontic, breathing pacifiers, etc.) Mustachifier Baby Pacifier company products (pacifiers with a mustache, in the shape of the teeth, balls) pacifiers with thermometer, soother with a variable flow and others. Today in the market are also represented new teats with antivacuum system which main element is a valve. This device, first, reduces the amount of air swallowing during sucking, significantly reducing the frequency of regurgitation, and secondly, prevents sticking of teat, allowing the baby not come off the bottle during feeding.

According to the State register of medicines and medical devices there are 27 items of soothers, of which 7 % are of domestic production and 93 % are imported.

In Ukraine only one company is engaged in the production of soothers - "Kyivguma."

We have carried out research of foreign manufacturers. It has been found that 15 foreign companies produce this type of product. Thus, according to our data, we can conclude that (according to the register data) baby pacifiers are most often imported to Ukraine from Germany, Poland, Thailand, China.

ANALYSIS OF PHARMACISTS' ERRORS AND MAIN WAYS TO PREVENT THEM

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Problems related to medications are common in all countries of the world including Ukraine, and they are responsible for significant morbidity, mortality, side effects and cost. True incidences are unknown and difficult to obtain for many reasons, ranging from poor reporting, differences in definitions of what constitutes a medication error, lack of awareness of reporting techniques, lack of time, fear of litigation, inability to determine causality, reluctance to admit error, cost etc. For example, even in advanced countries (e.g. United States) estimates for all types of medication errors (including such variants as missed dose, wrong dosage, wrong medication, wrong time, wrong route, etc.) range from 1.5 to 35%.

The purpose of this study was to record prospectively the frequency of medication order errors in Ukrainian pharmacies with the objective of assessing the impact of pharmacist intervention in preventing potential harm.

Errors due to look-alike or sound-alike medication names are most common in pharmacies and hospitals, and are responsible for thousands of drug diseases or even deaths. Up to 25% of all medication errors are attributed to name confusion, and 33% to packaging and/or labeling confusion. Thousands of medication name pairs have been confused based on similar appearances or sounds when written or spoken, or have been identified as having the potential for confusion. Systems and recommendations have been developed that may reduce the occurrence of such errors.

It has been proposed that INNs should be used to reduce errors due to sound-alike, look-alike proprietary names as well as to avoid duplicate prescriptions due to multiple proprietary names for the same active drug. There are multiple case reports in the literature of patients being admitted to the hospital for side effects resulting from overdoses caused by taking two or more prescriptions with the same active ingredient but different brand names. However, the opposite has also been proposed – that trade names be used due to similar-sounding generic names, particularly in certain drug classes. For example, the majority of the cephalosporin antibiotics have generic names that look and sound very similar, but often have very different proprietary names.

This study estimates the reasons for medication errors. However, proper graphic design of drug packages and marking is the best way to prevent them.

COMMODITY ASPECTS OF ADHESIVE PLASTERS RANGE RESEARCH

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At present, it is becoming important to expand the range of medical devices. The aim of our research is to review the current market of patches, and to identify new types and their manufacturers that provide basic range of pharmacies and medical institutions.

Plaster (from the Greek. Émplastron - ointment, patch, from emplásso - obscure, cover with) is a dosage form in the form of plastic mass that has the ability to soften at body temperature and stick to the skin, or in the same mass on a flat carrier, designed for external use only.

By appointment distinguish patches: to protect the skin from external stimuli, for holding bandages, plasters, having a specific therapeutic effect (eg, callus patch), lead (to treat boils, carbuncles), bactericidal (used in the festering wounds), pepper (at neuritis, neuralgia, etc.), skin adhesives and varnishes that form a flexible film after evaporation (colodium, cleolum glue BF-6, etc.).

In recent years, manufacturers of plasters are increasingly surprising with innovations. For example: the patch for skin care helps to reduce the manifestations of aging (anti-wrinkle patch), anti-cellulite, anti-aging collagen patch that helps to get rid of wrinkles on face, contraceptive, patches impregnated with special drugs that eliminate diarrhea causing poisons through the skin, reducing the number of epilepsy attacks and improving mood and also painlessly administering one or more medicines.

In Ukraine, the following companies are involved in manufacture of patches: Private Enterprise "Edel" "English- Ukrainian company "Sarepta - Mediplast»» LLC, Ningbo Chinmed Technology Co., Ltd. for «Styroloptpharmtorh", PJSC "Gemoplast."

The largest producer of adhesives in Ukraine is JSC "English- Ukrainian company "Sarepta - Mediplast."

In order to provide a wider range in the State Register of Ukraine are registered products of 12 foreign companies. As can be seen from the list of patches suppliers-companies in our country there is a need to improve their research in new types of products, and learn from foreign producers on the range and variety of methods to create them.

ACTUAL PROBLEMS AND PERSPECTIVE DIRECTIONS OF NUTRITIONAL PRODUCTS FOR BURN PATIENTS IN UKRAINE

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The aim of the research is to analyze actual problems and perspective directions of improvement of the assortment of products of nutritional support for burn patients in Ukraine.

The materials and methods used in this research are marketing, the analysis of secondary information, interview.

Every year in Ukraine thousands of people suffer from burns. Burned patients have different nutritional needs initiated to avoid hypermetabolism. Due to metabolic stress immediately after burn injuries, patients are at high risk for weight loss and nutritional deficits during the initial stages of treatment. They require a diet high in protein, calories, fluids, vitamin B, C and zinc in order to return to normal weight and restore damaged tissues. The increased protein, energy and micronutrient demands need to be met in hospital and sometime after. Many people can have their nutritional support at home.

The market of nutrition support is shared among of the top players accounting for 84 % of the market was estimated and presented for the following countries: USA-33%, Europe-33%, Japan-18%.

The problem for Ukrainian consumers is the high price of products nutrition support for burn patients. The assortment of Ukrainian products nutrition support for burn patients is absent. Consumer demand for specialized nutrition increases in many countries around the world and in Ukraine

Therefore, it is appropriate to extend the assortment of products nutritional support for people with burns by creating a balanced chemical composition of dry mixes. There are several formulas for determining the nutritional needs for burn patients. The criteria of structure optimization of dry mixes: protein 20-25%; carbohydrates 40-50%; fat less than 30-35%; certain recommendations for minerals such as copper, selenium, zinc, vitamins A, C, E, and the B group vitamins, L-glutamine, arginine.

The major factors impacting the growth of this market include increasing incidences of burn and affectivity of using mixes. The products may be prepared in dry form which may be subsequently mixed with water or liquid, ready to use. Thus, the creation of balanced foods for people with hypermetabolism is a perspective direction for expanding assortment of nutritional support in Ukraine.

STUDY OF MODERN RANGE OF BANDAGES FOR PREGNANT WOMEN

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Using a bandage during pregnancy and after it has not been paid as much attention as now. Currently, a large number of expectant mothers prefer an active lifestyle and a lot of time outdoors which is a great stress on the body, so in most cases there is need for bandages.

The aim of this work was to investigate the range of contemporary bandages for pregnant women in the pharmaceutical market of Ukraine and identify the leading producing countries.

Bandages for pregnant women - medical products which provide support for abdomen, and the correct position of the fetus in the uterus they prevent premature dropping of the fetus. Modern bandages are aimed at avoiding many unwanted manifestations during pregnancy: a feeling of physical fatigue, back pain, heaviness of the whole body, etc.

It was found that by far the pharmaceutical market of Ukraine has a wide range of bandages for pregnant women. They have different characteristics and properties. Most popular in Ukraine are bandages of Baltic, Italian and Russian manufacturers, but leading in quality are Germany and England. Their bandages are distinguished by balanced combination of medical relevance, functionality and aesthetics, which is very important for pregnant women. They use a variety of bandages color gamma - white, flesh, black and others.

Bandages like clothing are of different sizes. Choosing one, a person needs to try a couple of options on and stop on that in which a pregnant woman feels most comfortable. Size of belt-bandages corresponds to the size of pre-pregnancy clothes: S (42 to 44), M (46 to 48), L (50 to 52), XL (52 to 54), XXL (from 56 and above). Bandages for pregnant women are divided into prenatal, postnatal and combined. They exist as shorts, skirts, belts, elastic ribbons.

Recently, on the pharmaceutical market appeared novelties: a bandage with inbuilt player, which can record music via USB, or record parents' voice through the microphone. Sound is transmitted through vibration on the surface of women's abdomen. Bandages with silver threads, made of cotton on the classical technology providing comfort and ease of use, and the silver ions prevent bacteria growth, maintain the natural balance of the skin and suppress unpleasant odor.

Thus, leading producing countries have been found, and new forms of contemporary bandages have been explored.

ASSORTMENT OF GOODS AS A CATEGORY OF MEDICAL AND PHARMACEUTICAL COMMODITY SCIENCE

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In accordance with DSTU 3993-2000, commodity science - the scientific discipline which systematically studies the goods during all stages of the life cycle, methods of knowledge of their consumer value, regularities of forming assortment and quality requirements for the efficiency of their production, circulation and consumption.

Considering the fact that the medical and pharmaceutical commodity science (MPCS) is part of non-food products commodity science, it is clear that it has its own subject, category, methodology and objectives.

The aim of this work is the definition assortment of goods in the system of knowledge MPCS/

In accordance with DSTU 2398-94, category - the result of the division of the universal concepts of a general nature that can be applied in principle to all subject areas.

Concepts form through a set of categories, shapes which are determination (definition), the conception and theory. Therefore, considering the MPCS as a system of scientific knowledge about medical and pharmaceutical goods, there are several major categories, namely *commodity*, *assortment of goods*, *product quality*, *consumer properties and consumer value*.

According to DSTU 3993-2000, assortment of goods - a set of products of different groups, sub-species and variations that are divided on a certain consumer, commercial or industrial feature to characterize the composition of the mass of commodities in different conditions.

Specificity assortment of goods as a category of the MPCS is a broad range, which is limited to the license terms in the market.

To assess the assortment of goods, in practice, it uses the term nomenclature of goods - the set of all assortment groups of goods and trade items that are offered for sale by the subject of specific market.

In the classic sense of assortment of goods as part of the categorical apparatus of commodity science we can highlight such indicators:

1. the breadth of assortment - the ratio of nomenclature of goods to assortment of goods;

2. completeness of assortment - is characterized by the number of positions of the nomenclature in relation to registered and approved for use goods;

3. depth of assortment - is characterized by a variety of dosage, concentration, or packing one type of goods;

4. saturation of assortment - describes the number of existing goods on the market;

5 harmony of assortment – is characterized by the degree of uniformity nomenclature in relation to the doctor and (or) the patient benefits;

6. completeness of use - characterizes rationality of assortment chosen by institution. Calculated as the ratio of assortment sold to the positions available for a certain period of time;

7. stability assortment - the ability of a set of goods to satisfy consumer demand;

8. assortment update degree - the quantitatively expressed ability of a set of goods to satisfy changed consumer needs through new products.

These indicators are conditional, but they make it possible to quantify the success of the assortment management of a particular pharmaceutical facility or facilities network.

In the development of any pharmaceutical product establishment policy needs a comprehensive analysis of allowed to use and existing drugs on the market, their dosages, packings, dosage forms, price characteristics, quality, novelty of and so on.

Analysis of assortment of goods in pharmacies is now the subject of study of pharmaceutical marketing, however, based on the definition of commodity, it is clear that using known tools, the MPCCS can develop as an independent scientific discipline that has its own categorical and instrumental apparatus and methodological grounds.

Thus, in this work we have outlined the concept of assortment of goods as the category of MPCCS.

Moreover, it has determined the relevance of using quantitative and qualitative indicators of nomenclature of goods for product policy and to evaluate the competitiveness of health care institutions that are engaged in retail and wholesale of finished drugs, medical tools, devices, equipment, chemical reagents, items of medical care, etc.

PACKAGE'S MARKING AND DESIGN – IMPORTANT ASPECT OF DRUG'S SAFETY

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The importance of correct product labeling, marking and packing for exports cannot be overstated. Their regulations vary from country to country, however, certain basic information is constant in all regulations. For example, necessary information, which primary and secondary package of drug should contain, helps final consumers to identify it in a large range of different trade names of drugs, for pharmacist – to provide its inspection analysis with all-round studying of its quality and estimation of safety. In Ukraine the marking of initiate and outer package is regulated by: the law of Ukraine about drugs, 1996; the Branch Standard of Ukraine “Graphic Design of Drugs. General requirements.”, 2000. Now in Ukraine marking of drug package is regulated by Order of MoH № 426 with amendments introduced by Orders of MoH № 536 and 543.

However, not only marking of package, but also its design helps pharmacist to provide more comfortable control of drug's origin, it's quality, with high level of inspection's result. Packaging design should also take into account the needs and capabilities of the widest possible range of potential users, and in particular older and partially sighted users, and how they interact with the medicine in the home.

Purpose of our research was to work out recommendations to the design and labeling, which can be used in inspection analysis of drugs. Using the literature data we established, that if secondary packaging is cluttered with text and images, it can be difficult to recognize important information and identify the correct packaging, but using blank space, critical information such as the medicine name and strength can be emphasized.

Concerning the use of color, it can help to distinguish between, for example, different strengths of the same medicine and between similarly named medicines.

It can be used also for make the style of primary and secondary packages common, for such case, when patients take more than one medicine, or the same medicine in two or more strengths, and have be able to identify which blister strip belongs to which pack, even if they mixed it.

To prevent insufficient information about the medicine after cutting of single blister pockets, the medicine name and strength should be printed on each pocket of the blister strip. If the size of the pocket is too small, the information should be repeated in a pattern across the entire strip.

USE OF PATCHES WITH DRUGS EFFECT ON THE BODY

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Drug treatment is inextricably linked with the question of rational dosage form choice in which the drug substance or substances should provide complex therapeutic (or prophylactic) effect. It is obvious that with the expansion and change of drugs directory and improving methods of treatment the range of dosage forms expands and their technology improves.

In today's rhythm of life, such a dosage form as a patch is attracting increasing attention from scientists and opens up new opportunities for its use in medicine.

The purpose of this work was to study such dosage form as a patch with medicinal substances.

Patches (Emplastra) - a dosage form which represents plastic mass with the ability to soften and to stick to the skin. Designed for external use. The effect of the patch exposure is achieved by the fact that it affects the skin, subcutaneous tissue, and whole organism.

Depending on the medical indications patches are divided into: epidermal - patches in most cases containing no medicinal substances, used mainly as dressing material, to protect the skin from the harmful effects, to mask defects, convergence of wound edges and fixing bandages on the skin surface; endermal patches always contain medicinal substances of different therapeutic effect (e.g., keratolytic, depilating, etc.) and are used in diseases of the skin at the site of application; diadermal patches contain medicinal substances, penetrating through the skin and affecting the deep-lying tissues or possessing systemic effects on the body. Endermal and diadermal patches have softer consistence than epidermal ones and provide required action of medicinal substances, facilitating their penetration to certain predetermined depth.

Molecules of many drugs can diffuse out of the drug to the skin surface, to penetrate the stratum corneum and reach epidermis and dermis and then the vascular network transfers them to organs and tissues. Due to transdermal delivery stable drug concentration in the peripheral circulation is supported, which in comparison with other dosage forms increases the safety profile of patches.

Thus, it can be definitely said about the necessity and feasibility of developing transdermal patches for the provision of safe and efficient care to mankind.

COMMODITY ASPECTS OF CHILD-RESISTANT PACKAGING

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Medicinal products - a specific commodity that requires responsible actions for dealing with it. Due to the fact that most of the life cycle the commodity is in the process of storage, the important point is eliminate the risk of misuse by children.

There are many reported cases of poisoning of children with drugs, which was followed by improper storage and packaging disparity.

The aim of this study was to determine the place of child-resistant packaging among medical and pharmaceutical goods and providing him commodity evaluation.

No doubt, to follow the children's behavior is difficult, therefore the packaging has appeared, which has the objective of protecting potentially dangerous products from inappropriate use by little children. This packaging has some protective mechanisms that prevent children's access to content packaging.

Today in Ukraine is valid *DSTU ISO 8317:2005 Child-resistant packaging - Requirements and testing procedures for reclosable packages*. This ND establishes basic requirements to containers, closures and ways of multiple closing.

Analyzing the assortment of registered drugs, we have found that in Ukraine the issue of child-resistant packaging is without sufficient attention. Only a few manufacturers, such as Stinol, using child-resistant packaging for tablet form. There are also several foreign manufacturers whose products have similar packaging. But the total amount of drugs having child-resistant packaging is rather scarce.

This can be explained by the relatively high cost of the packaging and packaging equipment, as well as tough legal requirements during the medications registration, and as a result his unwillingness to use the manufacturer. However, the risk of poisoning children with potential possibility of opening packaging indicates acute urgency of this problem.

On the other side, the use of such packaging in combination with tamper evidence enhances the protection of drug from counterfeit, but makes impossible carrying out the inspection and expert examination of pharmaceutical and medical productst that is inside.

Hence, today there are needs in formal regulations, which could simultaneously solve the problem of inspection analysis, product protection against counterfeiting and protect children from inappropriate drug poisoning.

TUBE – OPTIMAL CHOICE OF CONTAINER FOR SEMI-SOLID MEDICINES

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At the moment, as containers for soft drugs jars and tubes are used. The advantage of a tube as the package that allows the tube to dose the required amount of product, extruding it directly to the application site. Furthermore, the product tube is protected from damage, evaporation, and other light effects, such as contamination with microorganisms. Throughout the world are widely used metal tubes, polymeric and composite laminates tubes. Construction material of modern tubes has good barrier properties, is inert to products, contained within, provides the strength and tightness of the case, and securely holds the decorative coatings and printing design of tubes. The undeniable advantage of tubes over other types of packaging is their compactness, tightness and high barrier properties. Tubes allows precise content dosing without any additional devices, provide long-term storage of the product and convenience in use.

Tubes are distinguished by the type of materials: aluminum (metal), plastic (extrusion), laminate. For today aluminum tubes which possess high barrier properties are widely distributed. They are certainly practical, but their consumer properties are far from perfect. For example, the ability to print on aluminum is limited. High-resolution image and the exact combination of colors can be applied on laminate. In other words, the picture on the laminated tube will look brighter, clearer and more multicolored than aluminum. In the production of laminate tubes colored and outer barrier layers can be combined, a unique appearance can be achieved. Laminate tubes can be offered to a customer without secondary packaging (packet) namely because of their reliability and colorful print. This reduces overhead costs associated with the packaging of the finished product. Laminate tubes keep their shape well during transport and use. Unlike aluminum, the laminate tube has neither wrinkles nor cracks. The tail parts of laminate tubes can be given different shapes (eg, a curve or hook). So laminate tubes are far ahead of metal ones on visual appeal, which is a strong advantage in the fight for the attention of customers. Laminate tubes have a distinct advantage over extrusion, due to its high barrier properties. Therefore, laminated tubes are used in areas where packing in plastic tubes is impossible or undesirable. Based on the above said, we have chosen laminate tube as a container for packing a topical gel for the treatment of the upper respiratory tract diseases.

STUDY FOR THE REASONS OF COUNTERFEIT DRUGS INCOMING INTO PHARMACIES OF KHARKOV CITY.

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Modern medicine is unthinkable without use of highly effective and safe medicines. It is known how hard consequences for human health the use of poor quality drugs can lead to. In this regard, it is extremely important to prevent entry of poor quality drug into consumption field and to ensure effectiveness of the control system. In this view the objective evaluation for quality of drugs circulating in Ukraine and study of functioning efficiency of quality control system are still very important problems, which is the aim of present research.

The need for such a study is caused by changed situation in the field of drug circulation associated with new social-economic conditions, increasing number of manufacturers and suppliers of pharmaceutical products, sharp increase in quantity of registered drugs and so on.

Under conditions of the changed situation the control-licencing system has been developed to provide state control over quality of drugs. Thereupon it's necessary to underline that realization of institutional arrangements for the purpose of effective functioning of the given system is not always based on the results of theoretical developments and objective practical estimation of them.

