

## ABSTRACT&amp;REFERENCES

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## SUBSTANTIATION OF PRODUCTION TECHNOLOGY OF TABLETS “AP-HELMIN”

p. 4-8

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**The aim.** The purpose of this work is to substantiate the technology of “AP-helmin” tablets preparation and to establish the possible critical parameters of the production process.

**Materials and methods.** Objects such as a mixture of pure substances albendazole and praziquantel in the ratio (1:4), tablet mass and tablet core samples were used in the research. The usual physicochemical and pharmacotechnological methods of the State Pharmacopoeia of Ukraine were used in the work, namely, the appearance, physical parameters, bulk density, compressibility, flowability, crushing force, determination of average mass, uniformity of mass, resistance to crushing and disintegration time were evaluated.

**Results.** It was found that the mixture of active substances has poor flowability, indicating the need to enter the stage of wet granulation in the development of tablet technology with them.

The wet granulation stage was carried out with the addition of such excipients as corn starch, microcrystalline cellulose 101 (MCC-101) and povidone (as a 10 % solution).

Studies of the 4 samples of tablet mass allowed establishing the most rational composition for the formation of tablets-cores – sample number 4. The samples of composition

No. 4 are white core tablets, homogeneous, without chips and cracks, and with respect to resistance to crushing and disintegration time meet the requirements of SPH U (96 N and 8 min 27 sec, respectively).

The next stage of the study was the development of a common technology for the preparation of the tablets “AP-helmin”. In order to ensure proper consumer characteristics, the Opa-dry II ®YS-1-7027 White (“Colorcon”) white coating was introduced.

**Conclusions.** On the basis of the obtained results, a technological scheme of production was prepared taking into account the critical parameters and the forecasted control methods at different stages

**Keywords:** technology, tablets, anthelmintic drugs

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## DESIGN, SYNTHESIS, MOLECULAR DOCKING AND ANTICONVULSANT EVALUATION OF 6-METHYL-2-ARYLAMINOPYRIMIDIN-4(3H)-ONE

p. 9-17

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**The aim.** *Synthesis of 2-aminoaryl derivatives of 6-methyl-pyrimidin-4(3H)-one, target-based virtual screening followed by the study of anticonvulsant activity and the establishment of structure-activity patterns.*

**Materials and methods.** *The standard methods of organic synthesis were used, synthesized compounds structure was proved with elemental analysis, <sup>1</sup>H NMR spectroscopy, chromatography-mass spectrometry. Molecular docking was performed using AutoDockTools-1.5.6 and AutoDock Vina. Anticonvulsant activity was studied in a model of pentylenetetrazole seizures in rats.*

**Results.** *Methylation of 6-methyl-2-thiopyrimidin-4 (3H)-one with dimethyl sulfate or methyl iodide gave a 2-thiomethyl*

*derivative. By heating the latter with aromatic amines at 140 °C, the target 2-aminoaryl derivatives of 6-methyl-pyrimidin-4 (3H)-one were obtained. The prospect of screening the synthesized compounds on the pentylenetetrazole model by seizure and the selection of the objects was performed by the results of binding energy and conformation evaluation at the active sites of GABA receptor and GABA-AT. The test substances did not show anticonvulsant activity: only 2 compounds tended to exhibit activity according to the criterion of integral protective index – a decrease in mortality compared to control, preventing mortality in 100 and 80 % of animals, respectively. Comparison with previous activity results of 2-thioacetanilide derivatives allowed to prove the positive role of thioacetamide and phenyl fragments, as well as 4-Br, 4-MeO radicals in the manifestation of anticonvulsant activity and increase of lethality in the presence of Cl atoms.*

**Conclusions.** *The synthesis was performed and construction of the 2-aminoaryl derivatives of 6-methyl-pyrimidin-4(3H)-one was proved. PTZ seizures model in rats did not show anticonvulsant activity. However, the obtained results allowed us to identify a number of structural fragments that influence anticonvulsant activity. A positive correlation between in vivo studies on PTZ seizures model and docking results in active sites of GABA<sub>A</sub> and GABA<sub>AT</sub> enzyme was determined*

**Keywords:** *synthesis, pyrimidine, docking, GABA, PTZ, anticonvulsant activity*

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**STUDY THE ATTITUDE OF THE UKRAINIAN CITIZENS TO THE ENVIRONMENTAL PROBLEMS IN THE CONTEXT OF THE THEORY OF GENERATIONS**

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**The aim.** To study the attitude of the Ukrainian citizens to the environmental problems in the context of the theory of generations X, Y, Z.

**Materials and methods.** Using the analytical-comparative, system-analytical, mathematical-statistical, logical methods of analysis and the method of questioning, as well as descriptive and abstract modelling and generalization, the environmental portrait of the Ukrainian citizens was studied.

