ABSTRACT&REFERENCES

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DEVELOPMENT OF THE METHODOLOGICAL APPROACH OF OBTAINING PREPARATIONS BASED ON SOLID DISPERSIONS

p. 4-8

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Nowadays, the innovative direction of pharmaceutical development is the application of methods to increase the biopharmaceutical efficiency and safety of the use of already existing APIs, including method of incorporating them into solid dispersions in which the substance molecules are included in the supramolecular formations by forming non-covalent bonds by excipients. Today, the preparation of solid dispersions is considered as the most effective way of increasing oral bioavailability, in which dissolution of the carrier facilitates the release of API with its rapid solubilization. According to the literature, it is established that today there is only an empirical approach to obtaining solid dispersions.

The aim *of the work was the formulation of the main approaches to the development of preparations on the basis of solid dispersions, taking into account the current trends in the development of the composition and technology of preparations with sparingly soluble active pharmaceutical ingredients.*

Materials and methods. *To develop a methodological approach, external situational content analysis of applied methods for increasing the bioavailability of active pharmaceutical ingredients used in the manufacture of solid dosage forms was used.*

Results. *In the course of accomplishing this goal, a classification of the types of solid dispersions was proposed depending on the structure and method of production, an algorithm was developed for choosing a method for obtaining a solid dispersion, taking into account the physico-chemical properties of the active pharmaceutical ingredients, which can be used in the technological process to increase their bioavailability. Critical components were also found in the development of solid dispersions.*

Conclusions. *Taking into account the physicochemical properties of the active pharmaceutical ingredients, was chosen an algorithm for selecting a method for preparing solid dispersions that can be used in the process to improve their bioavailability. Based on the results of the analysis of the literature data and our own research of the physico-chemical characteristics of the active pharmaceutical ingredients and excipients, type of the solid dispersion structure, the type of solvent and carrier, a methodological approach to the preparation of solid dispersions is proposed, the use of which will optimize the development of solid dosage forms*

Keywords: *solid dispersions, bioavailability, method of obtaining, structure, methodological approach, development stages*

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BIO-BASED SUCCINIC ACID SAMPLE PREPARATION AND DERIVATIZATION PROCEDURE OPTIMISATION FOR GAS CHROMATOGRAPHY-MASS SPECTROMETRY ANALYSIS

p. 9-13

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This study focused on bio-based succinic acid sample preparation and derivatization conditions optimization using GC-MS analytical method. Succinic acid, the precursor of a wide range bio-compounds, especially it is important in accumulation of mitochondrial metabolite succinate (citric acid cycle) and during ischemia controls reperfusion injury through mitochondrial reactive oxygen production. Accurate determination of analytes is the key in metabolomics to use as low molecular biomarkers in case to improve diagnostic methods.

Methods. *Gas chromatography-mass spectrometry (GC-MS) method. For the quantitative determination of the succinic acid applied derivatization process by silylation using -bis- (trimethylsilyl) -trifluoroacetamide (BSTFA).*

Results. *The derivatization agent BSTFA, the derivatization time of 3-4 hours and derivatization temperature at 70 °C were selected as the optimal derivatization condition for quantification of succinic acid by GC/MS in biological samples. The results show that GC-MS SIM method with evaporation was the most effective to quantify succinate in biological samples after ischemia/reperfusion injury. Selected ion monitoring (SIM) allowed to monitor a subset of fragments with their related mass values in a certain retention time (RT) range for a set of targets.*

Conclusions. *DC – MS has several advantages for measurements of succinate concentration in small kidney tissue samples (lyophilized mitochondria). The method can be applied in small pieces of tissue – biopy samples, tissues from various organs*

Keywords: *succinic acid, gass chromatograpy-mass spectrometry, derivatization, BSTFA, metabolomics, GC-MS*

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SCIENTIFIC AND PRACTICAL SUBSTANTIATION OF DIRECTIONS OF MUTUAL COOPERATION OF HIGHER EDUCATIONAL INSTITUTIONS WITH EMPLOYERS OF PHARMACEUTICAL SECTOR OF HEALTH CARE INDUSTRY

p. 14-19

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The aim *is to study, summarize and develop the directions of mutual cooperation between higher education institutions with employers of the pharmaceutical sector of the healthcare industry, which will allow making the preparation of competitive competent specialists in accordance with the requirements of the labor market.*