In Ukraine only in the first half of 2013 the State Service for Drugs has revealed 34 cases of counterfeit medicines sale. 47 batches of 25 names of counterfeit drugs have got under the ban on the basis of issued instructions. Taking into account this unfavorable situation in the field of medicines turnover it is necessary to analyze the reasons for incoming of fake drugs on pharmacies' shelves as well as to suggest ways for preventing this phenomenon.

The study used method of questioning and interviewing of pharmacists in pharmacies. The survey involved 100 pharmacists in different pharmacies of Kharkov. The chosen method was aimed to reveal violations during receiving of drugs by quantity and quality.

The data obtained have shown that in most of pharmacies in Kharkiv (approximately 85%) providing of incoming quality control of medicines is not fully executed. As the main reason of this violation pharmacists have noted the lack of time and physical ability to perform a full check of the input control of all drugs entering the pharmacy.

THE MAJOR CONSUMER PROPERTIES OF MODERN DISINFECTANTS

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Leading role in the complex of sanitary - epidemiological measures that ensure the prevention of contagious diseases and disinfection of germ on surrounding objects belongs to disinfectants. Also holding disinfection measures relevant for pharmaceutical companies, especially in classes purity A, B and C.

The aim was to analyze the properties and range disinfectants that are applied.

Disinfectants - are chemical substances used to destroy (disinfection) of pathogens in their ways of transition from the source of infection in the body. By modern disinfectant following requirements: breadth of spectrum bactericidal and fungicidal activity; low toxicity to animals and staff, default of corrosive properties ; security for the environment; compatibility with materials processing ; active in a wide range of temperatures, default of carcinogenic, teratogenic, immunosuppressive properties; default of flammability and explosion hazards; efficiency and ease of use.

The analysis of the Ukrainian market, showed that among disinfectants registered by the Ministry of Health, along with well-known and widely used , disinfectants foreign production (Russia , Germany , France, Switzerland) , as a significant portion - of domestic production. Ukrainian manufacturers of disinfectants should be called : "Ukrainian Research and Production Center disinfection problems", "Research and Production Enterprise" biocide", "Farmakos" (Kiev), Pervomaysk public enterprise "Khimprom" (Kharkiv region) , "Dniproazot " (Dnipropetrovsk region), "San Clean INT" (Odessa), etc. The chemical structure disinfectants are classified into : halogen-containing compound (Hlorosept, Medikarin, Hlorsept), oxygenated compounds (Sterioks, Sanosil, Oksivir); aldehyde containing compounds (PF Gigasept, Steranios) surfactants (Zenteks, biocide plus acarids plus Dezekon etc.); alcohols (no sharp edges, Septoderm, Vaygosept) composite drugs (Klinisept, Lizoformin, Ultratsid, Geksadekon etc.). The analysis of modern disinfectants showed that there are no universal disinfectants. Practically every one of them has limitations in the spectrum of antimicrobial activity, scope, degree of toxicity and effects on materials that who are exposed decontamination. .

Accordingly nowadays the most widely used composite agent - multicomponent disinfectants which comprise surfactants in combination with alkyl amines, aldehyde, guanidine, alcohol, etc. These agents effectively combine complex properties: cleaning, deodorizing and broad spectrum antibacterial properties.

SECTION № 17

SOCIAL STUDIES

CONCEPTUAL AUTHORITY AND ITS RESOURCES OF SOCIAL MANAGEMENT

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Conceptual authority is an authority of people and ideas capable to generate social processes including the life of society during a number of generations continued in accordance of developing concept.

Conceptual authority is realized through priorities of generalized resources of social management. Among the main resources are:

World outlook priority is a world view, methodology of cognition. The aims of development and basics of management are forming on this level in a considerable long-term period. Factual priority is an applied factology of all the branches of knowledge: ideology, technology (including social and political components), and religious doctrines. The authority is able to manipulate behavior of people first of all by the two ways:

- Urging of people for some actions with a help of enforced values and aims;
- Preventing and blocking of unwanted social movements, protests, and actions appearance.

Economical priority is an active using of international credit-financial system, state and world financial resources and schemes. International credit-financial system is a main resource of economical priority. Genetic priority is a destroying of gene pool, weakening and damaging of future generations. It includes such facilities as alcohol, tobacco, drugs, genetic engineering. Force priority is a focused using of all the legal and illegal force structures, such as army, police, militia, armed formations, terrorist groups, etc. Making conclusions about social and political situation in Ukraine it should be noted that mass communications demonstrated its possibility to provide a pressing on a public consciousness in a rather wide way. Though mass communications because of its original essence and organizational and functional nature are unable to (and don't have to) play a leading role in formation of public consciousness. Formation of public consciousness and world outlook should be based on scientifically grounded truth and implemented by optimal methods. Specify a place and a role of "crowd" and "elite" in a system of state management in conditions of transformational processes it should be noted the next statement. When a man located and functioned in general stream looking for similar it is hard for him to fix the differences going on gradually at the same time with all. He can see only the near surrounding area both literary and figuratively. Single external or subjective internal factors with a complex of measures developed and introduced in the life are the obstacles for getting of more completed information about a surrounding area. For example, "informational aggression" should be aimed on creation of closed informational space around a concrete person or the whole social group. Each person and nation in total has a certain power. From the other point of view not each person and social group wants or can use its power. There are persons fond of power and people who delegate its power with a hope that these delegates will represent public interests.

PHENOMENON OF IATROGENIC AND MEDICAL PRACTICE

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Verbal and nonverbal factors affecting the patient's condition became the object of studying considering a doctor and a patient interaction in the context of their mutual understanding. We are talking about actions that can cause a patient's complications of the disease or mental disorder. Iatrogenic is a mental condition characterized by painful reactions caused by communication with a doctor, which in some cases can lead to a pathogenic situation. The problem of iatrogenic was investigated by such authors as Oswald Bumke, Roman Luria, and Konstantin Platonov, who analyzed the mental aspect of iatrogenic. Now the meaning of this phenomenon has expanded and it is regarded as "a defect of medical work". Among the main sources of iatrogenic are: wrong conducted health education, doctor's or pharmacist's individuality (categorical statements of "all-knowing the pros" easily inculcating his views and opinion); the personal characteristics of patient: nervous patient with non flexible mind exposed to complications. Sometimes the role of the patient individuality may be so severe that it is not a fault of the paramedics but the "mistaken iatrogenic". The appearance of iatrogenic depends not only on the actions of the "man in a white coat", but also the perception of the patients. That's why the source of problems becomes a "far-fetched" component. The classification of iatrogenic is wide: psychogenic (caused by careless and misunderstood statements of medical worker about the health of the patient); medical (caused by effects of the medicine); traumatic (medical action of damaging factors of physical and mechanical nature), infectious (includes all the cases of infectious diseases, the contamination that occurred in the provision of medical care); mixed (caused by the action of several damaging factors). The main reasons of iatrogenic effects are: the imperfection of medicine, intensive development of treatment methodic, increasing of a number of damaging factors, inappropriate "over awareness" of patients. Subjective factors are associated with individual characteristics of pharmacist or doctor: lack of skills, lack of interest in the patient evaluation, etc. Adequate attitude of the patient to the process of treatment and readiness for a dialogue are very important factors. Exception of iatrogenic effects of treatment is an ideal for specialists. Among the main methods to prevent such kind of difficulties are: high level of ethic education of future doctors and pharmacists, following the principles of medical ethics, which are based on understanding and compassion for the patient. The content of documentation and other treatment information for patient should be analyzed better. Iatrogenic aspect of pharmaceutical practice could be minimized in the case of the correct reaction of provisor to the doctor's appointments and highly professional attitude to patients. It should be noted that biopharmacy is a special branch of pharmacy which deals with the prevention of some medical and iatrogenic complications.

Each medical practitioner should remember the golden rule of treatment: "Do not harm!" and the patient should have an adequate reaction to the process of treatment to preserve a health and solve the iatrogenic problem.

THE IMAGE OF HRYHORY SKOVORODA IN ART

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The honorable responsibility of artists is to respect the best representatives of Ukrainian people. For Hryhorii Skovoroda it was made by masters of a word, a sculpture, and a painting. The famous examples are such portraits and paintings as: the people listening a kobzar performing the song by Skovoroda by painter S. Vasylykivskyi, the graphic portraits of Skovoroda on the old engravings (anonymous without signature of engraver P. Mescheryakov, V. Mate), on lithography by Brukman, Zhuk, Uvarov, etc.

The most interesting portrait of Hryhorii Skovoroda is the one in Saint-Petersburg Public Library. Such features of face of Skovoroda as seriously, honor, thoughtfully although tired is worth to pay attention. H. Skovoroda is depicted as more old than on the previous portraits. This portrait was created shortly before his death when he already had 70 years old. According on the style of depiction, the materials and the condition the portrait can be considered as one of the oldest and well-turned one.

The most interesting monument to the philosopher is in Lokhvitsa, Poltava region, presented in 1922. The author is Ivan Kavaleridze. The monument to H. Skovoroda is a full-length sculpture installed on the granite plinth. The height of the monument is 4,17 meters. Skovoroda is depicted during a temporary rest. The ceremony of the monument presentation took place in Lokhvitsa on December, 22, 1922. The event was devoted to the 200-years' jubilee of philosopher's birthday. I. Kavaleridze was working with the cement but he created the illusion of stone. During that period the monument presented a good composition with the buildings around – museum, library and city theatre. But during the World War II the buildings of theatre and library was burned and the monument was damaged. That's why the new bronze monument to H. Skovoroda was installed in Lokhvitsa on November, 29, 1972 for the 250-years' jubilee of philosopher's birthday.

The monument to H. Skovoroda decorates Contractova Square in Kyiv. It was installed in the capital of Ukraine on March, 1, 1977. H. Skovoroda is turned to Kyiv-Mohylyanska Academy – the place where he spent several years. H. Skovoroda seems like coming back to his alma-mater. The author of this sculpture was also I. Kavaleridze. According on the project proposed by I. Kavaleridze H. Skovoroda was depicted barefoot, keeping armpit the Bible with the cross on his neck. This version

didn't like the authorities of Soviet Ukraine. The cross was removed, the philosopher took on the bast, and the Bible was changed for a bag so the original idea was destroyed. The monument became an integral attribute of Kyiv-Mohylyanska Academy. The students have a tradition to clean the monument on October, 14 (the Day of Academy). This good and symbolic action is called "pure Skovoroda".

The bust of H. Skovoroda was mounted in Chornukhy – the village he was born in Poltava region. The sculptor is M. Kogan. The bust is created of wrought copper (sizes: 1,45 X 1,35 X 0,95 meters) and installed on the labradorite plinth (sizes: 3,25 X 0,77 X 0,61 meters). On the center of the bust there is a copper belt with the sign "Hryhorii Skovoroda". The square around the bust is decorated with tile. On the left of the bust there is a memorial plaque in horizontal position. The first attempt to immortalize the memory about Hryhorii Skovoroda was made in 1914, but it was failed because of the war. The Memorial Estate of H. Skovoroda parents and the Local History Museum were opened in Chornukhy for 250-years' jubilee in 1972. Near the memorial complex the bust of H. Skovoroda by M. Kogan was installed.

The life and activity of H. Skovoroda was connected with Kharkov, that's why we have several monuments to our greatest philosopher. The monument to H. Skovoroda was mounted on the territory of H. Skovoroda National Pedagogical University of Kharkiv on Blucher str., 2, May, 27, 1992. The sculpture was created by I. Yastrebov of the sheet copper.

Another monument to H. Skovoroda of bronze was installed near the History Museum on Universytetska str., 10, on September, 3, 1992. The history of this monument was long and dramatic. The monument was created by I. Kavaleridze in 1971 for Podil in Kyiv. This version of monument was forbidden because of the Bible in the hands of philosopher. That's why it was mounted on Kobzar steep near the Monastery of St. Pokrova. The memorial plaque of H. Skovoroda on the territory of the Monastery of St. Pokrova was presented later.

The monument to H. Skovoroda by S. Gurbanov was presented on the territory of H. Skovoroda National Pedagogical University of Kharkiv 9 of October, 2012. The sculptor depicted H. Skovoroda as a man of exceptional features, poignant wit, always thinking. He wanted to present his internal world and to create his psychological portrait. Though the best monument to the great philosopher is an old oak tree in Skovorodynivka, under which H. Skovoroda liked to sit and to think so much.

YOUTH SUBCULTURE OF HIKIKOMORI

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Hikikomori represents the one of modern youth subcultures emerged in Japan and strengthening their positions in different regions of the world.

Hikikomori (“hikikomori” from Japanese means a “being in seclusion”) is a category of young people refused any forms of social activity, tending to an extreme degree of isolation due to the presence of certain personal complexes and phobias. Hikikomori are spending all the time at home, leaving such duties as school, university or work, wasting a free time engaging their hobby. The hobby is a whole time senseless staying online. The age of Hikikomori is varying from 17 till 27 years. The works by such Japanese psychologists as Genda, Hattori, and Saito are devoted to analysis of Hikikomori. According to these authors Hikikomori lifestyle is characterized by insularity, destruction of social relations, including within the family, the complete absence of any contact with the outside world except some basic needs such as paying utility bills and buying food.

The presence of such category of young people represents a sustainable process of atomization of the informational society. Training and labor activity, contacts with family and friends are not a priority for the Hikikomori and are discordant with their current way of life. They prefer the life in a confined space and consumption of various information products (anime TV series, computer games, comics, etc.). Direct communication is being replaced by technically mediated one. Hikikomori are immersive in virtual space, which is perceived as an ideal, “sterile” space free from domestic problems and communicating with relatives or friends. Internet addiction reaches critical proportions: online games, online communication free of registration and accounts are the communicational space of Hikikomori where they feels themselves comfortable and can contact with the same people. The real living space is narrowed to the boundaries of a room or an apartment. At the same time it becomes a multifunctional: a space for relaxing, everyday pastime, eating, sleeping, using a computer or a game console, storage space for necessary things and food.

All of the listed problems of modern youth socio-cultural space are indicating an alarming trend of deep and systemic social degradation of a significant part of today’s youth. Youth society and modern society in total don’t have a single established system of the hierarchy of values. The coexistence of continuity of traditional values typical for our society and the formation and mass distribution of consumer interests can be observed.

EUTHANASIA-PRACTICE TERMINATION OF LIFE

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Euthanasia - the practice of terminating the life of a person suffering from an incurable disease, experiencing unbearable suffering. The term "euthanasia" used in various senses: accelerating the death of those who are experiencing severe suffering, the cessation of life "extra" people, care for the dying, providing opportunities people die. "Euthanasia" is also sometimes called euthanasia of animals, including laboratory and stray animals.

The aim of our study was to investigate the notion of euthanasia, review its moral side.

Concept of euthanasia ambiguous is defined as in the ethical and philosophical, legal, and in the medical literature. Therefore, is complicated the process the study of sources in which is no single definition of euthanasia. For the first time this term introduces in the seventeenth century English philosopher Francis Bacon in one of his main works "On the dignity and augmenting of science." The term "euthanasia" comes from the Greek words "eu" - good, boon and "thanatos" - death. In theory, there are two kinds of euthanasia: passive euthanasia (the intentional termination of medical supportive care of the patient) and active euthanasia (controlled medications or other actions that result in a quick and painless death).

The idea of euthanasia in the late twentieth century is becoming more and more popular, along with increased use of another important concept of quality of life. However, the Hippocratic Oath in its traditional form is contrary to implement the idea of euthanasia: "I won't give deadly medicine to any one if asked, nor suggest any such counsel"

Life - this is the highest value for any person, but if life is only associated with intolerable anguish, in humans occurs reorientation his values, and death as a deliverance from suffering becomes a great boon Do we have the right to deprive a person of this good?

Euthanasia - is when of two evils choose the lesser. But death of a man more evil than his suffering, is not it.

THE PROBLEM OF ISLAMIC IDENTITY IN EUROPE

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Europe has built over the last decades a union that confirms to the world the identity of the countries included. Consisting different countries, the European Union has mixed cultures and borders that would seem a little bit unclear to some. Mixed with Western identity and Islamic one, Europe seems to face a challenging proximity. Being the second largest religion in Europe after Christianity, the Islamic identity is under argument whether it's a part of Europe identity or an intruder of it. Do they both share a unite identity of Europe? Can we call it a shared identity? Can one actually delete the other? Is it so dangerous to accept the Islamic culture in westernized countries? So, what is the Islamic identity? Why has it been under criticism for so long? How did it enter Europe and how Europe is accommodating?

Presenting some facts, we should know that when we talk about the spread of Islam in Europe first we should divide it into 4 quarters, Eastern Europe and Western Europe and the south east (Greece, Bulgaria, Serbia, etc.) and south west of Europe where the south part were Muslim countries and that didn't match the boundaries of Europe. When we look at the history, European and Russian leaders had Muslim allies and they had mosques in their countries where it wasn't a big deal. So, there was a time where Islam and Europe were conceded to one another.

So, we were inherited the idea that 'Europe' (North West Europe to be exact) is all about civilization, freedom, progress, superior. We were also inherited the Islamophobia, and that Islam is only related to Arabs knowing that there are 1.62 billion Muslims around the world, and that Muslims in the United Kingdom were found more than in Lebanon and in China more than in Syria in a study done by the Pew Research Center in 2014. Shedding the light on the media, it played an important role in passing on this in heritage from one generation to another. Not only feeding it more lies, but also shedding the lights on extremists in titling it with 'why we should hate Islam'.

Islamic identity and well-being are not antagonists to one another. It is not necessary correlated to Arabs and Middle East. The same way Christianity is not only related to west only. However, men in power knew how to create a shielded castle to their own ignorance and that is by spreading this ignorance among people. Wars caused by caliphs, rulers, kings, presidents, whatever they call themselves over time, in the name of any religion has done nothing over the years but increased the gap between people among each other and among people and religions.

From socio-cultural point of view, I think there is a claim from the Europeans that Islamic tradition and rules may not fit the westernized life style, and a fear that this may interfere with their social life. Europe actually cares about all people living within its lands to have the same rights. So, with great number of Muslim immigrants, Europe is in a complex between providing total comfort and equal rights

for the immigrants for their world image in one hand, and between taking precautions from the claimed effect of these immigrants in their countries. So, may a 'Muslim-Western' identity occur or even allowed from both sides? After all, Islam and Europe did share history once.

A turning point would be the events of 9/11 that brought Islam again to the number one media subject after being hiding in the shades for several years. The media played a major role in directing what happened to make it a campaign against Muslims. Ever since, it actually succeeded in creating that propaganda about Muslims and stereotyping them.

Terrorism has no identity; unfortunately, those terrorists who are killing, bombing, forcing their identity, are doing so in the name of Islam, knowing that Islam and all religions are free from these people and condemn them. So, I am with taking extra safety measurements to prevent these terrorists, but I am not with making campaigns against 'Islam'. I think the government and the people share the responsibility of being aware and acknowledged to realize that Islam is the number one victim of these terrorist. Europe has done an excellent job in the extra measurements against Muslims, but terribly bad in informing people about Islam.

Feeding people with ignorance, government increased the hatred against followers of this religion making them in the victim list again. So, a question is raised, are people in power, the ones who are capable of making decisions, associates in all the crimes? May it have been that they wanted this to happen so they lead people to it? Many became enchanted by the religion that they converted and some turned their hatred to respect and love. Others, some just kept on polluting the world with this propaganda. We all fear what we don't know, so just know; for, knowledge is power.

Islam, being viewed as an extreme religion in the west, it gained a worldwide hatred thanks to people in power who provoked and nourished that hatred among people. However, the beauty in God's creation of humans is that he created us with the ability to feel and think. In the last few years, we have witnessed an enormous breakthrough in the world; people are refuting against their rulers mainly because of feeling inequality, injustice, insecure, not having their rights, not treated well as human beings. These humane values are not for one kind of people with certain background, but are for all human races. It is wrong to label certain religion because of some extremists who happens to be holding that religion in their pockets on their identity card. Anyone can be bad or good regardless where they come from or what they believe.

The Islamic identity should be understood positively in other societies with positive interaction. Accepting Muslims in Europe and integrating them would enrich the culture and build a tolerant environment in the country they live and eventually in the whole world.