**Results.** In the context of the growing global environmental crisis, the environmental approach becomes a major trend for the country's sustainable development. Economic and social well-being is closely linked to the state of the environment, which can only be stable within certain environmental and resource boundaries. Therefore, special attention should be paid to the attitude of people to the environment as a public good and formation of their environmentally responsible behaviour, which is becoming an increasingly important element in international programs to protect our common environment. According to the research, the attitude of the Ukrainian citizens of different generations to the environmental problems was determined, and the main tendencies in the dominance of types of behaviour and character traits of the generation Z representatives were revealed. It has been found that the Ukrainian citizens of three generations (X, Y, Z) share common environmental values – they consider it is important to protect the environment and are confident that they can personally play a role in protecting the environment. However, it can be said that the environmental practices of the Ukrainian residents still need special attention from the state bodies and public organizations.

**Conclusions.** The attitude of the Ukrainian citizens to the environmental problems in the context of the theory of generations has been determined, and their common ecological values have been generalized. According to the results of the research, the main directions in raising the level of environmental awareness of citizens have been identified. The active work with young people has been proposed since the generation Z does not care about natural resources and the environment as a whole. In particular, such work is possible by introducing various eco-practices and raising public awareness concerning

*environmental issues. At the same time, it is important to introduce incentive and motivation mechanisms for environmental protection taking into account the needs and values of each generation*

**Keywords:** environmental portrait, theory of generations, surveys, awareness, environmental issues, environmental protection

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## DRUG DESIGN OF MEDICINAL PRODUCTS ON THE BASIS OF NATURAL CARDIOSTEROIDS

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**The aim.** The article describes works about designing a structure, predicting of biological activity and the chemical transformation of natural cardiosteroids to obtain promising drugs with specified properties.

**Materials and methods.** An effective modified method for the synthesis of aldimines of cardenolides, based on the interaction of natural cardenolides with organic amines, is proposed. The abnormal physical and chemical properties of bis-ketoimines, which consist in their resistance to hydrolysis and increased polarity, are revealed.

**Results.** It is revealed that electrostatic fields play a decisive role in cardiostonic activity, which should be located in the form of a “sandwich” – in the  $\alpha$ -plane there is a positive charge and in the  $\beta$ -plane is negative. The presence of a negative field at C3 is mandatory and the activity is higher if this negative field is extended further (the sugar component of the conditioned configuration, which does not violate the charges of the  $\alpha$ - and  $\beta$ -planes). It is shown why the molar activity (biological activity expressed in moles of substance per kg of animal mass) of cardenolide glycosides is higher than their aglycones, that is, the sugar component contributes to the activity through electron fields, and not only due to changes in the hydrophilic-lipophilic properties of the substance.

**Conclusions.** The hypothesis of the existence of a phenomenon of non-inducing binding to  $\text{Na}^+$ ,  $\text{K}^+$ -ATPase, in which the substance acts as an antidote for active cardiosteroids is formulated.

A detailed analysis of this relatively exceptional case involves the simultaneous occurrence of two isomerism – conformational (conformers) and geometric in the synthesis of aldimines of cardenolides

**Keywords:** cardio steroids, cardenolide, drug-design, aldimines, virtual screening, bis-cardenolides, cardiac glycosides, pharmaceutical development

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**PRIMARY SELECTION OF THE PREBIOTIC COMPONENTS IN THE COMPLEX DERMATOLOGICAL THERAPEUTIC AND PREVENTIVE MEDICINE WITH PROBIOTIC**

p. 33-39

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**The aim.** Selection of optimal prebiotic components for bacteria of the genus *Lactobacillus* for their joint use in a complex dermatological therapeutic and preventive medicine with a probiotic.

**Methods.** Co-cultivation of a probiotic strain in a liquid MRS nutrient medium with an active ingredient at selected concentrations. During the cultivation cycle, samples of growing culture were selected at specific intervals to determine bacterial concentration by direct seeding and acidity determination.

**Results.** During 48 h of co-cultivation of lactobacilli with selected components, were observed a significant increase of viable cells, both in control and with the addition of vitamins at selected concentrations (exponential bacterial growth phase), from 48 h to 60 h - decrease of the rate of cell growth as in control group, and in experiments, the number of cells remains almost constant (stationary phase of bacterial growth), after 60 h - decrease of the number of cells (phase of dying).

During cultivation, the oxidation of the nutrient medium resulting from the formation of lactic acid carbohydrates and other terminal metabolites were observed; that is, the addition of components slightly increases the biochemical potential of microorganisms, as evidenced by the increase in biomass and acid potential.

Although there was no significant difference between one series of experiments with different vitamin contents, the largest increase in viable cell was observed with vitamin B5 (concentration 1 %) and provitamin B5 (concentration 2.5 %).