Methods: *to achieve the aim, methods of scientific analysis were used, in particular generalization, comparison, system and logical methods. Graphic analysis is used to visualize the generalized results of the expert survey.*

Results: *scientific and practical approaches to determining directions of mutual cooperation between higher education institutions and employers of the pharmaceutical sector of the healthcare industry are substantiated. Modern directions of cooperation between higher education institutions and employers are presented, which contribute to the improvement of the organizational and methodological foundations of interaction, the optimization of the content of education and the educational process, the improvement of the quality of practical training and employment of graduates, the development of research and innovation infrastructure. The forms of cooperation of the National University of Pharmacy (NUPh) with pharmacy institutions and pharmaceutical enterprises are systematized, the introduction of which will improve the quality of practical training of pharmacists.*

Conclusions: *based on the results of the expert survey of pharmacy specialists, it is determined that the most significant motivations for the cooperation of the National University of Pharmacy with the employers of the pharmaceutical sector of the healthcare sector are the training of specialists in accordance with the labor market needs and access to skilled labor resources, and effective forms of cooperation - mentoring and training. Based on the results of the research on the specifics and forms of cooperation, the authors carried out their systematization and defined the areas of mutual cooperation between higher education institutions and employers, using the example of the NUPh, the implementation of which contributes to improving the quality of practical training for future pharmacists and the formation of competitive graduates in accordance with labor market requirements.*

Keywords: *pharmacy, education, employers, forms of cooperation, practical training, employment, labor market.*

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THE INFLUENCE OF INDOLINOREN ON KIDNEY FUNCTION IN CONDITIONS OF WATER AND SALT LOAD

p. 20-23

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Diuretics are widely used to correct kidney disorders. In turn, the ionic composition of food, mostly sodium ions, which directly affect the excretory function of the kidneys, can act as modulators of the action of diuretics.

***The aim** of the study was to investigate the effects of the new 2-oxoindoline derivative with the conventional name "Indolinoren" on the state of the excretory function of the kidneys under the conditions of water and salt load.*

***Materials and methods.** Studies were performed on white non-linear rats. The water load was modelled by introducing distilled water (5 ml per 100 g of body weight of the animal); salt load - intragastric administration of 0.45 % sodium chloride solution in an amount of 3 % of body weight. Indolinoren and comparison drug furosemide were administered intragastrically at a dose of 29.5 mg/kg and 5 mg/kg, respectively.*

***Results and discussion.** It has been established that indolinoren has a saluretic effect in conditions of water load, accompanied by an increase in sodium excretion by 132 % and potassium by 2.4 %. Against the background of the introduction of indolinoren, a significant increase in the sodium-potassium coefficient of urine was established 2.3-fold ($p<0.05$), which indicates a more pronounced natriuresis than kaliuresis. Under conditions of salt load, indolinoren promotes a significant increase in urine output by 381 % ($p<0.05$), increases sodium excretion by 127 % ($p<0.05$), potassium by 7 %. There were no significant differences in creatinine excretion. The expression of diuretic activity in conditions of salt load indolinoren exceeds furosemide and does not have a significant difference under conditions of water load.*

***Conclusion:** The increase in natriuresis and, to a lesser extent, the kaliuresis, as well as the absence of significant changes in the excretion of creatinine, a glomerular filtration marker, on the background of the introduction of indolinoren indicates that its diuretic effect is realized due to oppression of tubular reabsorption. In the mechanism of indolinoren action involved inhibition of mineralocorticoid control of the excretory function of the kidney, as evidenced by the increase in the sodium-potassium coefficient of urine. The obtained data justify the need for further in-depth study of indolinoren as a perspective diuretic*