**MY FAMILY PRIDE – KOVALIOV KONSTANTIN FEDOTOVICH,
HERO OF THE SOVIET UNION**

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The Great Patriotic War has left a significant imprint on the fate of the Soviet people. It was a war of the Union of Soviet Socialist Republics against Nazi Germany and its allies. Our ancestors fought courageously against fascism and now everyone can proudly share their family history of the wartime period.

Objective of the work: to nurture love for the motherland, patriotism of modern youth on the heroic examples of bravery and courage of our forefathers.

In 1941-45 my great-grandfather Kovaliov Konstantin Fedotovitch was a marine pilot, fighter, captain, flew in the sky of the Baltic. During 4 years of the War my great-grandfather flew about 500 sorties. On his battle account were 31 downed aircrafts, 12 of which he destroyed personally, and the rest were in group battles.

One of the most memorable events in the biography of K. Kovaliov was his acquaintance with the famous seer Wolf Grigorevich Messing.

In 1939, after the Second World War broke out, Wolf Messing fled to the Soviet Union where he performed with the "mind-reading ", first in the agitation brigades, and then with the individual performances of State Concert.

The Soviet patriot, an honorary member of many academies and universities in the world, wishing a speedy defeat of the fascism, Messing purchased on his personal savings a combat aircraft and decided to give it to an honoured pilot. The choice fell on Kovaliov, a native of Kuban.

On the fuselage of the donated aircraft there was the inscription: "A gift to the Hero of the Soviet Union, the Baltic pilot K. F. Kovaliov from the Soviet patriot W. Messing".

My great-grandfather shot down four enemy aircrafts on this fighter.

After the war, Wolf Messing came to visit my great-grandfather's house in the Krasnodar region, stanitsa Mingrelskaya. The friends lived in the same hotel, performed in front of factory workers, they met the pioneers.

The name of my great-grandfather is among the names of Heroes of the Soviet Union on the stele of the in Moscow Museum of the Great Patriotic War.

SECTION № 18

PHILOLOGY

MEDICAL AND PHARMACEUTICAL PROFESSIONAL PHRASEOLOGICAL UNITS, THEIR INFLUENCE ON FUTURE SPECIALISTS' CULTURE OF SPEECH

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The objective of research: to ascertain semantics of medical professional phraseological units and their usage in medical and pharmaceutical students' speech.

The subject of research: the role of medical phraseological units in formation of the future pharmacists' and doctors' culture of speech and in the development of the future specialists' important professional qualities.

The object of the research: various structural and semantic models of Ukrainian phraseological units on medical and pharmaceutical subject-matter.

The tasks of research:

- to study theoretical base on phraseological units;
- to investigate the interplay between the learning of medical and pharmaceutical professional phraseological units and the formation of medical workers' culture of speech and their mental outlook;
- to systematize the interpretations of the meanings of phraseological units on medical and pharmaceutical subject-matter.

The methods of the research: in the research the descriptive and the contrastive methods of analysis are used to investigate the studied language units.

The topicality of the research is predefined by the necessity: 1) to define the specific features of the meaning of medical phraseological units; 2) to investigate phraseological means of language as the source of the emphatic and figurative enriching of pharmaceutical students' speech.

The work has theoretical and practical significance: systematized theoretical material on medical phraseological units can be used at Ukrainian language lessons and at extra-curricular activities in order to enrich pharmaceutical students' speech.

Thus, understanding and reasonable usage of medical phraseological units develops skills of future medical workers' professional associative thinking and enriches their professional vocabulary. The usage of medical phraseological units facilitates the activation of students' communication skills and the improvement of comprehension of colleagues' professional speech.

A NEW LANGUAGE IS A NEW WORLD.

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The problem of language contacts is one of the main problems in modern linguistics, because any language is permanently changed. It reflects the cultural and historical background of each era, and it is fully understandable only for people living in this era. The problem of ignorance a language creates a problem of communication.

"Do you speak English?"- from this cliché starts communication between people speaking different languages who want to find a common language for communication. People from different countries have to get along with the progress in global trade and technology and also with each other.

There are many professions in our life where a person speaking foreign languages can successfully his work. Nowadays, business also means the ability to communicate foreign languages. We can also develop our intellectual and cultural potential with people from other countries.

We know the proverbs: "How many languages you know so many times you are human." They say: "A person who knows several languages, lives several lives".

Language is communication. Communication is life. Many events and scientific investigations were in the English language. In addition, if you learn language only as a thing that helps you to express yourself and discovers the world and different people you will find adventure here.

The English language is beautiful. It is a language of great literature. It is the language of William Shakespeare, Charles Dickens and other famous people. It is the language of computer technology. The great German poet Goethe wrote: «Who does not know a foreign language does not know his native language."

One must learn all the intricacies of a language, in order to use it in a proper way. Idioms, phraseology, dialects, slang, fill up quite a large part of the vocabulary. Understanding can put a person in an uncomfortable position. Learning foreign languages is hard work, maybe someone thinks that it is boring work, but it is true: "A journey of thousands miles begins with a single step ".

EFFECTIVE INSTRUMENTS OF TEACHING FOREIGN LANGUAGES

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Every few years, new foreign language teaching methods arrive on the scene. New textbooks appear far more frequently. They are usually proclaimed to be more effective than those that have gone before, and, in many cases, these methods or textbooks are promoted or even prescribed for immediate use. New methods and textbooks may reflect current developments in applied linguistic theory or recent pedagogical trends. Sometimes they are said to be based on recent developments in language acquisition theory and research. For example, one approach to teaching may emphasize the value of having students imitate and practice a set of correct sentences while another emphasizes the importance of encouraging 'natural' communication between learners. How is a teacher to evaluate the potential effectiveness of new methods? One important basis for evaluating is, of course, the teacher's own experience with previous successes or disappointments.

In addition, teachers who are informed about some of the findings of recent research are better prepared to judge whether the new proposals for language teaching are likely to bring about positive changes in students' learning.

LINGUISTIC ANALYSIS OF THE TITLES OF HOMEOPATHIC MEDICINAL PRODUCTS AND REMEDIES FROM PLANT AND ANIMAL MATERIALS

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In the early 21st century drugs of plant and animal origin and homeopathic medicines are gaining popularity all over the world. The number of such drugs in the Ukrainian pharmacies also constantly increasing. Interested in their names, we selected as the purpose of our work to explore from a linguistic point of view the names of drugs of plant and animal origin, manufactured in Ukraine and of homeopathic medicines domestic and foreign production, represented in Ukrainian drugstores.

During our work, we sought to find a way of forming, derivational elements, motivational priorities when creating titles, the choice of a language and adherence to traditional norms of letters. The object of research were titles of drugs of 3 groups:

1. medicaments from plant and animal materials, manufactured in Ukraine;
2. production of N. Zubicka's company «*Zelena planeta*»;
3. ready homeopathic remedies, represented in pharmacies of Ukraine.

Thus we have explored names of 353 remedies. In linguistic analysis have been reported existence of all derivation methods, the most common are the basics' compilation using **-o-** interfix, among prefixes the most common are **anti-, a-**; among suffixes **-an,-in,-at**. In general, manufacturers adhere to traditional spelling, but in some cases are inferior them for the sake of euphony. In the name of drugs dominate Latin term-elements, but often a tendency to use the term-elements in language of country of origin can be traced; the circle of most popular term-elements include those that indicate the names of organs and their diseases; using names of plants is also quite common, often in combination with the name of the organ or disease.

Motivational priority in the creation of titles can be considered to deliver to the consumer the maximum information about the drug. There is a tendency of the manufacturers to call remedies of effective, easy-to-remember names; this trend, increasing the drugs' attractiveness to the consumer, resulting in a decrease of pharmacoinformatical values of such names.

According to the results of work we can say that most informative (primarily for the practitioner, but also for non-professional consumer) titles can be considered the most successful ones. Informativity is achieved by appropriate using of term-elements, highlighting sphere of influence, effect and composition of the drug. Clarity and fruitiness of names have a positive impact on consumer.

INFLUENCE OF KAZAKH LANGUAGE ON RUSSIAN IN KAZAKHSTAN

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Russian in Kazakhstan did not lose the international language status. The main point of this situation is that most representatives of this title nation are bilingual, which means they speak Kazakh (their mother language) and Russian equally well. Bilingualism of the representatives of this nationality is one of the main factors of co-operation of Kazakh and Russian languages. The aim of this research is to set some influence vectors of Kazakh on Russian. Russian and Kazakh languages function within the framework of one state and, naturally, interact.

Nowadays Kazakh language influence on "Kazakhstan" Russian is limited to different types of lexical borrowings. Such borrowings are traditionally named kazakhisms. The first group is kazakhisms-renamings denoting existing realities. The second group is kazakhism-namings denoting new realities. Kazakhisms of the first and second group are borrowed by

Russian with strictly defined narrow meanings and are monosemantic expressions in Russian. They are phonetically and grammatically mastered and are already in language lexical system. The third group is so-called exoticisms regardless of their origin (Turkic and Kazakh), which according to ethnocultural positions belong to nonequivalent vocabulary. A small part of exoticisms is lexically mastered by Russian. Kazakh proper names-namings, often used in Russian, are the specific vector of Kazakh influence on Russian, f.e. names of magazines, newspapers, programs(educational, social and other). Such units are not considered to be Russian borrowings because of motivation absence: for Russian natives connection between a language sign and reality is absent.

However under the influence of regularity factor and high frequency of their usage some proper names-namings are able to lose the proper names status, able to acquire denominative features (abstract namings and act as borrowings). It is noticed that such occasionalisms are created by the representatives of well-educated part of the society with a certain stylistic task –positive or negative emotionally-expressive marking.

The pragmatic component of lexical meanings of the analyzed words make them attractive for Russian natives and perhaps will serve as a factor of their transition from occasionalisms to usual Russian vocabulary functioning in Kazakhstan.

ANALYSIS OF SLOGAN AS AN OBJECT OF ADVERTISING OF PHARMACEUTICAL PREPARATIONS AND PRODUCTS OF MEDICAL DESTINATION

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The actuality of this theme is conditioned the growing value of advertising in the life of modern society. Slogan is the most perceptible part of publicity text.

The subject of the investigation is the feature and specificity of advertising slogans of pharmaceutical products. The providing of the purpose of the investigation foresees the realization of the following tasks: to investigate the term “slogan”, to review modern conceptions, to do own complex classification of slogans; to discover and probe the features of creation of slogan; to investigate the publicity slogans of pharmaceutical products as to morphological, lexical, stylistic and syntactic features. A base is made by over 200 slogans of TV publicity rollers of pharmaceutical products. Linguistic features of slogans: use of pronouns “Your, Our” for creation of the impression that the choice of these medicines belongs exactly to them and he is already done; the use of imperative mood of verb for stimulation of positive choice of buyer; using of numerals for underlining of exclusiveness of means; and also the syntactic constructions of different types are used: ellipses, broken structures, incomplete suggestions, repetitions, nominative suggestions, advantage to simple sentences, which give dynamic, expressivity to publicity information, interrogative suggestions are used (a question describes a problem, an answer for such question is acquisition of the advertised mean). For creation of texts of publicity slogans different stylistic forms, stylistic figures are used. such, for example, as: puns, remade phraseological units, hyperbolae and metaphors, litotes and others like that.

It is possible to do conclusion, that a publicity slogan is inalienable part of successful publicity campaign. Every slogan must contain a «spirit», its presence contributes to memorizing, and as result — positive choice of user and the increase of demand for goods. To this purpose one use the special syntactic constructions, specific vocabulary, facilities of stylistic and graphic expressiveness and others like that. A few elements for bringing in of attention can be used in one slogan. However we must not forget about enormous responsibility before consumers because their conscious or unconscious choice can cause damage to the health. Therefore, to our opinion, publicity slogans (and rollers, that they are accompanied) must not create feeling of imaginary lightness in the decision of medical problems and popularize self-treatment.

RUSSIAN PROVERBS AND SAYINGS ABOUT NUMBERS

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Russian proverbs and sayings about numbers appeared with man's life and activity, with the development of economic relations. Numbers personification started the era of their usage in folk proverbs. The quantity category which is in close connection with the quality category plays a great role in proverbs. Measure understandings, quantity gradation via metaphors, gradation of good and bad things were transmitted in sayings with the help of numbers: *Лучше один раз увидеть, чем сто раз услышать* (*Seeing is believing*). Numbers in proverbs and sayings often possess not direct, but indirect and symbolic meanings. Russian proverbs analysis allows to make a conclusion that the most often used numbers are numbers 1, 2, 3, 7, which have the special magic meaning in Russian linguistic. Number 1 in Russian proverbs and sayings has direct meaning and denotes quantity equal to one, and also in indirect meaning, denoting a small amount of smb, smth or nothing: *Один в поле не воин* (*One man, no man. There is safety in numbers*). Number 2 is more frequently used in its direct meaning: *Два медведя в одной берлоге не уживутся*. Proverbs and sayings with this number in figurative meaning contain comparisons and denote an indefinite quantity, which is greater in comparison to other indefinite quantity, expressed with the word "one": *За двумя зайцами погонишься – ни одного не поймаешь* (*If you run after two hares, you will catch neither. Grasp all, lose all*); *Старый друг лучше новых двух* (*Old friends and old wine are best*). Number 3 in Russian culture has a magic character: a fairytale hero performs three deeds; three sons or three daughters usually grow in a family; in Bible God is presented in three persons; width, length and height are distinguished in space. In the meaning «much/manу»: *Обещанного три года ждут* (*It is never long that comes at last / Between promising and performing, a man may marry his daughter*). In the meaning «little/few»: *от горшка три вершка*. Antithesis principle is presented in a proverb: *Не узнавай друга в три дня – узнавай в три года*. Number 7 is also very often used in Russian culture: seven holes are in a human head; seven virtues; seven sins; seven rainbow colors; seven skies; seven week days; God created the world for seven days, devoting the seventh day to rest. Even patients were treated repeating: *Сделай настой из семи трав на семи водах, пей семь дней по семь ложек*. Psychologists found out that one man's glimpse is able to see not more than six objects at once; therefore "seven" is already «a lot». That is why such proverbs are used: *Семь раз отмерь, один раз отрежь* (*Measure twice, cut once. Second thoughts are best*); *Семеро одного не ждут* (*For one that is missing there's no spoiling a wedding*).

MUSICAL CULTURE OF MEDIEVAL WESTERN EUROPE

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The main objective of our work is to study the laws of musical art development in Middle age.

Subjects of research: collections of medieval songs (“Carmina Burana”, “Llibre Vermell de Montserrat”); samples of Gregorian chant (“Dies Irae”).

Latin in Middle age was the base of educational system – “seven liberal arts”. Latin also was a universal language of communication and so underwent major changes, sometimes unacceptable from the positions of Classical Latin. Thus many coevals granted Medieval Latin name of “vulgar” or “cuisine” Latin.

Musical art of Middle age was developing in two different directions: ecclesiastical (official art) and unclerical (temporal art). Birth to medieval ecclesiastical music was given in Antiquity by Saint Ambrose (340-397 A.D.). The most significant innovation of his was called “Antiphony” and implied separation of church choir in two parts located on both sides of the altar. Each part had to sign particular musical fragments in turn.

Pope Gregory I (590-604 A.D.) standardized ecclesiastical singing that eventually was named “Gregorian chant” in his honor. Gregorian chant is the basic element of modern catholic services. Spread of unclerical music in Middle age was implemented by wandering musicians (bards, minstrels etc.). Folk musicians were illiterate. Goliards and vagrants were literacy teachers in artistic environment. They were unsuccessful bishops and students who despised Church and its laws. “Carmina Burana” is the most famous collection of unclerical medieval music and contains songs that describe events of Migration Period. There are many medieval music bands nowadays (In Extremo; Saltatio Mortis; Corvus Corax etc.). They play different genres of medieval music (folk, rock, metal) and are very popular around the world. “Symbiosis” of church and temporal traditions of musical composition in Middle age became a turning point in history of music in general. Art of this “mutual” kind was created for pilgrims to replace folk songs that weren’t godly enough for performing in monastery. “Llibre Vermell de Montserrat” contains vivid song samples of mentioned type. They were composed on junction of two eras and symbolize moving of humanity from Middle age to Renaissance.

SECTION № 19

PEDAGOGY AND PSYCHOLOGY

THE ROLE OF LEARNING THE “CLINICAL PHARMACY” DISCIPLINE IN THE PRACTICAL ACTIVITY OF FUTURE PHARMACISTS

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Clinical pharmacy, as a branch of pharmaceutical industry, according to its purpose, establishes the theoretical foundation and is the practical basis of pharmacist professional activity during realization of consultation work among medical specialists and population regarding issues of individual rational therapy. Participation of pharmacist in the process of treatment, from the drug assignment to the estimation of distant consequences, after the end of medication intake, encourages the timely availability of high-efficiency drugs for patient, establishment of rational routes of administration and dosage regimens, prevention of incompatible medications assignment, minimization of indirect drug action, and also decrease of polypragmasy. Knowledge of fundamentals of internal medicine, clinical pharmacology principles, issues of interaction of medications from different pharmacological groups is the very thing that allows a pharmacist to provide pharmaceutical care in the most effective way during assignment to patient OTC-drugs (at a pharmacy) and prescription medications (in hospital conditions).

The discipline “Clinical Pharmacy” is integrative and combines the pharmaceutical and clinical aspects of pharmaceutical science. Its main task is the creation of reliable theoretical principles and methodological approaches of rational use of medicines. This discipline is the theoretical and practical foundation of forming the professional activity of a pharmacist during realization of consultative work among doctors and population regarding issues of rational medicinal therapy. The value of the discipline “Clinical Pharmacy” in future practical activity of pharmacist is rising, coming from the following trends of industry progress. Practical medicine, passing to the formulary system, needs the individual approach to medicines selection. New knowledge regarding to pathogeny of diseases, medical standards regarding to their diagnostic, prevention and treatment in the last few years have established the requirements not only to physicians but also to pharmacy specialists, which must have systematized knowledge about major diseases occurring in pharmacist practice.

PSYCHO-PEDAGOGICAL CONDITIONS OF FORMATION OF STUDENTS' MOTIVATION WHEN STUDYING THE SUBJECT OF "PHARMACOLOGY".

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Motivation of students' learning activities is one of the most important factors of effective implementation of the educational process. In order to identify the psychological and pedagogical conditions of motivation when studying the subject "Pharmacology" at the Department of Pedagogy and Psychology of the NUPh has been research conducted. The results showed that as the following conditions should be considered such as: provision of teaching learning activities to stimulate students learning activities, organization of training activities based on gaming technologies and the formation of collective students group.

The work identified ways to implement psychological and educational conditions. To implement the conditions to ensure the teaching learning activities to stimulate students the advice of a psychologist, which included a range of techniques to encourage students to succeed academically was used. Formation of training activities was conducted with activation of positive teacher's interaction with students.

Among the ways to implement the conditions for the organization of learning activities based on gaming technologies we have identified, the following:

1. Using gaming devices in the students learning activities (crosswords, scanwords, themed tasks, slovohrams, chaynvords).
 2. The use of gaming technologies in the course of practical training (conducting situational role-playing, group discussions , etc. .).
 3. Using creative situations during practical lessons based on game design.
- Ways to implement terms of the impact of the collective students group on motivation of students to study included:

1. Revitalization of the supervisor to ensure the formation of the group.
2. Trainings to influence the cohesion of the group as a collective.

Experimental verification of implementation of these conditions in the educational process of the subject "Pharmacology" allowed to have a positive impact on the formation of learning motivation of the students. Thus, the motive of obtaining deep and sound knowledge increased by 21.74 % of the students of the experimental group compared with the control one. Further research will be aimed at identifying measures to specify the ways to implement psychological and pedagogical conditions of student's motivation in learning.

PHYSICAL EDUCATION PROGRAM IMPROVES STUDENTS' EXECUTIVE ATTENTION

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Regular physical exercise improves cognitive functions throughout the life span. In particular, executive functions (EFs) that are highly important for learning achievement can be improved by physical activity. Because exercise interventions in early childhood programs and schools can be effective in enhancing school readiness and academic success through their influence on EFs, it is important to study possible beneficial effects of school sports programs in this age groups.