**Conclusions.** Optimal prebiotic components for use with lactobacilli as part of dosage form were selected. Despite

the pronounced synergism of action of the vitamin B5 and D-panthenol, all other components are also promising due to the positive effects on human skin and lack of negative effects on lactobacilli

**Keywords:** lactobacilli, probiotics, prebiotics, skin microbiome, dermatological diseases, therapeutic and preventive medicine

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#### RESEARCH OF FEATURES OF DEVELOPMENT OF EPIDEMIOLOGICAL SITUATION ON LYMPHOGRANULEMATOSIS IN UKRAINE

p. 40-50

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**The aim.** To analyse the peculiarities of the epidemiological situation on lymphogranulomatosis in the country during 2012–2018.

**Materials and methods.** The studies used data from the National Cancer Registry for 2012–2018. Historical, analytical, comparative, systemic, logical, hypothetical-deductive, mathematical-statistical, as well as methods of epidemiological studies were used.

**Results.** It was established that morbidity and mortality of the adult and children's population from lymphogranulomatosis, expressed in absolute terms during 2012–2018 in Ukraine decreased. Thus, the number of patients with lymphogranulomatosis in 2012 compared with the data in 2018 decreased by 26.9 %, and mortality – by 41.2 %, among children – by 37.7 % and 25.0 %. All absolute indicators were complex in terms of the nature of the changes, with peak values in 2015 and 2018 (incidence among adults), as well as in 2016 (mortality among adults) and in 2015 (incidence of children). At the same time, not a single indicator reached or exceeded the value of the 2012, with the exception of data on the incidence of children with lymphogranulomatosis in 2015 (an increase of 11.8 % compared with the previous 2014). It is gratifying that after 2015, the incidence rates of children with Hodgkin's disease have steadily declined. It was proved that women prevailed taken together indicators of morbidity (53.4 %), and in the mortality structure, on the contrary, the proportion (%) of women was less (43.0 %). Among the children's contingent of patients, there were more men (53.0 %). According to the analysis of the relative incidence rates among men, it was found that their average value (2.29 per 100 thousand of the population in Ukraine) did not exceed the corresponding data of world epidemiology (2.3 per 100 thousand of the population of indicators) for lymphogranulomatosis. Among women, the average incidence rate (2.46 per 100 thousand of the population) significantly exceeded the corresponding world indicators (1.9 per 100 thousand of the population). The average value of the indicators of relative mortality from lymphogranulomatosis, which we calculated for 2012–2018 amounted to 0.69 for men and 0.47 for women per 100 thousand people against world figures of 0.4 and 0.3, respectively. Thus, we can conclude that the level of male mortality in Ukraine from lymphogranulomatosis was 1.7 times higher than the corresponding world indicators and 1.6 times higher for the female population.

**Conclusions.** From 2012 to 2018, Ukraine was able to reduce morbidity and mortality rates significantly, expressed in absolute data. At the same time, with regard to relative indicators, the fact of an increase in the incidence among women, as well as mortality from lymphogranulomatosis among adult patients causes our concern. This allows us to conclude that it is necessary to implement early diagnosis programs and chemotherapy regimens further, which can increase the 5-year survival of patients, as well as achieve stable and long-term remission in these patients

**Keywords:** epidemiology of lymphogranulomatosis, lymphogranulomatosis, lymphomas, oncohematology, Hodgkin disease

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## CALTHA PALUSTRIS. ANALYTICAL OVERVIEW

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**The aim.** Analysis and synthesis of data on the area of growth, content of biologically active compounds and the spectrum of use in pharmacy and medicine *Caltha palustris*.

**Materials and methods.** Literary and electronic sources of information regarding the distribution, chemical composition and pharmacological activity of *Caltha palustris*.

**Results.** *Caltha palustris* is a perennial herb of the Ranunculaceae family. The plant is unofficial, widely used by folk medicine as an anti-inflammatory, antispasmodic, bactericidal, antimicrobial, analgesic, diuretic agent. The main biologically active substances of *Caltha palustris* are tannins, glycosides ( $\gamma$ -lactones of protoanemonin and anemonin), saponins, berberine, bitterness, vitamin C, choline, carotene, flavonoids and alkaloids. *Caltha palustris* is a regionally rare plant in the administrative territories of Ukraine. Given the relevance of expanding the range of medicinal plant raw materials for the creation of modern therapeutics and chemical composition, pharmacological action of *Caltha palustris*, it is advisable to conduct further resource, phytochemical and other studies of the plant.

**Conclusions.** Considering the extensive experience in folk medicine, the wide range of pharmacological activity, the content of valuable biologically active compounds *Caltha palustris* is a promising and valuable raw material for the preparation and production of phytochemicals and their practical application.

**Keywords:** Ranunculaceae, *Caltha palustris*, protoanemonin, anemonin, biologically active substances, pharmacological action

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