***Keywords:** diuretic activity, water load, salt load, indolinoren, 2-oxoindoline derivative, furosemide*

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DEVELOPMENT AND VALIDATION OF SPECTROPHOTOMETRIC METHOD FOR THE DETERMINATION OF MELDONIUM DIHYDRATE IN DOSAGE FORMS

p. 23-27

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Aim. *Spectrophotometry is one of the most widely used methods in the pharmaceutical analysis. The main advantages of this absorption method are the highly sensitive, cost-effective and available to quality control laboratories for dosage forms. However, there is a need to find new analytical reagents. Therefore, the aim of the present work was investigation and development of spectrophotometric method based on reaction with p-chloranil for the determination of meldonium dihydrate in dosage forms.*
Methods. *In the study were used working standard of meldonium dihydrate, p-chloranil, DMF, the sample of finished dosage forms. Absorption of the reaction products was measured using spectrophotometer Specord 200.*
Results. *The optimum conditions of the spectrophotometric analysis has been established during the process of development this procedure. The influence of various parameters such as nature of the solvent, concentration of reagent, temperature, time of heating were investigated. It was experimentally established that meldonium dihydrate reacts with p-chloranil in DMF medium to form the coloured reaction product with absorption maximum at 556 nm. The proposed method was subjected to validation tests. The method was validated for the parameters like linearity, precision, accuracy, robustness and range of application. Beer's law was performed at the concentration range of 8.00–20.00 mg/100 ml with correlation coefficient 0.9995. The linearity ranges were calculated with the help of regression analysis by means of least squares. The proposed procedure meets the requirements of State Pharmacopoeia of Ukraine.*
Conclusions. *The spectrophotometric method for the determination of meldonium dihydrate was developed and validated. This procedure is successfully applied for dosage forms analysis. Results of the study showed that the procedure is accurate, simple and relevant for application at the quality control laboratories for dosage forms*
Keywords: *spectrophotometry, derivatives of quinone, p-chloranil, meldonium dihydrate, analysis, quantitative determination, validation*

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RESEARCH OF 1,3-OXAZOLE-4-IL-PHOSPHONIC ACID DERIVATIVE ON THE CONTENT OF FATTY ACIDS OF LIPIDS IN RATS WITH ARTERIAL HYPERTENSION

p. 28-31

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The number of patients with arterial hypertension (AH) continues to increase. Significant negative effects of arterial hypertension are structural, metabolic and functional disorders in the tissues of the myocardium, vessels and other organs, in particular, changes in the content of fatty acids (FA) and their correlation. The purpose of the study is to investigate the change in fatty acid composition of lipids in blood serum and tissues of rats with arterial hypertension under the influence of a new original compound, 1,3-oxazole-4-yl-phosphonic acid derivative (abbreviated name – oxazole derivative).
Materials and methods. *The studies were conducted on white, sexually mature rats. Arterial hypertension was modeled by salt load – salt drink (1 % solution of sodium chloride) with free access to it for 21 days. Animals from the 14th day received oxazole derivative at a dose of 25 mg / kg intraperitoneally, once daily, for 7 days. The content of fatty acids of centrifuged blood serum and homogenized in 0.9 % saline NaCl tissue was determined by gas chromatographic analysis.*
Results and discussion. *The administration of oxazole derivative in the background of increased blood pressure in rats did not significantly affect the amount of SFA and USFA in serum in contrast to*

the group of rats with hypertension due to the tendency to restore the stearic acid content, but the changed content of linoleic and arachidonic acids practically did not differ from the values in the blank group. There was a restoration of the content of palmitic, stearic, linoleic and arachidonic acids in aorta. In heart, the change in the content of linoleic and arachidonic acids in the reverse direction compared with the blank group was established.

Conclusions. *The administration of 25 mg/kg (ED_{50}) of oxazole derivative intravenous intraperitoneally once daily for 7 days with simultaneous simulation of arterial hypertension by salt load did not cause any adverse changes and led to the restoration of lipid parameters of SFA, USFA and PUFA*

Keywords: *arterial hypertension, fatty acids, 1,3-oxazole-4-yl-phosphonic acid derivative, oxazole derivative, rats*