Executive Functions and Learning Achievement

EFs are of major importance for learning achievement in content areas such as language, mathematics, and science throughout the school years. Working memory stores about seven elements (such as words, objects, and numbers) for only a few seconds. Moreover, working memory allows operating with short-term stored information. Working memory is also needed to retrieve long-term stored information. Behavior is thus not only induced by current but also by (reactions to) earlier information. A functioning working memory is therefore a precondition for goal-directed behavior.

In physical education (PE), for instance, students with high self-regulatory skills are much less willing to foul teammates in order to reach a victory. Self-regulation that supports positive and suppresses disruptive emotions is an important key to success in life, and successful goal-directed and self-regulated behavior enables students to put their knowledge to appropriate use. An additional element of EFs is cognitive flexibility that is based on inhibition and working memory. Cognitive flexibility is the ability to react on altering conditions and demands. Cognitive flexibility supports the taking up of different perspectives respectively to switch between different perspectives, and therefore to think and react in a flexible way.

Executive Functions and Physical Activity

EFs can be improved by acute and chronic physical activity (especially aerobic endurance exercise) in populations of depressive patients, in healthy old and young adults as well as in preadolescents and adolescents. One possible mechanism for improving EFs by physical activity could be based on changes in brain chemistry. EFs are influenced by transmitter systems such as dopamine and serotonin. Physical activity influences central dopaminergic and serotonergic systems. Aerobic endurance exercise, when carried out for approximately half an hour and longer leads, first, to a lipolysis-elicited increase in blood-free tryptophan.

Indeed, studying the effects and benefits of physical activity and physical performance in students is a promising research area because school and therefore PE are mandatory for students. Furthermore, because EFs are of major importance for students' learning achievement, it is essential to clarify to what extent EFs can be improved by school sports programs of different duration and intensity. Today, compared with other school subjects, PE is still given a low level of attention especially with regard to the promotion of academic achievement.

Objective - theoretically and experimentally justify the use of physical education in higher education for improving students' executive attention.

Methods: theoretical analysis and synthesis of the literature; anthropometric methods, physiological methods of research; teacher testing; psychophysiological research methods;

Two different exercise programs were standardized for the study. The PE program consisted of a 30-min predominantly aerobic endurance exercise session. This treatment condition was executed by the PE teachers and was focused on exercise intensity of students' individual performance. In the control condition, students were listening to a 30-min audio book. The MB was also an aerobic endurance exercise session but with a duration of only 5 min. In the control condition, students watched the other students taking part in the 5-min MB. Initially, the teachers were introduced in the PE program and in the MB program.

DISCUSSION

In our study, we showed that a single PE program of 30 min leads to an improvement in the maintenance of ontask attention in the face of distraction. This in turn may support students' selective, sustained, and focused attention processes.

We further suggest that a possible increased synthesis of serotonin after the 30-min PE program may directly lead to an increased serotonergic tone and consequently to the improvement in the incongruent condition of the flanker task. Study results suggest that a serotonergic modulation in the prefrontal cortex occurs simultaneously with decreased impulsivity to increased attentional selectivity

Our study results provide arguments for an increase in PE and suggest that PE should be scheduled before important subjects like mathematics and not at the end of the school day, as is often the case. Because students' physical fitness seems to be more relevant than an acute bout of exercise for improving students' EFs, this further strengthens arguments for more PE because higher fitness could not be achieved with short MBs. Short MBs could have effects on cognitive functions if they include coordinative exercises of 10 min; or, if they are highly intensive (two sprints of 3 min. However, if one wants to expose students to high-intensity physical exercise, they should be well trained. This argues again for more, ideally daily, PE lessons

It is worthy of further investigation.

IMPLEMENTATION ACTIVE LEARNING METHODS IN THE STUDY OF THE HUMANITIES IN HIGHER EDUCATION

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Among the main conditions that determine the effectiveness of the teaching - learning, a special place is occupied by teaching methods because they directly determine the form and nature of the relationship of teachers and students significantly influence the formation of relationships between them. The nature of the relationship between teacher and student defines a paradigm of the national education system, the entire focus of the educational process.

In recent decades, under the influence of general didactic science, educational psychology and humanization and democratization of education created modern active learning methods were created, called in didactics active methods of teaching and learning activities. The use of active methods in the learning process can improve the effectiveness of learning activities of students. When it refers to the purposeful activity of the teacher directed the development and implementation of methods, tools and learning that would enhance the skills of productive communication in terms of the learning process , the development of skills to argue complex situations, identify major and minor , their causes and find ways and means to solve them, the development of mental processes (attention, memory, thinking), maintaining a constant interest and motivation, independence, and the ability to predict the development of different situations and make decisions. The ability of the teacher to reveal the internal resources of the student, using active methods of teaching can provide constructive changes in education, helping the young person to assess their skills and capabilities to properly define their place in life and open the way for him to carry out a full career.

So, based on the foregoing, we have set a goal of research - theoretical basis and experimentally verify the effectiveness of the use of active learning methods of teaching principles in the study of humanities.

This study used the following methods:

- Theoretical: Analysis of psychological, pedagogical and educational literature on the study, study and theoretical understanding of the experience of academics;
- Empirical: monitoring training activities of students, surveys of teachers and students, analysis of written work of students and their responses in the classroom;
- Pedagogical experiment, qualitative and quantitative analysis of its implications.

Analyzing psychological, pedagogical and educational literature, conducting monitoring of training activities of students: answers to exercises, written work, came to the conclusion that it is active learning helps to keep students to generalize and develop their independence of thought, teach important to highlight the learning material, develop speech. Active learning methods are also helping to train and develop students creative thinking, generate them appropriate practical skills and knowledge, to stimulate interest in and increase employment, enhance and sharpen the perception of educational material.

In practice, teachers of humanities harbor such as active learning case study, Timelines, Socratic Method, "brainstorming" ("attack"), teaching and thematic discussion, role play, professional game, professional consultancy, organizational and active play.

Summarizing all the above, we note that the use of active learning methods in high school in the study of humanities is a prerequisite for training highly qualified specialists and leads to positive results: they can generate knowledge and skills of students by involving them in active teaching and learning activities as educational information goes into the personal knowledge of students.

FACIAL ASYMMETRY AND HUMAN BEHAVIOR TRAITS (EXTRAVERSION/INTROVERSION AND NEUROTICISM)

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The face plays a crucial role in human social cognition. Facial expressions are important signals of internal states – emotions and intentions. Humans also see in the face signals of internal qualities that are more stable over time, like attractiveness as a mate or dominance, etc. The belief that the face reveals information about underlying character cuts across national, cultural and geographical boundaries. Widespread interest in physiognomy – the study of the face and its relationship to human ability, potential and character – peaked at the end of the eighteenth century when a physician and pastor named Johann Kaspar Lavater produced a formal classification system and set of rules specifying the relationship between the face and the mind. Among contemporary applications of face analysis not only psychological interpretations are accomplished, but also medical results are obtained. For example, more than 700 genetic issues influencing facial structure and facial features are known, and special software for disease identification from face had been developed.

The aim of the current research was to evaluate relationships between facial asymmetry and extraversion/introversion and neuroticism (two axis of human temperament) in a sample of Ukrainian people. The expression of extraversion/introversion was measured in points: >19 – a bright extrovert, >15 – an extrovert, 12 – the average value, <9 – an introvert, <5 – deep introvert. The expression of neuroticism was measured in the same way: >19 – very high level of a neuroticism, >14 – high level of neuroticism, 9 to 13 – the average value, <7 – low neuroticism. Among males and females the mean levels of an extraversion were 13.2 and 13.6 and the mean levels of a neuroticism were 13.4 and 13.8.

It was shown, that only in males one statistically significant correlation coefficient was found. Particularly, r between neuroticism and ratio of a measurement difference between the wings of the nose of the right and the left side related to a face midline to the measurement of the wings of the nose of the right side related to a face midline ($r = -0.50$, $p < 0.05$). So, in this context, facial asymmetry is not of medical importance and does not reflect a negative trend for to some extent clinically significant neuroticism.

FEATURES of ADAPTATION of STUDENTS-FRESHMEN of MEDICAL COLLEGE

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For the modern system of medical education the problem of educational adaptation of students-freshmen of higher educational establishments goes out on the first plan I - II levels of accreditation. In fact from passing by them to educational adaptation personality development and achieving of future physician will depend in a great deal, that in future will affect forming of professional career.

With the purpose of research of features of passing of adaptation of students of the Kharkov base medical college №1, a questionnaire was conducted of 197 students by counsels . This job performances allowed to do next conclusions. In the number of most difficulties on the way of adaptation to the new educational terms 157,6 % of students marked the growing volume of the educational loading. The new system of evaluation caused problems for 188,2 % of students, complication of mastering of new educational disciplines marked 98,5 % of respondents. Problems in relationships with comrades on studies arose up for 59,1 % of students, and lining up the new system of relationships with teachers was caused by complication at 39,4 % of those, who took part in a questionnaire. Thus only 78,8% of freshmen regard, that they need a psychological help in the decision of adaptation problems. First of all it is needed at overcoming of stress before the first session, including in a new collective, decision personality problems. At the same time it was educed on results the same research, that 59,1% of all polled freshmen categorically deny the necessity of psychological help. Among respondents there was 59,1 % of such, who had difficulty with an answer for this question.

Further researches will be sent to the exposure of pedagogical terms of successful adaptation of students-freshmen in a medical college.

PEDAGOGICAL TESTING – ADVANTAGES AND PROBLEMATIC OF THE APPLICATION

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Nowadays, in the context of the credit-module system of the educational process, it is hardly possible to find a teacher who does not understand that pedagogical control and students ratings are crucial tasks.

The main intention of this work is to reveal positive sides of the rating process and to describe the problematic associated with rating system for validation of student's achievements.

It is important to note the presence of experience in employment of pedagogical tests in Kharkov National University of Pharmacy and Kharkov National Medical University. This experience shows that first of all pedagogical tests attract educators by its novelty compared to traditional rating forms. In second place, pedagogical tests stimulate students to study systematically since it is an inevitable or a necessary form of control. Teachers work hard to instill education's most enduring and profound rewards: self-confidence, academic growth, joy in learning and intellectual curiosity. In third place, testing creates a unique motivation for learning based on healthy competitiveness and strong focus on achievement. Finally, systematic testing allows to modify the final form of the pedagogical control mainly emphasizing on learning skills and higher level of the knowledge. Also, it creates a system of current grade for every student, which permits to make the final control more effective, objective and sometimes an automatic pass.

There are numbers of fundamental differences of pedagogical test from other methods of the pedagogical control. Pedagogical test is a scientifically aproved method of empirical research. It permits to eliminate conceptual evaluation of the student's knowlege. The most important distinction of pedagogical tests from other pedagogical task is its processability. It means that each test question has a clear

unequivocal answer and rated standardly based on the answer. Processability realizes completely in the implementation of automatic system of the test control and assessment.

The aspects of pedagogical tests mentioned above enable to formulate one of its advantages. The pedagogical test allow to grade all students on all questions of educational material under the same conditions using previously developed objective rating scale without any exception. That's exactly what aspires to improve the pedagogical control. Why pedagogical tests are not so widely used in teaching practice? What is the problem?

First of all, we can talk about conceptual problem that defines an ambiguity of opinions for possibility of applying pedagogical tests for comprehensive evaluation of the student's knowledge. This is due to the fact that tests narrow the possibility of assessing student's logical thinking and argumentativeness of their decisions. Next problem is the evaluation of test results. Which aspects have the most impact on test result: the quality of students' knowledge or the quality of development of pedagogical tests? This question remains unsolved. Had all levels of learning been taken into account? This question causes the necessity of test quality assessment not only by some statistical characteristic, but also by their complexity. Last evaluation requires repeatable approbation and correction before appliance in pedagogical practice.

Thus, advantages of pedagogical tests listed above and implementation problem into pedagogical control appear worthy of more close attention and research. Also, it should be noted that application of pedagogical tests should not have self-sufficient value. It should be combined with other forms of pedagogical control. These are the massive opportunities for creative activity of professional educators.

MORPHOMETRIC ANALYSIS OF FACIAL ASYMMETRY

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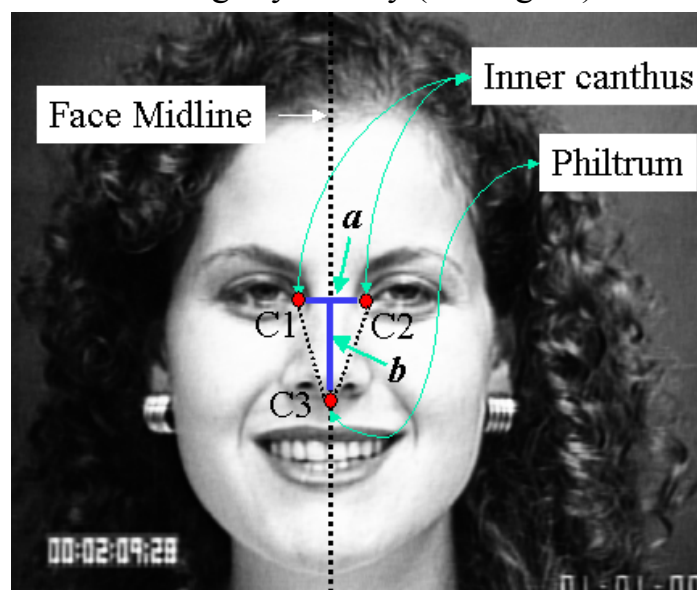
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Studying bilateral asymmetry in vertebrate organisms is carried out for a long time and involves various types and characteristics: dental and behavioral traits in humans, rats and mice; skull peculiarities in rats, cats, rhesus monkeys and humans, skeletal elements in mice and birds, sexual ornamentals in birds etc. One of the first classifications of symmetry and asymmetry was given in 1962 by Van Valen. He demonstrated three types of asymmetry to be: directional asymmetry, fluctuating asymmetry and antisymmetry. All asymmetries can be measured as a size difference between the left and the right sides of the body. Fluctuating asymmetry is often referred as minor variations of morphological landmarks from a perfect symmetry. Examples can include any signs of bilateral animals and plants. Directional asymmetry reflects a characteristic deviation which is constant within a species and can be seen as a greater development of the body in one side comparatively to the other (for example, dominant left and right position of the heart/liver in humans). Antisymmetry is expressed with a bimodal distribution curve R-L differences around zero. Examples of an antisymmetry in the nature can be observed in the development of signaling claws in a male crab. Both left and right claws can be signaling with an equal chance, and it is impossible to predict it.

An interest to the study of fluctuating asymmetry is high because it can reflect the instability of ontogenesis. Yet not all possible causes are known. Facial asymmetry is a kind of fluctuating asymmetry (see Figure).



The aim of the current research was to obtain morphometric characteristics of facial asymmetry in a sample of Ukrainian people.

85 people (24 males and 61 females) were enrolled. All participants were photographed or provided their high resolution photos. From a face midline to left and to right the following indexes of facial morphometry were measured: the distance to the inner corner of the eyes, the distance to the outer corner of the eyes, the distance to the wings of the nose and the distance to the corner of the lips.

Due to the fact that the absolute size of various images was different in some participant photos, all measurements were adjusted to a uniform scale by using ratios of a measurement difference between the same distances of the right (D_r) and the left (D_l) side to the measurement of the right side. So, relative indexes of asymmetry were further used. The results obtained have shown that all distributions were related to standard normal distribution (Table).

Table

Results of a distribution checking by Kolmogorov–Smirnov (D-value) and Shapiro–Wilk (W-value) tests

Names of relative asymmetry measurements	D-value and p	W-value and p
$(D_{r, \text{inner corner of the eyes}} - D_{l, \text{inner corner of the eyes}}) / D_{r, \text{inner corner of the eyes}}$	0.095, $p < 0.05$	0.963, $p > 0.05$
$(D_{r, \text{outer corner of the eyes}} - D_{l, \text{outer corner of the eyes}}) / D_{r, \text{outer corner of the eyes}}$	0.05, $p > 0.05$	0.967, $p > 0.05$
$(D_{r, \text{wings of the nose}} - D_{l, \text{wings of the nose}}) / D_{r, \text{wings of the nose}}$	0.075, $p > 0.05$	0.987, $p > 0.05$
$(D_{r, \text{corner of the lips}} - D_{l, \text{corner of the lips}}) / D_{r, \text{corner of the lips}}$	0.075, $p > 0.05$	0.987, $p > 0.05$

Note. The statistical significance is stated comparatively to alternative hypothesis.

Levene's test had shown the equality of variances, and ANOVA has shown the equality of mean values for all morphometric traits calculated for males and females. The Pearson correlation coefficients demonstrated that a relationship between different morphometric indexes was only direct both in males (r from 0.53 to 0.81) and females (r from 0.35 to 0.86).

So, the results demonstrated that some facial asymmetry is present in both males and females, but no sex differences were found between males and females in morphometric indexes of a face asymmetry. A facial asymmetry is a typical quantitative trait with a normal (Gaussian) distribution. The tendency to one-side asymmetry (right or left) of all measures was found in both males and females.

IMPLEMENTATION INTERAKTIVE METHODS OF TEACHING MATHEMATICS

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Interactive teaching is a form of organization of cognitive activity that has a specific prescribed purpose - to create a comfortable learning environment in which every student will feel his need, will discover his abilities and demonstrate proficiency in the subject, to feel confidence.

During interactive teaching learning process is carried out by continuous active participation of all students. Interactive teaching requires each student's the ability to communicate with one another, to think, to make decisions. Depending on the interactive forms student learns to process information, make reference circuits, algorithms and notes, imparting his knowledge to others, express his opinions, solve a variety of different levels and make the task to evaluate his own work and his other students.

Learning mathematics is also of great importance to the scientific perception of the world, to develop creative, intellectually developed person. The modern educational system of mathematics education requires improving the methods of teaching mathematics. You must provide the student store of knowledge through interaction with the teacher, with other students, with the group, while interest in employment and increase its effectiveness. Therefore, we believe that the subject of our research to date is relevant.

Objective: to identify and justify the use of interactive teaching methods in the classroom for math in high school I and II accreditation levels, improve and enhance teaching and learning of students.

At various stages of the study, the following methods:

- Theoretical - analysis of psychological and educational research literature on the subject of research to uncover the concepts of "interactive teaching", "interactive methods", classification and systematization of theoretical and experimental data, analysis and synthesis of interactive methods in terms of the feasibility of their use in the educational process.

- Empirical - methods of mass gathering information (surveys, tests, interviews, pedagogical supervision), which contributed to the study of the problem; pedagogical experiment.

- Methods of processing the results of research - comparative methods, quantitative and qualitative analysis.

After analyzing a number of scientific and technical literature, my own experience of teaching mathematics, experience of colleagues, we concluded that the introduction of interactive teaching methods helps to activate learning, positive impact on various areas of future professionals, provides a high level of communicative activities in the performance of tasks forms the collective skills of cooperation makes it possible to combine theoretical knowledge with practical activities.

The introduction in the educational process, particularly in teaching Mathematics interactive teaching methods contributes to a culture of debate, the ability to make joint decisions, the ability to communicate, to report. Interactive teaching methods also allow students to act as authors, creators, raise the level of practical knowledge of the material forming the skills of self-employment, provide non-standard lessons, and make creative, fun, exciting and effective lessons.

As the results of the study, it is appropriate for classroom use in mathematics interactive methods such as "Brainstorm", "Circle of ideas", "Troubleshooting", "Find Error", "Finish this sentence", work in groups, pairs.

After the introduction of interactive methods can state the following changes: deepened motivation, increased activation in the classroom, students have acquired cultural debate, evolved the ability to make joint decisions, improved ability to communicate, report, has changed the level of perception - it became personal meaning, rather than "learn", "remember" has become "consider", "apply", has changed the main level of mental operations - analysis, synthesis, generalization, abstraction.

Interactive methods of making the educational process varied, interesting and effective and the most useful in this study is that students begin to like Mathematics.

REACTIONS TO FACES OF INDIVIDUALS WITH DIFFERENT MEDICAL CONDITIONS: POPULATION ASPECT

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The study of reactions to different types of human faces is of a special interest to psychologists, psychiatrists, criminologists, anthropologists, ethologists, sociobiologists, image-makers, personnel of marriage agencies etc. Based on faces with different behavior deviations, a lot of diagnostic procedures are developed. Some of them are based on picture response evaluations. Leopold Szondi is a Hungarian psychiatrist who suggested one of such methods known as Szondi test. It is based on portrait choices of people with some mental conditions. Szondi approach is applied in the current paper.

A face plays a critical role in a subject's acceptance by other people, because it's the most exact external identification characteristics. Initially, Szondi test was used in clinical practice. Szondi considered that people could be diagnosed by prevalent "attraction" to the portraits of individuals with specific disorders. It was suggested that the prognosis of a disease progression could be estimated in such a way. Currently, these speculations are considered to be not scientifically ground, and that the diagnostic value of the procedure is doubtful. Nevertheless, application of Szondi test for other non-diagnostic purposes are not rejected if specific types of individuals will be concentrated in groups of certain behavior deviations.

Szondi test was rarely used for a general population study. Recently, Hungarian and Portuguese community samples were analyzed for their reactions to Szondi's portraits. The aim of the current study was to receive distribution characteristics of reactions to faces of people with different medical conditions and peculiarities in population of Ukrainian megapolice Kharkov (eastern Ukraine).

The aim of this research is to study population-related distribution of certain aggression types among the population of Ukraine in two successive generations.

355 volunteers (90 males and 265 females) participated in the research. All participants lived in Ukraine and were Slavs (predominantly Ukrainians and Russians). Most of them were Kharkiv city residents and were students of schools, colleges and universities. The study design was cohort and cross-sectional.

The following results were obtained from the population distribution of different portrait type reactions and analysis. Both males and females found pictures of individuals with some behavior peculiarities more or less attractive. Nevertheless, no

sex differences were found for four portrait type reactions out of eight disorders. Similar male and female face reactions were described as well for Hungarian and Portuguese community samples. These findings were a ground to combine males and females to one group for a further analysis.

Volunteers responded in the most tolerant way to faces of individuals with mania disorders. So 54% of participants considered that faces of patients with these mental disorders are less unpleasant, comparatively with faces of other individuals in portraits. For comparison, it should be mentioned that respondents from a general population in Hungary and Portugal had very similar rate of positive response to faces of maniacs. The second place on tolerability in Ukraine belongs to faces of individuals with homosexuality. Positive reactions to homosexual faces were found in 41% of cases. About 1/3 of respondents tolerantly perceived the faces of individuals with epilepsy and paranoid schizophrenia, about 1/4 – responded to faces of individuals with hysteria disorders and sadists. The faces of patients with depressive disorders and catatonic schizophrenia were less pleasant to respondents.

The results obtained, herein, may help to explain famous criminology and psychology phenomena. For example, many maniacs and serial killers are able to attract a potential victim. It is easily explained by data obtained that an evident hostility to faces of individuals with mania disorders is rarely observed. Among Ukrainian sample under examination, only 12% of respondents disliked the faces of people with mania disorders.

33% of individuals expressed null reaction to faces of sadists. These people can potentially form a group risk on face, differentiating difficulty of normal individuals and those who are predisposed to violence. But this will be true only if associations between specific phenotypic face features and personality traits are proved.

About 4/5 of respondents did not express attraction or did not react at all to faces of individuals with depressive disorders. This may partially explain why these subjects are lonely. In such a situation of a lack of attention and support of other people, their relative isolation may facilitate suicide attempts completely.

The current study of Szondi test was applied not for diagnostic purposes. It was found out that there were found no sex and age differences in individual reactions to portraits presented. The results obtained can contribute to facts described by other scientists such as reactions to faces with different mental conditions and hence, serve as a control for studies conducted with diagnostic aim.

POPULATION DISTRIBUTION OF AGGRESSION TYPES AMONG UKRAINIANS

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The number of works devoted to biology of aggression in both animals and human is enormous. It has been recognized that a human in terms of his biological natures is an aggressive creature. This aggression has been evolving during evolution of *Homo sapiens* as of a biological species. It is believed that inherent for a human are both pro-social behavior with its utmost trait of altruism and antisocial behavior with its utmost form as aggression. Aggression of a human is a species characteristics which means that a human possesses physical, cognitive and emotional systems capable for inflicting intentional harm to others. In animals and in humans aggression is an inborn response to potential threat or provocation. This conclusion is based on the researches of outstanding ethologists, anthropologists and psychologists: C. Laurentz, E. Wilson, S. Freud, R. Baron, D. Richardson etc.

Apart from aggression which is typical to all the members of population antisocial behavior generally includes psychological disorders in particular psychopathy, antisocial personality disorders diagnosable in 5-10% of population as well as offensive patterns of behavior demonstrated by 20-30% of population. The variants of antisocial behavior interpretation by psychologists, psychiatrists and criminologists are highly inter-correlated. For this reason the behavioral genetics often most researches both antisocial behavior as it is and its individual components like aggression. Knowledge of the nature of aggression, genetic control of its physical and biochemical processes we can find a means of positive aggression control.

The aim of this research is to study population-related distribution of certain aggression types among the population of Ukraine in two successive generations.

The research covered 2305 people of Ukraine aged 14 to 72 from Kharkiv City and Kharkiv region mostly who gave informed consent for questionnaire survey.

The information was collected in compliance with ethical standards of communication. The questionnaire gave social and demographic information. The probands were 741 men and 1501 women. The researched population comprised 74 married couples, 105 couples of siblings and 352 parent-child couples, 1174 peoples were researched with no relative. The groups were formed depending on the task of research. One group included the persons aged under 35 with the youngest one being 14 years old. The second group included the people who are more than 35 with the oldest being 72 years of age. The average age of the examined from younger generation was 19.3 ± 0.1 years old ($s = 3.8$), modal age was 17 years old and medial

age made 17 years old. Among the older generation respondents the average age was 43.8 ± 0.3 years ($s = 7.2$), the modal age made 40 years and medial age was 42 years. The difference between the average ages of younger and older generations of respondents is 24.5 years which corresponds to the time segment equal to one generation in terms of genetics.

Different types of aggression were assessed under Buss-Durkey Inventory.

Verification of data for compliance with the law of normal distribution in big groups ($n > 30$) was made by the method of Kolmogorov-Smirnov. The parameters of symmetry and excess with subsequent verification of zero hypothesis about their equaling to zero were calculated. Comparison of two groups arithmetic average was accomplished by Student method. The conclusion on statistical hypotheses was made at $p \leq 0.05$ level.

The database was formed with Microsoft Excel software. The calculations were made in Microsoft Excel и Biostat software.

Study of population distribution in terms of behavioral features is not only a means of behavior polymorphism assessment but rather an essential preliminary stage of genetic analysis, determination of population incidence, risks, etc. It was found that distribution of aggression is mostly normal. The signs of sexual dimorphism and cohort effect were revealed which are related to the disparities between generations. For example physical aggression is more common for men of both generations. There are signs of verbal aggression and negativism among older generation. On the whole in terms of the majority of aggression types the differences between generations are traceable among women only.

Some scholars explain aggression from the evolutionary point of view. According to this view the people having common genes tend to show less aggression towards each other.

The analysis of aggression types in terms of different population has shown that distribution of the most of these types correspond to Gauss' Law. Defining the character of behavioral features distribution will make it possible to select the proper methods for assessing heritability coefficients in the subsequent genetic analysis. The value of gender differences was in average 10% of the range of features deviation. More significant differences between representatives of different generations were fixed among females.

THE IMPORTANCE OF THE SUBJECT „CLINICAL STUDY OF PHARMACEUTICALS” IN PRACTICAL TRAINING OF CLINICAL PHARMACISTS

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The main task of national health care at the present stage of its development is the improvement of care delivery and access, including provision of medicines. The solution of this task requires the increase of clinical pharmacist's status and level of responsibility. In this situation the importance of pharmacists in the general system of national health care substantially increases, because the main goal of pharmaceutical aid is the provision of medical therapy reliability in order to prolong patient's life time and improve quality of patient's life. As such, the inclusion of subject „Clinical Study of Pharmaceuticals” to the clinical pharmacist training program in National University of Pharmacy is methodologically reasonable, and its teaching in the conditions of real clinic carrying out clinical research is an organizationally rational approach to the solution of this task. In the process of studying the subject students get familiar to the principles of drug trials and GCP, methods of proving of pharmaceuticals efficiency and safety, clinical trial document. They acquire the skills of finding and registration of adverse effects of pharmaceuticals, assessment of clinical information quality, methodology and criteria of information selection; they also learn how to analyze and interpret data obtained and further implement it in patients' treatment.

Obtained knowledge is useful in detection of clinically and economically effective pharmaceuticals, data concerning effectiveness and safety obtained by methods of evidence based medicine. It permits engaging the pharmacist to creation of pharmaceutical formularies in order to form risk-benefit strategy at selection of medicine for every patient. Clinical pharmacist ability to advice doctors and patients on interpreting the data of complex clinical trials and its use at individual medical treatment is of the highest importance as well.

Thus, studying the discipline „Clinical study of pharmaceuticals” allows training of a clinical pharmacist in the area of clinical research with respect to modern requirements, gives him a possibility to participate at the professional level in forming of drugs administration policy, to cooperate with professionals in the process of preparation of textbooks and guidelines on treatment of diseases, to take part in procurement and distribution of pharmaceuticals.

FOOD PREFERENCES IN THE POPULATION OF UKRAINE

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Human food choice is conditioned by a number of factors. A human being has genetically deterministic systems underlying the taste evaluation of innate preferences for sweet, salty and fatty food. Sweet food is a fast and easily accessible source of energy. Taste sensitivity to sweet food is an evolutionary advantage for all kinds of animals. A certain amount of a table salt is necessary for normal functioning of the body, particularly for functioning of excitable tissues and maintenance of buffer properties of a blood. Less obvious, but still consistently present innate preferences for fatty food may be explained by the necessity of lipids for a myelination of nerve fibers, ensuring the synthesis of sex hormones and sexual behavior, formation of cell membranes, solubility of a number of vitamins, elevation of the organoleptic properties of the food. In a modern society these initially useful food preferences have moved beyond their adaptive borders, promoting the development in the population of a number of metabolic disorders, such as diabetes mellitus, obesity and mental disorders. The lack of genetic and population studies in the field nutrigenetics in the population of Ukraine, as well as overburdenness of a population by the genetic load on the “diseases of civilization” dictates the need for these studies.

Food preferences were studied in 288 Ukrainian inhabitants, mainly from Kharkiv and Kharkiv region. Food preferences were studied by special interviewing, which places the examinees under the conditions of the equal accessibility of food, lack of hunger and an opportunity to choose several food categories. As the food groups seven following groups were chosen: sweet (high-calorie carbohydrate group), meat (protein group), fruit (cellulose and vitamins), salty food (the source of NaCl), first vegetable courses (cellulose and vitamins, “healthy” food), fast food (“junk” food containing food additives, colorings, preservatives), fatty food (the source of essential fatty acids, high-calorie food).

45.5% of examinees detected the compatible food preferences. According to the relative order by individual food preferences, the examined groups were allocated in this way: sweet, fruit, meat, “fast food”, fatty food, first vegetable courses, salty food. The comparisons were carried out in preferring and non-preferring groups, which were called “testers” and “not testers” accordingly. It was shown that with an

age there was a decrease in preferences for sweet and fruit for males and “fast food” group for females (Table).

Table

The correlation coefficients (r) between food preferences and age

Food group	Males (n = 66)	Females (n = 222)
Sweet	-0.25* ± 0.12	-0.10 ± 0.12
Fruit	-0.30* ± 0.12	-0.07 ± 0.12
Meat	-0.02 ± 0.12	0.03 ± 0.12
Fast food	-0.06 ± 0.12	-0.33** ± 0.11
Fatty food	-0.08 ± 0.12	-0.04 ± 0.12
First vegetable courses	-0.08 ± 0.12	0.10 ± 0.12
Salty food	-0.20 ± 0.12	-0.06 ± 0.12

Note. - n – the number of examinees, $r \pm Sr$ – the biserial correlation coefficient and its statistical error. The difference between the correlation coefficients of people of the opposite sex is not significant in all cases.

It is obvious that in the population sample under study there is a tendency of decreasing of food preferences for sweet with age. It can be considered as a risk-reduction factor of obesity in this age group. The studies in the field of the obesity correction by the opiate antagonists, naloxone and naltrexone, selectively reducing the consumption of chocolate, are known. The age-related decrease in food preferences for fruit, the source of vitamins and cellulose, appears as the unfavorable trend among Ukrainians. It is known that many fruits and vegetables, for example, grapefruit, green tea, brussels sprout and soy products contain phytochemicals with the oncoprotective activity. These particularly include citrus flavonoids, green tea and red wine polyphenols, cruciferous vegetables glucosinolates and soy products isoflavones. The statistically significant differences in preferences for fruit and first vegetable courses between persons of different sexes were found. Thus, every fifth male and only every fifteenth female in the absence of tangible hunger prefer first vegetable courses, which we referred to the category of “healthy” food. At the same time the sex differences concerning fruit testify that half of all females and a third of males prefer this food category.

Thus, in general, in the population of Ukraine the highest preferences for sweet food, fruits and meat has been revealed. A negative correlation between the age and preferences for sweet food and fruit among males and “fast food” group among females have been found out. More evident preferences for fruit among females and for first vegetable courses among males has been shown.

ORGANIZATION OF INDEPENDENT WORK OF STUDENTS OF MEDICAL COLLEGES IN THE STUDY OF A FOREIGN LANGUAGE

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Of particular importance in the context of the Bologna Process takes to improve the system of independent work of students, which should play a major role in the training of future professionals and to develop their skills and readiness for professional learning.

Analysis of research to determine that the individual work required at all stages of education: at the stage of acquiring new knowledge and the repetition stage, securing and using them in practice.

Organization of independent testing work should consider two important aspects:

- 1) the subject of the educational process in higher education;
- 2) the specific academic subject "Foreign Language" .

Independent testing work is leading students learning a foreign language, which develops the skills of independent research and information work, increases research and creative activity of students engages them in depth study of the achievements of advanced science and use of these advances in everyday activities. She points to a great education and the educational value of independent work that contributes to the creative skills of research students, needs a lot of knowledge and skill to manipulate and use in practice.

The main objective of self-study practice for learning a foreign language in high school is to achieve an appropriate level of language proficiency that allows fluent in technology transfer and scientific skills of rapid reading of literature, specialty and training graduates able to work independently and effectively with others sources of information upon graduation.

Through independent testing work students have the opportunity to experience the joy of receiving the information exchange and its ability to use it in

their future careers, by the help of favorable conditions for the formation of the professional as a specialist, the psychological and practical readiness to perform its major professional functions.

For successful students work on assignments in specialty instructor should be somewhat familiar with the contents of this specialty and foreign literature by profession, to use a system of pedagogical influence to achieve specific educational goals.

The main task of the teacher is reduced by the development of objects with which the student has to work, and to create the necessary conditions self-activity, student self as a person that allows himself to identify additional learning objectives.

New organizational forms of self-study, in addition to the traditional performance of independent action with lyrics - participation in conferences, seminars, meetings of scientific societies and student research work.

The content material that is offered for independent study should be interesting, informative, emotive and not leave indifferent students. The ability of young people to creatively process information is one of the main criteria of the future specialist training to work after graduation.

Thus, through the effective use of leading learning and purposeful exchange of information on verbal-logical level of the students observed sustained motivation to further improve the knowledge of a foreign language. It's clearly reflected in the planning of conscious self-study students with foreign language texts vocational guidance , the ability to actively use their knowledge of a foreign language in the communication process outside the learning process that will help them self-activity, mobility and allow themselves to identify additional learning objectives .

SECTION № 20

**PSYCHO-PEDAGOGICAL FUNDAMENTALS OF FORMATION OF
FUTURE SPECIALIST IN MODERN HEIS**

BASIC SCHOOL BIOLOGISTS HISTORICALLY OF KHARKIV REGION

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Still the outstanding historian of Ukraine D. I. Bagaley, studying history of slobozhansky edge, he paid attention to love to education and sciences at Slobozhan. Schools appeared in the 17th century, and in the 18th century already there were many schools and printing houses. Starting from the Kharkov Collegium as a center of education and science Slobozhansky edge in the 18th century, where G.S. Skovoroda worked for the famous, to contemporary great scientific potential of Kharkov with his fully developed and diversified science, in any historical period were outstanding scientists, researchers, teachers.

Essence of such difficult phenomenon as "life" at all levels of development of the live interested and carried away scientists. Starting specialized biological research in Kharkiv came at the end of 18 the first half of 19 century at this time began to form botany, zoology, anatomy, with 19 century - plant physiology, paleontology. Researches of that period had rather descriptive character. The second half of 19 century characterized by a great impetus for the development of biological science. At this time, the transition from description to studies that reveal the laws of the development of organisms. Especially biology began to develop rapidly in the 20th century, a large role in this was played by the creation of the Academy of Sciences of Ukraine with numerous research institutions. In Kharkov unfolded study a variety of new or relatively young biological sciences, which were previously not been developed or scarcely explored - biochemistry, genetics, biocenology, parasitology, molecular biology, cytology, developmental biology, virology, cryobiology.

Many scientists not only accumulating Kharkiv own material, but also created a whole school in their respective industries. The most famous of them: school of the Kharkov botanists: Korshikov A.A., Matviyenko A.M., Tkachenko N.M., Dogadina T.V., Prokudin Yu.N.; school of the Kharkov gerontologists: Mountain A.V., Bulankin I.N, Nikitin V.N.; school of cryobiologists: Pushkar N.S., Utevsky A.M., Grishchenko V.I.; school of ecologists: Visotsky G.N., Kalabukhov N.I.; school of geneticists and selectors: Yuryev V.I., Didus V.I., Delon L.N., Eisner F.F., Tkachenko F.A., Shakhbazov R.G., Shkorbatov Yu.G., Atramentova L.O., Grechanina E.Ya and others. Thereby we studied in detail, a systematic knowledge of the main areas of biological science in the Kharkiv region, prominent leaders in various industries and determined their basic scientific heritage for the preservation and transmission of cultural and scientific heritage to succeeding generations not only professionals but also the general public.

MAIN STAGES DEVELOPMENTAL BIOLOGY

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History of the origin, formation and development of biological science can be interesting not only professional - biologist, whether researcher or student, but simply the modern intelligent human. It first of all concerns specialists and students of the medical-biological profile of various higher education institutions since each stage of the development, each direction of biology has so many examples, the actual material, traces evolution of scientific thought, is a devotion illustration to science, favorite occupation on examples of biographies of scientists, history of inventions, opening, supervision. Such material has informative value since biological values of various areas (botany, zoology and their subsections on objects of studying, and also all-biological disciplines, for example, theory of evolution, morphology, anatomy, cytology etc.) created base for formation and development of a large number of the modern scientific directions such as immunology, a path physiology, genetics etc. Educational value is that it substantially promotes increase of interest and activity of students, brings up positive traits of character, forms outlook, broadens horizons.

In this regard, the aim of our work was to investigate the history of biology, the definition of a vector of its development in certain periods, as well as major discoveries and their implications for scientific, technical and practical progress of mankind. In the work characterized the era of practical prescientific knowledge, science antiquity Middle Ages, and design of the basic biological sciences, the development of biology in XVI-XVIII, the first and second half of the XIX century; identified and characterized the major scientific schools and their leaders - outstanding scientists of different industries and value their development.

In our work, we limited the term only to the twentieth century, as the history of biology XX and XXI centuries has such a wealth of material that requires a separate study.