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THE RESEARCH OF FREE AMINOACIDS OF WATER-SOLUBLE PROTEIN-POLYSACCHARIDE COMPLEX OF OYSTER MUSHROOM PLEUROTUS OSTREATUS

p. 32-37

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Recently, the share of medicinal products of natural origin has increased in the pharmaceutical market of Ukraine. This is due to the fact that the pharmacological effect of natural substances provides a complex of biologically active substances, which has a high therapeutic effect and the minimum number of adverse reactions. Therefore, the study of chemical composition and standardization of natural substances is an important stage in pharmaceutical research.
A promising source of active ingredients is the mushroom Pleurotus ostreatus. The chemical composition of this fungus is represented by a large number of biologically active substances, which ensures its many-sided use in folk medicine.
***Aim.** The determination of qualitative and quantitative composition of free amino acids in the composition of water-soluble protein-polysaccharide complex (WPPSC) of oyster mushroom Pleurotus ostreatus was the aim of research.*
***Methods.** Physicochemical methods are the most commonly used to study active substances of natural origin. This is due to the fact that they provide high informative, accurate, efficient a nd reproducible. The method of high performance liquid chromatography (HPLC) was used to analyze the amino acid composition of the WPPSC of oyster mushroom Pleurotus ostreatus. This method is based on the separation of individual components due to different adsorption capacity.*
***Results.** Research of the amino acid composition of the WPPSC of oyster mushroom Pleurotus ostreatus showed that the complex contains 10 (7 %) free amino acids, among which 5 are essential. The detected aminoacids are aliphatic, heterocyclic and aromatic compounds. They are presented by glycine, alanine, leucine, isoleucine, threonine, selinum, lysine, arginine, histidine and phenylalanine.*
***Conclusion.** The qualitative and quantitative composition of the free amino acids of the WPPSC of oyster mushroom Pleurotus ostreatus was established. The method of determination and separation of free amino acids by the method of high-performance liquid chromatography is proposed. The obtained results are proposed for standardization of the initial substance in the process of production of medicines based on WPPSC of oyster mushroom Pleurotus ostreatus*
***Keywords:** Pleurotus ostreatus, biologically active substances, amino acids, high performance liquid chromatography, standardization*

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IMPACT OF DRY EXTRACT OF GINGER ON MORPHOLOGICAL STATE OF PANCREAS OF SYRIAN GOLDEN HAMSTERS ON THE BACKGROUND OF HYPERCALORIUM DIET

p. 38-44

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***The aim** is to study the effect of dry extract of ginger on the morphological state of the pancreas of Syrian golden hamsters against*

the background of a metabolic syndrome induced by a hypercaloric diet.

Materials and methods. *The metabolic syndrome was modeled with the help of golden male hamsters, 20 weeks old, that had a hypercaloric diet enriched with energy sources (including 29 % fat – predominantly saturated lipids) and fructose (1 g per 100 g body weight) for 6 weeks. Dry extract of ginger in a dose of 80 mg/kg, species "Arphasetin" at a dose of 16 ml/kg and metformin tablets at a dose of 60 mg/kg were administered intragastrically once a day, starting at 4 weeks of experiment for 14 days.*

On the histological sections of the pancreas, the total number of pancreatic islets in the micropreparation was determined, their area was measured, the islets were divided into small, medium and large, and the percentage of each category of pancreatic islets was determined.

Results. *Prolonged consumption of food rich in fat and carbohydrates by hamsters leads to the development of the state of prediabetes, which is characterized by the morphological inhibition of the insular apparatus: an increase in the relative proportion of small and a decrease in the proportion of medium pancreatic islets, a decrease in availability. According to the morphological characteristics, the introduction of a dry extract of ginger at a dose of 80 mg/kg to hamsters with a metabolic syndrome restores the state of pancreatic islets, their area, β- and α-cells of the pancreas to the level of intact animals. The pharmacological effect of the dry extract of ginger is most likely due to the phenolic compounds that make up its composition - gingerol and shogaol, which may modulate the release of insulin due to the antioxidant effect.*

Conclusions*. According to the severity of the protective action, the dry extract of ginger exceeds the reference preparations – metformin at a dose of 60 mg/kg and the species of "Arphasetin" in a dose of 16 ml/kg. The obtained results testify to the prospects of further experimental and clinical study of the pharmacological properties of dry extract of ginger with the aim of creating an effective antidiabetic phytopreparation.*

Keywords: *metabolic syndrome, high-calorie diet, dry ginger extract, pancreas, histological examination*

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