IMPROVEMENT OF FUTURE PHARMACISTS PREPARATION FOR PASSING THE LICENSE INTEGRATED EXAM «KROK-1. PHARMACY»

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Taking into consideration the demand of the society in the competent specialists preparing, the problem of standardization and formalization of the student progress level assessment system has been raised. In view of the fact passing the license integrated exams (LIE) by students is relevant in the system of pharmaceutical education.

Taking into account the issue we have aimed to identify the problems of students preparation for the LIE «Krok-1. Pharmacy» and to define the organizational and pedagogical conditions (OPC) which would improve of future pharmacists preparation for this exam.

LIE are standardized test methods of pedagogical diagnostics and are the part of the students majoring in pharmacy state attestation. It is the successful passing LIE that is one of the indicators which determines the quality of pharmaceutical education and its conformity to the State standards of higher education and establishes a minimum level of the professional competence of the appropriate educational qualification specialist.

The system LIE for the specialists with higher pharmaceutical education includes two separate tests «Krok-1» and «Krok-2». The LIE «Krok-1. Pharmacy» is the test exam in the fundamental disciplines, and it is passed at the end of the 4th year after the fundamental disciplines having been studied. It includes 8 disciplines such as analytical chemistry, biological chemistry, microbiology, organic chemistry, pathological physiology, pharmacology, pharmaceutical botany and physical and colloid chemistry.

The exam is carried out in writing (blank) form and consists of 200 tests from the so-called examination booklet. Each booklet consists of two units, the first one contains «anchor» tests used in previous years, and the second one contains tests from a closed data bank. 60.5% of correct test answers indicate that a student has passed the exam.

The questionnaire survey conducted among the students and teachers of the pharmaceutical faculty has shown the following problems of future pharmacists preparation for the LIE «Krok-1. Pharmacy»:

- the inability of most students to carry out preparation independently;
- the lack of teachers consultative assistance in the process of preparation;

- insufficient attention is paid to individual approach to each student during the preparation for the LIE «Krok-1. Pharmacy».

- students preparation focusing on the «learning» test questions, and not on understanding them;

- the existing test base imperfection for preparation;

- the lack of an additional time to prepare for the LIE «Krok-1. Pharmacy» and its implementation only as a part of educational process;

- the lack of knowledge «survival»;

- students formal attitude both to the preparation process and to the exam.

Proceeding from the above we consider it is expedient to develop OPC which would improve the future pharmacists preparation to the passing LIE «Krok-1. Pharmacy». In this context the following is proposed:

- to develop teaching manuals with the test tasks separated on the topics and information blocks united with them and containing the basic concepts and regularities used in the LIE «Krok-1. Pharmacy».

- to conduct regular consultations on which discussing test tasks often encountered in the examination booklets and mistakes students often made;

- to contribute to the databases for self-study training for LIE «Krok-1. Pharmacy» created by the students.

- to introduce a mechanism of peer-tutoring that means the assistance of the advanced students to the so-called «risk group»;

- to create an individual training schedule for each student to prepare for the LIE «Krok-1. Pharmacy» with regard to his level of educational achievements and «weak points»;

- to monitor the current level of students preparation not only with the help of computer testing at the departments, but also by means of a written test where a student should choose the correct answer and substantiate it;

- to discuss in the concluding part of the seminars and practical classes test tasks referring the topic being studied;

- to introduce the elective class on which one must pay attention to highlighting the key issues necessary for the solution of test tasks and filling gaps in the studying disciplines included in the LIE «Krok-1. Pharmacy».

All the measures proposed should be systematic and planned and that will contribute to the successful passing the LIE «Krok-1. Pharmacy» by future pharmacists.

IMPROVEMENT OF INDEPENDENT WORK OF MEDICAL COLLEGE STUDENTS

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At the present stage of the higher medical education system modernization the system of organization and management of independent work of medical colleges students which allows providing qualitative training of the future experts is important, that causes the topicality of the research.

The purpose of these materials is to highlight the main point of students independent work and the possibilities of its improvement at the medical college in the process of studying the professionally oriented educational discipline «Fundamentals of Nursing».

Students independent work (SIW) is the primary means of mastering the educational material in the time free from the required classes. Modern normative documents of the MES of Ukraine determine the SIW as the main form of organization of educational process in higher educational institutions, and its volume according to the curriculum is regulated from 1/3 to 2/3 of the total volume of student's class hours. Due to the lack of methodological foundations and approved organization technologies the effectiveness of the SIW is still predominantly low.

Traditional forms of the SIW organization at the medical college are the studying of new material (reading and note-taking literary sources of information; watching video and listening to audio tapes of lectures); advanced studying of the material of the certain discipline (preparation for tests, practical, laboratory works and seminars; performing common tasks; compilation of summaries, essays on a given topic).

To enhance the students cognitive activity, particularly in the academic discipline «Fundamentals of Nursing», it is reasonable to plan the SIW introducing the technology of project-based training.

The technology of project-based training provides for the protection of the individual projects. The project is a prototype of the object, the type of activity. Project-based training enables to evaluate not only the result, but the process of training. Students work on the project may include six stages: preparation, planning, research, conclusions, project presentation or project report, evaluation of the result and the process. The role of the teacher is mentoring or advising and includes the following actions: sharing his (her) own experience, helping in finding the sources, supporting and encouraging students, coordination and adjustment of the project preparation process, supporting of continuous feedback .

The example of adoption of the project-based training technology during studying the discipline «Fundamentals of Nursing» at the medical College is the preparation of projects «Health Lesson» by students with the aim of further educating activities among children. Students must teach this target audience the basic rules of a healthy lifestyle.

For the preparation of the author's projects students are divided into micro groups (3-5 students). Students are encouraged to intellectually competitive role-playing system of cooperation (ICRPSC), within which they cast roles independently testing their abilities. Standard model of casting roles in a micro group includes «generators-seekers» (a person who is able to generate project ideas, find and process necessary literature sources), «analysts» (a person who is able to detect the rational and discard unnecessary in the collected data), «critics» (a person who is able to evaluate critically the material submitted by an analyst, to make comments, suggestions), «operators» (a person that has reciting skills, an ability to express thoughts clearly, skills of working with the audience).

During the presentation of the project «Health Lesson» at the Kharkiv Medical College № 2 future nurses demonstrated their professional knowledge and creative skills offering kindergarten children tales, poems, interesting tasks, games, coloring books developed by them in micro groups . It was proposed to conduct a «Health Lesson» in the form of a costume play. After conducting the «Health Lesson» the students presented the personal certificate on passing the training on the basics of a healthy lifestyle to every child.

Thus, the organization of the SIW in medical colleges allows to increase the motivation of students to study, to form the sanitary and educational thinking of the future expert, encourages students to get new knowledge and skills.

Using technology of project activities in the process of the SIW organization while studying the discipline «Fundamentals of Nursing» promotes creative thinking, introduction the components of research activities, development of personal qualities of future specialists (capacity of reflection and self-concept, the ability to make choice and understand both the consequences of that choice and the results of their own activities).

PSYCHOLOGICAL AND PEDAGOGICAL CAUSES OF ORIGIN OF CONFLICTS IN A SYSTEM “TEACHER–STUDENT”

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Where there are opinions that differ from each other, where there are people who have different views about the purpose and methods of achieving them, the plans and principles of life, there is inevitably conflict situations. The problem of conflict is related to the number of problems that are global in nature. In recent years significantly has increased the urgency of studying the problem of educational psychology, as pedagogical reality generates a lot of controversy and conflict situations, the output of which requires special training of teachers of high school.

The aim of our research is to study the causes of conflicts in the system “teacher–student”.

Considerable attention in the psychological and pedagogical literature paid to the problem of pedagogical conflicts. The issue devoted their researches as foreign (S. Freud, C. Jung, K. Horney etc.) as domestic psychologists (S. V. Banykina, N. Y. Voronova, E. I. Stepanov, B. S. Bratus, V. V. Stolin, F. Yu. Vasylyuk, A. A. Faizullaev, T. M. Titarenko, O. A. Donchenko, G. V. Lozhkin, A. F. Bondarenko, M. I. Pyrene, S. R. Kartashov, etc.)

Conflict is a sharp way of resolving contradictions arising in the process of communication, which is accompanied by negative emotions. It is clash of principles, opinions, estimates, characters and standards of behavior. Pedagogical conflicts include interpersonal conflicts, as in the student group, and in the system “teacher–student”. A distinctive feature of pedagogical conflict is the opposition social-role positions, which in turn is determined by the status of the participants of the conflict.

A conflict between the teacher and the student may occur due to various reasons, which can be divided into the following groups:

- *motivational* (poor motivation of students in the teaching and learning activities, they learn without interest, do not want to do study tasks);

- *behavioral* (violations of the student code of conduct in school and out of it);
- *personal* (individual characteristics are the cause of both students and teachers: age, temperament, character, perception, experience, etc.).

In a process of search for effective conflict resolution conditions teachers of higher education institution should specify the reasons for the conflict, and understanding the nature of their origin, use specific mechanisms of action for the successful their resolution in the context of their teaching. Conditions of conflict resolution are so diverse, as are conflict situations. However, they can be summarized as follows:

4. Termination of counter parties to a conflict situation.
5. Control of the emotional sphere (the human capacity for self-control and self-control in conflict situations).
6. Try to avoid using irritants in communication. Need to control their verbal and nonverbal behavior, not to provoke conflict through conscious or unconscious use of irritants.
7. Conflict can be successfully resolved only on the condition that both sides are showing a desire to that and looking for a way to reach understanding.
8. Timely and accurate diagnosis of its causes (identifying objectively existing contradictions, interests, goals of opponents).
9. Mutual interest in overcoming the contradictions and mutual recognition of each party's interests (free from hostility and mistrust each other).
10. Joint search for ways to overcome the conflict (the use of a whole arsenal of tools and techniques: direct dialogue between the parties, negotiating through a mediator, negotiations with involving a third party, etc.).

During the research we concluded that because of the conflicts is often a contradiction subordinate to certain laws, teachers, understanding the nature of their origin, should use the specific mechanisms of action for the successful resolve them in a variety of teaching situations.

THE FORMATION OF THE PROFESSIONAL FOREIGN COMPETENCE OF THE FUTURE MEDICAL WORKERS IN THE PROFESSIONAL TRAINING

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Democratization of the society, radical transformation processes in the field of international relations and social economic structures, broadening of international collaboration within the framework of European economic and political globalization, changes in the requirements to the graduates of Ukrainian higher medical establishments from the position of improvement of professional foreign competence through the necessity of close collaboration with foreign colleagues lead to changes in priorities in the organization of professional training of medical students at higher educational establishments.

The actual present day problem in the system of higher medical education in Ukraine is foreign education content renovation. In accordance with the requirements of such documents of the Council of Europe as «Bilingual education: key strategic task» (1998), «General European recommendations of language education: learning, teaching, evaluation» (2001), «European language portfolio» (2002). The new language policy demands modern approaches to broad the professional foreign competence.

The research has shown that a considerable number of students – future medical workers have conscious need to realize the foreign knowledge in the practical professional activity (60% from 325 surveyed) connected with high social motivation in reality, creation of joint companies, foreign medical firms in Ukraine, necessity and real opportunity to work with foreign colleagues that is still unrealized during the professional training and the higher educational establishment.

The index of traditional techniques inefficiency is incapability of the graduates to communicate effectively in professional sphere in the English language. Consequently, the main task of the professional training of students at the higher medical educational establishment is to create conditions that stimulate individual scientific research activity, to provide the possibility to communicate in English in the professional sphere.

Moreover, the received data make actual the problem of the future medical workers' professional foreign competence formation, as well as research for ways to provide the efficiency of this process.

Thus, an objective need in the formation of professional foreign competence of the future medical workers, actuality and insufficient study of the research problem in theoretical, methodological and practical aspects as well as the necessity to eliminate the contradictions have stipulated the choice of the topic of the master paper.

FORMATION OF PEDAGOGICAL CULTURE BASES IN FUTURE TEACHERS TRAINING

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The topicality of the problem of a teacher's professional and pedagogical culture formation is determined by the Ukrainian education entry into the global cultural and educational space, and consequently poses educators the problem of solving social and pedagogical tasks taking into account world trends and patterns of general and professional education development. Meanwhile, the discussion of higher education development prospects in Ukraine in the main does not touch upon the issues of the pedagogical culture formation. Not readiness of pedagogical culture study bases, the lack of a complete, holistic theory of its formation hinders the development of cultural and creative functions of teacher's and lecturers pedagogical activity. Under the modern conditions the competitive resource of the teacher's activities is general and pedagogical culture ensuring personality development, overrunning regulatory activities, the ability to create and send values rather than special knowledge, competence, mastered training and education technologies.

A teacher's pedagogical culture is the universal characteristic of pedagogical reality, that part of human culture in which spiritual and material values of education and upbringing as well as creative pedagogical activity methods required for a historical process of generations alternation and personality socialization have been impressed.

High pedagogical culture is regarded as a personality fundamental characteristic, a teacher's activity and pedagogical communication. It is implemented as a dynamic system of pedagogical values, creative ways of teaching and a teacher's personal achievements in the creation of pedagogical practice samples from the perspective of human culture. In this connection it is necessary to identify and raise the level of a teacher's pedagogical culture. Maturity of all components of individual pedagogical culture affects significantly a teacher's professional behavior, gives him integrity as well as his own teaching and individual style. Observations show that the most efficient factor and incentive of pedagogical culture level increasing is a teacher's involvement in the pedagogical creativity, the innovative activity and research.

FORMATION OF PROFESSIONAL CULTURE OF HIGH SCHOOL TEACHERS.

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The main purpose of higher education is not to provide the quality of professional training, but also opportunities for its recontinuous self-development on based on the requirements of modern scientific and technological progress. Science Ukraine has joined the Bologna process social values and determination of qualitative activities have taken place in social professional groups such as high school teachers. Reforms in higher professional education put new challenges to modern in teaching. The problem is that by its very nature the professional culture of teachers can't be changed as fast as the other subsystems of culture. All this gives rise to contradictions in the very culture of high school teacher. Consequently, the relevance of the study is also linked to the need to studying these contradictions and their resolution.

Educational activity can be both professional and non professional. Subject of unprofessional teaching activities can be any person who influence another person in one way or another, but the work is not professional for him (mentor, a family member, a member of the reference group, etc.). Specificity of professional pedagogical activity is that the results of the teacher labor delayed in time, they are not immediately visible, as in the work of an architect or engineer. Educational activity has no repetition of one and the same situation as the educational environment is extremely variable, and what happened today, as a rule, won't be repeated tomorrow. Legal regulation of behavior and interaction of teachers is complemented by ethical one it is expected that should be moral example of civil and social responsibility due to his status – of teacher, teaching, tutor. Therefore, teachers are limited in the choice of means to achieve both professional and their personal goals. Educational activity like no other professional activity, requires an immediate reaction from the teacher to any event occurring in the educational environment, and creativity. Under the professional culture of high school teacher and teacher interaction is understood educational

environment based on shared professional knowledge, norms, values, ensuring the successful acquisition of learners to acquire specific, due to the interaction of objective and subjective factors.

Formation and development of the professional culture of high school teacher serving as subsystem of common culture, due to a set of interrelated objective and subjective factors of socio-economic, socio-cultural character. At the same time factors have both direct (for example, the economic factor, status (prestige) profession in society) and indirect (for example, having a family, media) influence on the formation and development of the individual elements of the professional culture.

The main objective factors influencing the state of the professional culture and defining the values and norms of professional culture of high school teacher, should be highlighted: the economic factor, the education system, the occupational mobility of teachers within the university, the prestige of the teaching profession in a society value system of society, the media and family. The subjective factors include: personal experience teaching activities (experience), self-interest to the profession, educators personal value system.

Thus, normative and knowledge elements are dominant in the professional culture of high school teacher. First of all, it is because the teacher constantly need, both professional and non-professional knowledge, that he translates their student daily. And as knowledge becomes obsolete in modern conditions with tremendous speed, he is compelled to replenish their stock every day. In this case, knowledge of its completion is the main professional norm-value. Secondly, it is also due to the fact that there are legalists (Law of Ukraine «On Education», State Standard, etc.), covering all aspects of the high school teacher.

THE ACTIVITY APPROACH IN THE FORMATION OF FUTURE ECONOMISTS' VALUE ATTITUDE TO PROFESSIONAL ACTIVITIES

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The analysis of tendencies of formation and development of the national education system reveals the necessity of its modernization. The priority task is forming specialists of new formation: with a high level of professional competence, personal development, mastering of proper professional and value priorities.

Future economists training in this context is no exception and also needs improvement. Therefore the problem of identification and substantiation of the methodological approaches to the formation of future economists' value attitude to professional activity has been actualized.

Thus along with axiological, competence, personality oriented, systematic and environmental approach the activity one has acquired a particular importance. In the scientific literature it has been presented by the psychological theory of activity (K. Abulkhanova-Slavskaya, L. Vygotsky, P. Galperin, G. Kostyuk, S. Rubinstein and others) and by the theory of educational activity (V. Davydov, A. Markov, V. Slavonin and others).

In the context of formation of future economists' value attitude to professional activity its main idea is the following: the process of formation of future economists' value attitude to professional activity is mediated by the development of different activities (educational, scientific, research, professional, creative and other ones) at the time of training and education with using principles of development, historicism, objectivity, activity, interiorization and exteriorization; the unity of building external and internal activities; the system analysis of psyche; dependence of mental reflections from the place of the object which is reflected in the structure of activity; the unity of consciousness and activity; gradual mastering of activities.

In the framework of the activity approach forming future economists' value attitude to professional activity is the element of professionally oriented activities which provides transferring objectively significant professional values to subjective level in the training process at higher educational institutions.

PSYCHOLOGICAL CHARACTERISTICS OF MOTIVATION STUDENT LEARNING ACTIVITIES

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The problem of motivating educational activity is relevant both in theoretical and practical terms. That it affects the cognitive activity of students the result of teaching and learning activities.

An important contribution to the disclosure of the theoretical aspects of motivation training activities carried A.V.Leontyev, A.K.Markova, V.Morhun that focused on the study of features of the construction of the motivational sphere of the individual stages of the motives and mechanisms of their functioning in the mind, intensification and optimize the teaching process.

An important condition for the development of the individual desire for a profession are features of motivation of trains learners, their values, cognitive and professional interests, social needs, commitment to professional self-development. Motivation determines professional orientation and activity of students, describes the causes and mechanisms of their conscious behavior has impact on the professional and personal self-development. Under the motivation of learning activities, we understand the motives of the group that motivate students to master the professional knowledge and skills, consciously treat training exercise cognitive activity.

In motivating learning activities can be defined the following groups of motives:

1) cognitive motives related to the content of training and the process of its implementation;

2) educational - cognitive motives associated with a desire for future professionals to gain professional knowledge and skills and are implemented by the pleasure of teaching and learning activities;

3) motives related to the impact on the minds of students a number of factors: the authority of teachers, group of peers, parents, etc. requirements;

4) social motives related to the desire by students learning to assert their social status;

5) professional value reflecting the desire of students to get training to participate in the productive sphere of life. These motives come into effect immediate mastery of professional education.

Today, despite the existence of different conceptual approaches to motivating the consideration of the nature of teaching and learning of the following requirements: a) the necessity of targeting student learning motivation on the part of teachers and student; b) taking into account the characteristics of the motivational sphere of learners; c) creating conditions for transfer external motivation to internal.

Efficiency and outcome of motivation depend on the content and organization of learning activities, respect for psychological and pedagogical principles, conditions and factors of human development, milestones and actions of psycho - pedagogical process.

Motivation plays a specific mode of interaction between the teacher and a particular student, and therefore is unique.

Professional personal development begins with self – discovery from the standpoint of "I'm - the expert" restructuring of own attitude to teaching and learning activities.

Thus, the motivation for teaching and learning activities is a measure of individual student achievement, which is characterized by a set of emotional and volitional processes determining motives competition chosen specialty and prospects of self-realization as a specialist.

THE EXPERIENCE OF FEARS AND ANXIETY INTO (IN) ADOLESCENCE

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Period of adolescence is a stage of students adolescent, therefore, it is the relatively independent life period.

Adolescence – is a stage of human life, in which happen a life choice, a world view formation, becoming independent, distancing parents, professional choice, training in high school, , in some cases, creating a family etc.

Thereby, young men and women may feel discomfort, stress, anxiety and fear in any conditions in which they have to be in connection with the adulthood and changing lifestyles.

According to this, the aim of this research is the concepts consideration of "fear" and "anxiety", and the empirical experiment manifestation of fear and anxiety in adolescence.

The study of fear and anxiety is the basis of psychology emotion study. There are different points of view on these two concepts. Some authors say, that anxiety – is a reaction to the uncertain danger signal, and the fear is a reaction to a specific danger. There are also differences in the perception about benefit or harm of fear and anxiety influence on the person. There is no the single point of view for today.

In this paper we consider fear as "an emotional state that occurs in the presence or anticipation of a dangerous or harmful stimulus", and therefore, do not share the fear and anxiety, and consider these two concepts together, because anxiety and fear characteristically a state of anxiety, danger presentiment.

In the age-related psychology, there is such thing as a crisis for 17 years. A distinctive feature of this crisis is the emergence of variety fears that may have boys and girls. These fears include correctness fear of the chosen profession, of the responsibility which falls on them, of the presence or absence any successes and

achievements, the fear of potential difficulties in the university, in dealing with people, etc.

To confirm this, we present the results of our study, which took place on the basis of NUPh. 120 students of first course of specialty "Pharmacy" took part in the experiment. The aim of the study was to identify the various fears that are associated with educational activity of students.

Thus, we were obtained the following results: the most common fear - "fear of being allotted" (100% of respondents noted this), further there is "fear of the test" (81.4% noted), third place is "fear of public speaking "(72.9%). The fourth and fifth place is occupied by "fear of finish university badly" (50.8% noted this) and "fear of getting sick and miss a lot" (also 50.8%).

It can be concluded that the fear and anxiety affect to the success of student learning in an educational institution. One can say that the learning success is important to the students, is imported the correct choice of future profession, their further personal and professional development, they tend to achieve good results in training.

Fears that arise in terms of teaching and learning activities, as the problem of pedagogical and age-related psychology require further study and experimental research.

APPLICATION SHEET

**«CHEMICAL-TOXICOLOGICAL EVALUATION OF LIDOCAINE
HYDROCHLORIDE IN OBJECTS OF BIOLOGICAL ORIGIN», IN
ACCORDANCE WITH THE PROBLEM OF «HUMAN HEALTH», THE
DEVELOPMENT OF NEW AND IMPROVEMENT OF EXISTING
METHODS OF RESEARCH OF TOXIC COMPOUNDS FOR USE IN THE
CLINICAL PRACTICE OF ACUTE POISONING**

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1. Purpose:

drawing up guidelines for the implementation of evidence-based clinical and toxicological studies diagram of body fluids (blood, urine) of living persons for diagnosis of poisoning in specialized clinical health institutions.

2. Objectives of the study:

-the development of effective methods of isolating lidocaine hydrochloride from biological fluids of living persons and other subjects as material evidence;

-the development of effective methods for retrievals with lidocaine hydrochloride from biological objects of study;

-the development of sensitive and specific chemical methods of detection, identification and quantification of lidocaine hydrochloride in extracts from biological material (blood, urine);

3. Relevance:

-diagnosis of poisoning lidocaine hydrochloride; control over the breeding of lidocaine from the body of the victim when detoxification activities; the causes of

poisoning from an overdose of lidocaine hydrochloride in biological material (blood, urine).

Academic significance:

1. For the first time, will be examined and evaluated by the lidocaine hydrochloride with chemical-toxicological view on laboratory animals.
2. Will be designed and developed guidelines for clinical and toxicological analysis.
3. Will be installed mechanism of distribution in the body and metabolism of lidocaine hydrochloride in experiments on laboratory animals.
4. Will be set the persistence of lidocaine hydrochloride in biological material (blood, urine).

Practical significance:

developed methodology will be implemented in practical activities of chemical-toxicological laboratories Center for forensic medicine.

4. Research methods:

for isolation has been used method of Vasilyeva A.A., for the detection and quantification of lidocaine hydrochloride used chemical and physico-chemical methods (chromatography in thin layers, gas-liquid chromatography, spectrophotometry).

5. Conclusions: during the study

-was developed a powerful technique for isolating lidocaine hydrochloride from biological fluids of living persons and other subjects as material evidence;

-has developed a powerful technique for purification of extracts with lidocaine hydrochloride from biological objects of study;

-have developed a sensitive and specific chemical methods for detection, identification and quantification of lidocaine hydrochloride in extracts from biological material (blood, urine).

**«CHEMICAL-TOXICOLOGICAL EVALUATION OF LIDOCAINE
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DEVELOPMENT OF NEW AND IMPROVEMENT OF EXISTING
METHODS OF RESEARCH OF TOXIC COMPOUNDS FOR USE IN THE
CLINICAL PRACTICE OF ACUTE POISONING**

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2. Will be designed and developed guidelines for clinical and toxicological analysis.
3. Will be installed mechanism of distribution in the body and metabolism of lidocaine hydrochloride in experiments on laboratory animals.
4. Will be set the persistence of lidocaine hydrochloride in biological material (blood, urine).

Practical significance: the methodology developed will be implemented in practical activities of chemical-toxicological laboratories Center for forensic medicine.

4. Research methods:

for isolation has been used method of Kartashova V.A., for the detection and quantification of lidocaine hydrochloride used chemical and physico-chemical methods (chromatography in thin layers, gas-liquid chromatography, spectrophotometry).

5. Conclusions: during the study

-was developed a powerful technique for isolating lidocaine hydrochloride from biological fluids of living persons and other subjects as material evidence;

-has developed a powerful technique for purification of extracts with lidocaine hydrochloride from biological objects of study;

-have developed a sensitive and specific chemical methods for detection, identification and quantification of lidocaine hydrochloride in extracts from biological material (blood, urine).

STUDY OF SELECTION OF BIOLOGICALLY ACTIVE SUBSTANCES FROM THE GERMINATING POTATOES

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Steroidal compounds are always of interest as active substances. On one side of the individual agents (solasodin, diosgenin, etc), this group of natural compounds used for the synthesis of hormone preparations in the pharmaceutical industry. However, increasing interest in steroid compounds as substances possessing a wide range of biological effect on living organisms. In these compounds were also found to inhibit the growth of some forms of cancer, reduce cholesterol in the blood and stimulate the ovulatory process in animals, as well as fungicidal, antimicrobial and antiviral activity. Steroidal compounds have proved effective in the treatment of rheumatism, asthma, hemolytic anemia and gemodiateza.

Such compounds include steroid structure glycosidic alkaloids potato plants (*Solanum tuberosum* L.) - alpha solanine and alpha chaconine during hydrolysis split off three molecules of sugars and aglycone-solanidin.

In all parts of the ground as well as in potato tubers contain a different number of glycoside alkaloids (GA) - solanine, chaconine and aglikonsolanidin. This class of compounds of interest that this group of glycoalkaloids, such solasodin is valuable medicament for the cortisone type. Other members of this series, published sources, as have antitumor, antimicrobial, antibacterial, anticholinesterase, antitussive and psychotropic effects, as well as effective in the treatment of cardiovascular diseases. The proximity of the chemical structure of HA and potato plants solanidina with the steroid compounds also causes concern. Since there are reports of receipt of solanidina Androstane derivatives.

For primary extraction as a cheap and affordable we have chosen extractant purified water. As water acidifying agents were used sulfuric acid, hydrochloric acid and acetic acid. To assess the effect of the nature of germs acids in potato tubers extraction was studied their influence on the yield of the active substance as well as purity extracts.

TOXICOLOGICAL SITUATION IN ALMATY IN THE PERIOD FROM 2000 TO 2010 YEARS

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Research is analytical, toxicological situation characterizing the state of the population of Almaty in the period from 2000 to 2010, analysis was carried out on the main aspects relevant toxicological services, it figures negotiability nosological character analysis of age, gender categories, as well as the analysis of mortality. According to the toxicology department of the hospital for emergency care Almaty.

Age category poisoned mainly represented by about 80%, from 21 years to 59 years, that is a working-age population, adolescents and the elderly, poisonings occur on average 6-7% of cases.

If we consider the data, that showed a reduction in uptake in adolescence with 10% in 2000 to 2% in 2010, it's probably due to a decrease medication poisonings over the past 10 years, and at this age is most common, this nosology, in particular suicides. According to statistics from acute poisoning occur mainly in men, and for the past 10 years there has been increase in the percentage of occurrence of poisoning in men from 60% in 2000 to 80% in 2010, respectively, in women - about 40% at the beginning and 20 % in the late 2000s, which also explains the reduction of the weight of medicinal poisoning. At the beginning of the two thousandth's (2000 and 2002). Severe degree of poisoning, that is life-threatening condition of the patient accounted for one third of the total number of poisonings, and by 2010 the proportion of severe poisoning fell to 8%.

Percentage mortality



Figure 1. The age of the patients

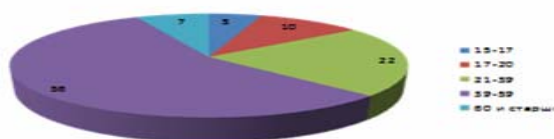


Figure 2. The percentage of mortality for 10 years

Conclusions: Thus, over the last 10 years the numbers uptake by acute exogenous poisonings remain high, and the average for the past six years are about 14,000 calls a year. In the first place - alcohol poisoning products, including surrogate alcohol poisoning, followed by poisoning medicines. An increase in suicidal poisoning in periods of severe economic situation in the country in the late 90s and early 2000s, and the stabilization of social problems and reduced the number of such poisoning. Mortality in poisoning decreased by more than 3 times.

DEVELOPMENT OF THE PHARMACEUTICAL COMPOSITION AND TECHNOLOGY OF COMBINED EYE DROPS FOR GLAUCOMA TREATMENT

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Glaucoma is a disease that ranks top in the list of eye diseases and is an important medical and social problem, as evidenced by statistics on the number of patients with glaucoma and visually impaired people among them, chronic nature of untreated disease and irreversible loss of vision, difficulty of early diagnosis and the level of financial expenses for medical treatment. Pharmacotherapy of glaucoma is aimed at normalization of intraocular pressure (IOP), intraocular blood circulation improvement and normalization of metabolic processes in the retina and optic nerve, and includes multimodality therapy with several drugs having differently directed action. Improvement and development of new effective combined ophthalmic drugs with differently directed action, which would ensure not only normalization of IOP, but also minimal side effects and affordable to the general population, is always relevant. An earlier our study allowed substantiating relevancy and promising directions in combining drugs that affect different chains of pathogenesis, and creation based thereon of an effective drug in the form of eye drops. The aim of this study was the choice of the optimal pharmaceutical composition and the development technology of new combined eye drops for glaucoma treatment.

The objects chosen for investigation: an adrenergic receptor blocking drug and an amino acid derivative. To assess the quality of model mixtures the following methods were used: determination of clarity and degree of opalescence of liquids (SPU, 2.2.1) and degree of coloration of liquids (SPU, 2.2.2, Method II), potentiometric determination of pH (SPU, 2.2.3), capillary viscometer method (SPU, 2.2.9), determination of refractive index (SPU, 2.2.6), determination of osmolarity (SPU, 2.2.35), determination of conductivity (k) (SPU, 2.2.38), liquid chromatography (SPU, 2.2.29), absorption spectrophotometry ultraviolet (SPU, 2.2.25).

At the stage of pharmaceutical development combined hypotensive eye drops the behavior of drugs in aqueous solution depending on their chemical nature and pH of solution have been analyzed. Based on the calculated molar particle ions the optimum area of pH where drugs are present in the form of ions has been proved. The results of appearance of freshly prepared aqueous solution of drugs showed that at acceptable to eye drops pH range from 3,5 to 8,5 test solution is clear. This has

allowed to substantiate optimal range pH at which saved the stability of drugs in the form of aqueous solutions. A preliminary assessment of the compatibility of drugs in their joint presence in aqueous solution depending on the pH of the medium in terms of clarity, color, pH and electrical conductivity have been carried out. In the pH range of 3,5 to 8,5 aqueous solution of drugs in their joint presence has been clear and colorless, that indicate the presence of both drugs in the form of water-soluble ions. The value of conductivity of the solution of drugs in their joint presence, which is the sum of the values of electric conductivity of individual solutions of everyone drug, indicate no interaction between the studied drugs. The research allowed to prove scientifically the pH, which provides stability and comfort during application of eye drops that combined with drug substances of different chemical nature.

The chemical compatibility of drugs with the excipients from different chemical nature and with different functions, for example, such as buffer systems (phosphate, citrate, borate), tonicity agents (sodium chloride, propylene glycol, glycerin, mannitol), antimicrobial preservatives (benzalkonium chloride, methyl parahydroxybenzoate, propyl parahydroxybenzoate, decametoxin) viscosity and penetration enhancers (methylcellulose, hypromellose, povinilpirolidon, various species of dextrans, alginates, carbopols, polyethylene glycols) as well as various combinations thereof was studied.

According to the optimal values of physicochemical indexes of dosage form (osmolarity – 300-500 mOsm/l, pH – 6.0-7.5, refractive index – 1.333-1.357, viscosity- 1-30 mPa·s) the optimal pharmaceutical compositions of eye drops, which comply with modern requirements to ophthalmic medicines, were chosen.

The technological parameters of eye drops obtaining process of the pharmaceutical compositions in form of stable solution (order and temperature regime of ingredient dissolution, rate and duration of mixing) were studied. The compatibility of the different filter materials with the ingredients of eye drops was carried out and the process of eye drops filtration with the use of chosen filter materials was worked out. The complex research concerning development of the technology was determined considering typical schemes of eye drops production that exist at the domestic pharmaceutical enterprises. The study of influence of different primary packaging materials and storage conditions on stability of the eye drops during storage continues.

The complex research have helped to choose the optimal eye drops compositions and to develop the technology, which allowed to obtain the eye drops with indexes in accordance with SPU requirements of quality to ophthalmic drugs and there are acceptable physiologically to eye.

SELECTION TECHNOLOGY OF HA AND SOLANIDINA OF POTATO TUBER SPROUT PLANTS

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The interest to steroid compounds studies which are conducted in several directions is not reduced. Representatives of this group of natural compounds (solasodin, diosgenin, etc) are used in the pharmaceutical industry for the synthesis of hormones. Increases the role of steroid compounds, as with a wide range of biological effects on living organisms. In these compounds were found an ability to inhibit the growth of some forms of cancer, reduce cholesterol levels in the blood and stimulate the ovulatory processes in animals and determined their fungicidal, antimicrobial and antiviral activity. Steroidal compounds have been shown to be effective in the treatment of rheumatism, asthma, hemolytic anemia and gemodiateza.

Steroidal compounds are widely used in Pharmacy and food industrial. One of the source of the steroid compounds are the Potato tubers.

The experiments were conducted as follows: Crushed to 1.5 -2.0 see potato sprouts after air drying were filled with water to a mirrored surface, asidify to pH 2.0 -3.0 on universal indicator sulphuric, hydrochloric and acetic acids. Insist at room temperature during 24 hours. Extraction percolates through a dense, coarse meal again flooded with water, the acidated with suited acid and continued insistence additional 24 hours. After 24 hours checkout was separated and both extract is combined, handled 25% solution of ammonia to pH 9.0-9.5 for universal indicator. Selected sediment filter through filter paper. Was dried in the thermostat at 40° c to constant weight. The results, the average of the 5 series of experiments are given in table №1.

№ p/p	Taken raw materials	Output with sulfuric acid. %	Hydrochloric acid. %	Acetic acid %
1	5 кг	2,4	2,2	2,0

As you can see from the table on the way out steroid link from potato sprouts has a higher impact does sulfuric acid. Further examined the effect of acids on the yield of interest of substances depending on the concentration of acids. Crushed long 1.5 -2.0 cm 5 kg potato sprouts air drying was poured by solutions of these acids with concentrations of 2, 3, 5% to a mirrored surface, raw material been pressed at room temperature during 24 hours. Checked the pH environment. Extraction of percolate through the dense, coarse meal again continued to insist additional 24 hours. After 24 hours checkout was separated and both extract were processed by 25% solution of ammonia to pH 9.0-9.5 for universal indicator. Selected sediment filter through filter paper. Was dried in the thermostat at 40° c to constant weight.

Studied for solanidina and glycoalkaloids from plants of potato plants. 3% solution of sulfuric acid is recommended as an extractant for allocation of the amount of active substances from the raw material extraction during the period of 48 hours.

CONTENT

1. SYNTHESIS OF PHYSIOLOGICALLY ACTIVE SUBSTANCES	4
Galimskiy I.O., Vlasov S.V., Kovalenko S.M., Chernykh V.P.	5
Grygoriv G.V., Redkin R.G., Syumka E.I., Shemchuk L.A., Chernykh V.P.	6
Derecha Yu.O., Vlasov S.V., Kovalenko S.M., Chernykh V.P.	7
Dolya O.V., Vlasov S.V., Kovalenko S.M., Chernykh V.P.	8
Yeromina H.O., Isaev S.G.	9
Zaviazun M. A., Bereznyakova N. L.	10
Ivanova I.I., Devijatkina A.O., Yeromina H.O., Isaev S.G.	11
Ivanova K.S., Yeromina H.O., Isaev S.G., Yeromina Z.G.	12
Krolenko K.Yu., Vlasov S.V., Zarembo O.V., Silin O.V., Kovalenko S.M., Chernykh V.P.	13
Lysyana A.A., Sytnik K.M., Shpychak T.V., Chernykh V.P.	14
Ovsjanykova Yu.O., Sytnik K.M., Shemchuk L.A., Chernykh V.P.	15
Prokopets S.V., Lega D.A., Levashov D.V.	16
Rayter L.M., Altuhov O.O., Kolesnyk O.V.	17
Semko M.M., Lega D.A., Redkin R.G.	18
Chan T.M., Levitin Ye.Ya., Kryskiv O.S.	19
D. P. Chumatchenko, D. V. Bondarenko, L. O. Perekhoda	20
2. STUDY OF MEDICINAL PLANTS AND CREATION OF HERBAL MEDICINAL PRODUCTS	21
Avidzba Yu. N., Koshovyi O.M.	22
Boshkayeva A.K., Omarova R.A., Iskakova M.K., Aktayeva A.M., Toktabekova A.M., Saurzhanova M.R.	23

Baranchikova O.S., Popova N.V., Lypovetskyi P.V., Tkachenko M.F.	24
Popova N.V., Baraschovets O.V.	25
Bovt Y.G., Kryzhna S.I.	26
Verhovod A.M., Krasnikova T.A.	27
Dunchak J. A., Evanesyanyan N. A., Novosel O. M.	29
Zhygul'ska A.V., Lypovetskyi P.V., Tkachenko M.F.	31
N. I. Ilyinska, T. M. Gontova, Y. S. Kichymasova	32
Kirichenko D. A., Oproshanska T. V.	33
Kishkan A.I., Samoylenko D.I., Burda N.Ye.	34
Kolychev I.O., Krasnikova T.O., Koshevoy O.M.	35
Komissarenko M. A, Koshoviy O. M.	36
Kravchenko O.O., Lypovetskyi P.V., Tkachenko M.F.	37
Kuranda E. A., Krasnicova T. A.	38
Myha M.M., Vovk G.V., Koshevoy O.M.	39
Osmachko A.P., Kovaleva A.M., Grishina E.V.	40
Ochkur A.V.	42
D.I. Prikolota, G.P. Kazakov	43
Rami Assaad, N.V. Popova	44
Ryabov V.O., Rudenko V.P.	45
Samoilova V. A. and Kovalev V. N.	46
Upyr T.V., Komissarenko N.A., Koshevoy O.N.	47
Shostak T.A.	48
Yudicheva D.M., Lypovetskyi P.V., Tkachenko M.F.	50
Iakovenko O.V., Radko O.V.	51

Nmemelu Franklin Chisom, Ocheredko L.V., Kruchkova T.M.	52
3. THE STANDARDIZATION OF MEDICINES. PHARMACEUTICAL AND CHEMICAL-TOXICOLOGICAL ANALYSIS	53
Arigbe Uyiosa, Useinova E. R., Klimenko L. Yu.	54
Baiva P.P., Baranova I.I., Kulikov A.Y.	55
O.A. Vislous, I.A. Dvoynos, N.Yu. Bevz	57
Ryabov V.O, Dolja O.V, Moroz V.P.	58
Ekpo Basse Olive, Klimenko L. Yu., Mykytenko O. Ye.	59
Yesbatur A.E., Shulnova G.K., Chernova A.A., Grudko V.A., Omarova R.A.	60
O. V. Shtrimaitis, O. A. Zdoryk, A.H. Valiev, V. V. Prokopec, V. A. Georgiyants	62
Ituen Ekomobong, Novitsky A. I., Klimenko L. Yu.	63
Kovalenko O. V., Zaharenko A. V., Moroz V.P.	64
Blazheyevskiy M.Y., Koretnik O.I.	65
M.S. Korolyova, A.V. Glushchenko, N.Yu. Bevz, V.A. Georgiyants	66
Mykola Y. Blazheyevskiy, Lyubomyr S. Kryskiw	67
Kucher T.V., Merzlikin S.I.	68
Lazurenko T.S., Moiseeva A.S., Akhmedov E.Y.	69
Malay B.B., Blazheyevskiy M.Ye	70
Maltseva T.I., Bardash O.A., Kolesnyk S.V.	71
Blazheyevskiy M.Ye., Mozgova O.O.	72
Moldakarimova M.D., Zhaparkulova K.A., Sakipova Z.B.	73
Nemr Nur Eddin Fatima, Klimenko L. Yu., Kostina T. A.	74

Popovich O.Yu., Yevtifieieva O.A., Proskurina K.I., Mordinson A.Yu.	75
Rymar M.V. Vetitneva N.A.	76
Tomarovska L. Yu., Bayurka S.V.	77
Bryzitsky O.A., Topchiy L.O.	78
Trut S. M., Klimenko L. Yu.	80
Khokhlova N.O., Migal A.V., Dobrova A.O., Golovchenko O.S., Georgiyants V.A.	81
Shevchenko O. G., Kizim O. G., Petukhova I. Yu.	82
Shkarlat G. L., Zhuravel I. A., Klimenko L. Yu., Showkova Z. V., Showkova O.V.	83
4. TECHNOLOGY PHARMACEUTICAL PRODUCTS	84
Agaev A., Vishnevskaya L. I., Zujkina S. S.	85
Bobro S.G., Tikhonov A.I.	86
Vaschuk V. A.	87
Vlasova K.V. Bobrov S.G., Tikhonov A.I.	88
Dolja O.V., Sichkar A.A.	89
Zaiter Hussein, Sichkar A.A.	90
S. I. Kapanistaya, I. V. Kovalevskaya	91
Kolisnyk T.Ye., Slipchenko G.D.	92
Strus O.E., Konovalenko I.S., Polovko N.P.	93
Kononenko K.A., Chushenko V.N., Levachkova Yu.V.	94
S. Korkosh, V. Chueshov, D. Soldatov	95
Korovyakova T.S., Kovalevskaya I.V., Pulyaev D.S.	96
Kriukova A.I., Kovaleva T.N.	97
Kudryk B.T., Tikhonov A.I.	98

Lahlifi Abdelkbi, Benomar Reda, Berhruz Zainuddinov, Bogutska O.Ye, Tikhonov O. I.	100
Lohosha R.V. Kukhtenko H.P., Stepanenko S.V., Gladukh E.V.	101
Maletska Z. V.	102
Marochkina T.A., Chushenko V.N., Rukhmakova O.A.	103
Tikhonov A. I., Melnyk I. M.	104
V. V. Mohylyuk , L. L. Davtian	105
Nezdolii A. O., Maletska Z. V.	107
Petrovskiy M., Buryak M.V., Yarnykh T.G.	108
Procenko V.P., Shpychak O.S.	109
Sourany R., Tolochko K.V.	111
Reva D. V.	112
Ruban O.I., Yarnykh T.G.	113
Sinitsyna E.V., Kovalevskaya I. V.	114
Skyter S. M., Levachkova Yu. V., Chushenko V. M.	115
Sklyarova A.Yu., Zhilinkova A.Yu., Zerdau A., Vishnevskaya L.I., Zubchenko T.N.	116
Smelova N., Kovalyov V.	117
Teslenko I.A., Bobro S.G., Tikhonov A.I.	118
Chernova A.O, Manscy O.A., Saiko I.V.	119
5. MODERN BIOTECHNOLOGY	120
Alekseeva Y.S.	121
Astafyeva E.Y., Strilets O.P., Strelnikov L.S.	122
Atanova H.O., Hladkov O.K., Ivakhnenko O.L., Strelnikov L.S.	123
Bazyuk D.S., Kalyuzhnaya O.S., Striletc O.P., Strelnikov L.S.	124

Britan M.V., Manoukian A.A., Kalyuzhnaya O.S., Kalyuzhniy A.B., Strelnikov L.S.	125
Glupak O.Y., Zavolod'ko O.O., Ivakhnenko O. L., Strelnikov L. S.	126
Goncharova V.V., Yakushko Y.D., Strilets O.P., Strelnikov L.S.	127
Zubeyko M.V., Lakhva D.N., Kalyuzhnaya O.S., Kopytina N.I., Strelnikov L.S.	128
Kamyshnikova V.O, Lapina E.A., Ivakhnenko O. L., Strilets O. P.	130
Kashcheyeva A.I, Metelkina K.I., Ivakhnenko O. L., Strilets O. P.	131
Korolkova Y.S., Babaeva A.V., Strilets O.P., Strelnikov L.S.	132
Kulyk R.V., Kalyuzhnaya O.S., Strilets O.P., Strelnikov L.S.	133
Mishareva V.V., Panchenko A.S., Brechka N.M., Strelnikov L.S.	134
Molchanova O.O., Kovalenko A.L.	135
Reznik R.A., Kalyuzhnaya O.S., Strilets O.P., Strelnikov L.S.	136
Reshetnyak O.P., Bondarchuk M.S., Strilets O. P., Strelnikov L. S.	137
Rybalkin M. V., Strilets O. P., Strelnikov L. S.	138
Sugrobov M.O., Tymchuk N.F.	139
Trembach O.O., Trembach H.O., Strilets O.P., Strelnikov L.S.	140
Shul'ga E.Y., Sherbak E.V.	141
Hawilo Ali, Yudina Yu.V.	142
Fakih Mohamad, Yudina Yu. V.	143
6. PHYSIOLOGICAL AND BIOCHEMICAL FUNDAMENTALS OF THE ACTION OF BIOLOGICALLY ACTIVE COMPOUNDS	144
Anas Fattal, Derkach N.V.	145
Bilyanska U.P., Bichko T.P., Fylymonenko V.P.	146
Butenko O.V., Shevchenko E.O., Pristenskaya A.V., Yatsenko E.Yu.	147

Gorinenko E. S., Chalyy V.V., Tishchenko I.Yu.	148
Grudko E.V., Garaji K.V., Galuzinskaya L.V., Zagayko A.L.	149
Zhurenko D.S., Tsubanova N.A.	151
N.O. Kurochka , L.A. Andrushkova, E.I. Voitenko, A.L. Zagayko	153
Mistyuk A.S., Tishchenko I.Yu.	155
Musmari Mohamed	156
Nikulina O.Yu., Shevtsov I.I.	157
Slyvnaya M.V., Zagayko A.L.	159
Haddushi Mohamed Jalal, Senyuk I.V.	160
Tsubanova E.S., prof. Zagayko A.L.	161
Eze C.I., Krasilnikova O.A.	162
Iakovenko O.V., Markiv V.I., Derkach N.V.	164
7. PRECLINICAL PHARMACOLOGICAL STUDY OF NEW	165
MEDICINES	
Arishin S.N., Buhtiyarova I.P., Shchokina K.G.	166
Bagauri O.V., Braverman L.B., Khodakivskiyi O.A.	167
I.P. Gucaluk, G.P. Fomina, G.L. Litvinenko	168
Gurdgiy O.I.Zaliubovska, M.E.Berezniakova	169
Deyko R.D., Shtrygol' S.Yu., Kolobov A.A.	170
Dmytrenko S.V., Drogovoz S.M.	172
Zakrutny R. D., Shtryhol' S. Y., Merzlikin S. I.	173
Kavushevskaya N.S., Tiupka T.I.	175
Kalapko O.N, Shtrygol' S.Yu.	176
Kalko K.O., Drogovoz S.M.	178
Kirshenbaum E.V., Fomina G.P., Avidzba Y.N.	179

Kolisnyk O.A., Drogovoz S.M.	180
Konovalenko E. V., Rybak V. A.	181
Luneva M.S., Drogovoz S.M.	182
Minaieva A.O.	183
Naboka V.U., Zaliubovskaya O.I., Fomina G.P.	184
Petryk I., Khodakivskyi O.A.	185
Sevryukov A.V. , Volkovoy V.A., Kolesnik S.V., Sutnik K.M.	186
Taran K.A., Shapoval O.N.	187
Khouari Samer, Naboka O.I., Glushchenko A.V.	188
Tsyvunin V.V., Prokopenko Yu.S., Zaginaychenko B.A., Shtrygol' S.Yu.	189
Chikitkina O.M., Tcukanova O.O., Kononenko N.N., Chikitkina V.V.	190
Shakhvatova N.N., Volkovoy V.A.	191
8. MODERN ASPECTS OF PHARMACEUTICAL MICROBIOLOGY AND IMMUNOLOGY	192
Boyko N.N., Zaytsev A.I., Nefedova L.V.	193
Geyderikh A.S., Filimonova N.I.	195
Gorobets K.P., Silayev A.A.	196
Adnan Khalil Dagher, Kliuchka Ye.O.	197
Lysenko A.S, Kovalyova G.O.	199
Priymak L.A., Filimonova N.I.	200
Rakeyev P.V., Dubinina N.V.	201
9. CLINICAL PHARMACY	202
Ekwomadu U.K Gerasymenko O.V.	203
Bevz O.V., Vetrova K.V., Davishnya N.V., Sakharova T.S.	204
Bondarchuk I.S., Ratushna K.L.	206

Inginova K. O., Piskarova A. M., Litvinov I. O., Ganziy T. V.	207
Kolodeznaya Tatiana, Dobrova V. Ye.	208
N. S. Mazur, V. E. Dobrova, S. V. Misyurova, V. V. Propisnova, I. A. Otrishko	209
Prisich K.S., Zhurenko D.S., Tsubanova N.A.	211
Rabochaya Anna, Dobrova V.	212
Ratushna K.L., Zupanets K.O., Dobrova V.Ye.	213
Strelnikova D.S., Gerasymenko O.V.	214
R. L. Furman, P. A. Kravchuk	215
10. MODERN PHARMACOTHERAPY	217
Antsybor A.G., Kashuta V.E.	218
Boyarskiy A.A., Tikhonova O.O., Ananko S.Ja.	219
Verkhovodova Y.V., Kireyev I.V.	221
Holovach A.R., Savokhina M.V.	223
Emirova E.I., Kashuta V.E.	224
Kazarinova M.V., Kireyev I.V.	225
Kirdan V.T, Tryshchuk N.M	226
Kolodeznaya T. Yu., Krivinos K.A., Savokhina M.V.	227
Korolenya Y.M., O.A. Kyrychenko	228
Krivos K. A., Kolodeznaya T. Yu., Savokhina M.V.	229
Litvinenko E.U., Rybak.V.A.	230
Pantuckh A.A., Zhabotynska N.V.	231
Ryabov V.O., Zhabotynska N.V.	232
Savan Alaa, Lebed L.V.	233

Savina M.V., Savina M.A.	234
Smelova N.N, Ryabova O.A.	235
Solovyova V.O., Zhabotynska N.V.	236
Chumak I.V., Storozhenko O.M., Kabachnyy V.I.	237
Tolmacheva K.S., Ryabova O.A.	238
Tsemenko K.V., Kireyev I.V.	239
O.V. Tsulun, L.V. Derymedvid	240
11. PHARMACOECONOMIC RESEARCH OF MEDICINES	241
Adonkina V. Yu., Terentyeva Yu. K., Mishchenko O. Ya.	242
Bondarchuk I. S., Chynush I. V., Bezditko N.V.	243
Vasilieva A.A., Iakovlieva L.V.	244
A. A. Leontyeva , N. V. Bezditko	245
12. MANAGEMENT AND MARKETING IN PHARMACY	246
L.R. Ablayeva, A.R. Shopabaeva, S.V. Khimenko.	247
Arakelyan M.A., Bobrytska L.A.	248
Baklanova R.I., Marianska S-V.V.	249
Shopabayeva A. R., Khimenko S. V., Aktayeva A. M., Bekkozhaeva A.G., Toktabekova A.M.	250
Volodin A.D., Yastrebova A.D.	251
Oliinyk O.E., Evtushenko O.M.	253
Paziuk Daryna-Mariia Valeriivna	254
Pechenizhska N.S., Dorokhova L.P.	256
A.A. Ruban, M.N. Kobets, Yu.N. Kobets	258
Uzbekova A.A., Abdilova Sh. M., Bakhtybaeva M.R.,Kobets M.N., Kobets Yu.N.	259

Sholpanbay A.O., Ibragimova L.N., Sakipova Z.B., Shopabayeva A.R., 260
Khimenko S.V.

13. SOCIO-ECONOMIC RESEARCH IN PHARMACY 261

A.A.Kotvitska. I.O.Surikova 262

Aulova Irina 264

Kotvitska A.A., Puzak O.A., Bevz O.V. 266

Wael El Ariss, Podgayna M.V. 268

Vozyyanova A., Korzh J. 270

Davidenko I.V. 271

Ignatenko M.A., Kotvitska A.A., Kubaryeva I.V. 273

Ilyushik O.R., Nemchenko A.S, L.V. Tereshchenko 274

Carlo V.V., Kotvitskaya A.A., Volkova A.V. 275

Kisyeyeva K.V., Kotvitska A.A., Cherkashyna A.V. 276

Kononenko O.V., Kotvitska A.A., Kubareva, I.V. 277

Kotlyarevska A.O., Vynnyk O.V. 278

Lobova I.O., Kotvitska A.A. 279

Pastukhova O.A., Kotvitska A.A. 281

Portnyagin V., prof. Sagaidak - Nikitiuk R.V. 283

Pchelnikova T.M., Bratishko Y.S. 284

Fursa L.I., Sevoyan A.A. 286

Shamray A.S., professor Posylkina O.V. 288

Iurchenko G.N. 290

**14. QUALITY CONTROL IN THE PHARMACEUTICAL AND 292
HEALTHCARE INDUSTRY**

Fayoumi H.A., Kovalenko S.S. 293

Hamoud H., Kovalenko S.S.	294
Sobh M., Kovalenko S.S.	295
Gorodetskaya V.I., Lebedynets V.A., Kovalenko S.N.	296
Davidova O.V., Lebedynets V.O.	297
Veronika R. Plaksina, Vyacheslav O. Lebedynets	298
15. INFORMATION TECHNOLOGIES IN PHARMACY AND MEDICINE	300
Ananko A.S., Korolev V. D.	301
Bobrova A.N., Boyko Y.S., Korolev V.D.	302
Balandin V.I., Efremova V.Y., Korolev V.D.	303
E.S. Pasechnik, V.N. Zefirov	304
Fedoseeva A.A.	305
S.S.Shershnyova, S.V.Velma	306
Prisyazhnyuk A, Schetinina M., Kokodii N.G.	307
16. COMMODITY SCIENCE	308
Anikina A.Yu., Dem'yanenko V.G., Breusova S.V.	309
Bezpala Y.O., Baranova I.I., Procenko V.P.	310
Grynenko U.V., Trunova T.V., Baranova I.I.	312
Hurkivska I.V., Breusova S.V., Dem'yanenko V.G., Baranova I.I.	313
Dulneva Ju.I., Dem'yanenko D.V., Breusova S.V.	314
Zhdanyuk N.A., Breusova S.V., Dem'yanenko V.G., Baranova I.I.	315
Kuchinska A.M.	316
Lytovchenko A.A., Trunova T.V., Baranova I.I.	317
Litovchenko A.G., Proskochilo A.V., Demianenko V.G., Baranova I.I.	318
Kazan M., Braidy A., Elherihi F., Mamedova S. O.	320

Myga M.M., Trunova T.V., Baranova I.I.	321
Protsenko V.P., Proskochilo A.V., Demianenko V.G., Baranova I.I.	322
Pul V. V., Baranova I. I., Zaviazun M. A.	323
Khokhlova N.A., Dem'yanenko V.G., Breusova S.V.	324
Shaban L.N, Kovalenko Sv. N.	325
17. SOCIAL STUDIES	326
Malay B. B., Shitov S.I.	327
Miskova K.V., Lantuh A.P.	328
Podolyaka Angela, Hirina Anna	329
Rakeev P.V., Shitov S.I.	331
Ryabov V.O., Shitov S.I.	332
Nur Eddin Fatima, Artemenko A.P.	333
Tsibulya D., Maliutina O.K.	335
18. PHILOLOGY	336
Dmytrenko I.S., Berestova A.A.	337
Toryanik L. , Karpenko M.	338
Toryanik L. , Konovalenko Ye.	339
Konovalenko E. V., Svitlychna E. I.	340
Kumarova A., Dolga E.A.	341
Rakeyev P.V., Lisenko N.O.	342
Andrianantara Ravaka Rivera, Tsyganenko V.V.	343
Fotesko K.O., Tomarieva N.O.	344
19. PEDAGOGY AND PSYCHOLOGY	345
Andrieieva O. O., Shtefan L. V.	346

Shtefan L.V, Bilovolenko V.O.	347
Ben Sliman N., Korolinska S.V.	348
Gulyaeva I.V., Kaydalova L.G.	350
George Yaw Osei, Filiptsova O.V., Filippova M.A., Kotenko V.V., Sivalnyova D.O., Burlaka I.S.	352
Ilina T.E., Shtefan L.V.	353
Komyshan A., Kozub S., Levashova O.	354
Meskini Dalila, Filiptsova O.V., Filippova M.A., Kotenko V.V., Burlaka I.S., Sivalnyova D.O.	356
Kaydalova L.G., Mironenko L.V.	358
Pirlik D.O., Filiptsova O.V., George Yaw Osei, Dyomina E.V., Sivalnyova D.O., Burlaka I.S.	360
Rakeiev P.V., Filiptsova O.V.	362
Tarasenko O.A., Shtefan L.V.	364
Timoshyna I.A., Filiptsova O.V., Ovezgeldiyev Dovran, Burlaka I.S., Sivalnyova D.O., Dyomina E.V.	365
Yukhno N.V., Shchokina N.B.	367
20. PSYCHO-PEDAGOGICAL FUNDAMENTALS OF FORMATION OF FUTURE SPECIALIST IN MODERN HEIS	369
Kirshenbaum E.V., Tymchuk N.F.	370
Kirshenbaum E.V., Tymchuk N.F.	371
Komyshan A., Tsarkova J.	372
Lutaeva T., Telegina A.	374
Plyaka L. V., Nieviezhina O. A.	376
Shtefan L.V., Ovsiannikova G.V.	378
Sabatovska I.S., Lyhvar A.	379
Sabatovska I.S., Sherbina T.	380

Tymoshchuk A. V.	382
Chueva I. M., Plyaka L.V.	383
Shapovalova V.S.	385
APPLICATION SHEET	387
K. K. Abdullayeva, T.B. Bajzoldanov, A.S. Kozhamzharova, H.M. Ilahunov.	388
A.B.Mukanova	390
K.T.Rozieva, Zh. Zh. Zhusupova	392
K.B. Temirbayeva, A.P.Nurzhanova	393
A.N. Yakubchuk, E.G. Fetisova, L.N. Andryukova, S.N. Kovalenko	394
T.B. Zholdasbekova, T.B. Bajzoldanov, A.S.Kozhamzharova	396

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