ABSTRACT&REFERENCES

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RESEARCH OF TRENDS OF DEVELOPMENT OF THE HEALTH INSURANCE MARKET IN THE CONDITIONS OF SOCIO-ECONOMIC CRISIS IN UKRAINE

p. 4-11

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***Aim**: to analyze the development trends of the health insurance market in the context of the socio-economic crisis in Ukraine.*

***Materials and methods.** The studies used data from the National Commission for State Regulation of Financial Services Markets and the League of Insurance Organizations of Ukraine on the results of the activities of insurers (number of concluded contracts, gross, net premiums and payments) for 2014–2018. Financial indicators were standardized in accordance with macroeconomic standards that were established in state budgets for different years (minimum wage, minimum wage per person, NBU rate of 1 US dollar, minimum cost of a consumer basket). We used historical, analytical, comparative, systemic, logical, hypothetical-deductive, mathematical and statistical methods.*

***Results.** The significance of the relationship between all indicators is mathematically proven. In addition, all data for 2014–2018 showed positive growth dynamics. This cannot be argued after their normalization by macroeconomic indicators. According to the normalized data on the minimum wage, in 2017 there was a significant decrease in indicators with a slight increase compared to 2018. A positive fact is the growth of financial indicators during 2014–2018, which were normalized to the subsistence level for the working population. In 2015, there was a sharp decrease in the values of all financial indicators normalized at the dollar exchange rate, which is the result of fundamental changes in the monetary policy in the country. The indicated indicators reached the minimum value in 2016. The indicators normalized by the value of the minimum food basket showed a zigzag pattern of changes in all indicators with a sharp drop in data in 2016 and their subsequent increase in 2017. All indicators that were normalized by the minimum wage, the NBU dollar exchange rate, the value of the minimum food basket in 2018, did not reach the initial values typical for 2014.*

***Conclusions.** The health insurance market was characterized by complexity of development and dependence on the main macroeconomic indicators used in the calculation of many socially significant indicators of the development of society. Negative trends in the development of the segment of the health insurance market were due to the direct or delayed influence of changes observed in the macroeconomic environment during the socio-economic crisis*

***Keywords:** health insurance market, insurance premiums, insurance payments, the level of insurance payments, medical insurance*

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DESIGN AND IMPLEMENTATION OF GREEN CHEMISTRY APPROACHES INTO PHARMACEUTICAL ANALYSYS OF BENZYDAMINE DOSAGE FORMES

p. 12-17

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Aim. *The development of the pharmaceutical industry of Ukraine and the world has led to an increase in the need for the use of hazardous and toxic chemicals and solvents, which affects the safety of the environment and directly employees of pharmaceutical companies.*
Therefore, one of the solutions to this problem is the implementation of "green chemistry" approaches in pharmaceutical quality control laboratories.
Materials and methods. *Chromatographic separation methods are used for the qualitative and quantitative analysis of raw materials and finished dosage forms, the determination of substances that are formed during the degradation of active substances and allow rapid analysis of complex mixtures.*
Results*. For the implementation of green chemistry principles in the laboratory of pharmaceutical companies, it is necessary to evaluate the possibility of using rapid quality control methods such as gas chromatography, ultra-high*

performance liquid chromatography, and absorption spectrophotometry in the ultraviolet and visible regions.

***Conclusions**. Approaches to "greening" of analytical procedures used in quality control of pharmaceuticals have been studied. Ways of implementation of modern approaches of methods of "green chemistry" to chromatographic methods are offered. On the basis of the developed decision tree the design of development and "greening" of the methods of quality control of benzidamine dosage forms is proposed*

***Keywords**: green chemistry, benzidamine, liquid chromatography, gas chromatography, absorption spectrophotometry*

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DEVELOPMENT OF A DESIGN RESEARCH FOR DETERMINING THE QUALITY INDICATORS OF POTENTIAL API. 1. NEWLY SYNTHESIZED SUBSTANCES FOR PRIMARY PHARMACOLOGICAL SCREENING

p. 18-26

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The constant growth in the world of medicinal products of synthetic origin determines the search, directed synthesis and pharmacological studies of new biologically active substances. The establishment of the structure of the substance and the study of physo-chemical properties requires the use of a number of methods and tests that allow obtaining a substance with "pharmacopoeial quality" already at the stage of synthesis of potential API. Changes in the further conditions of synthesis, solvents for crystallization, etc. can lead to a change in the profile of impurities and their quantity, obtaining other polymorphic modifications, isomers, etc. and as a result – to a change in the pharmacological properties. To prevent this, the requirements for substances that are transferred for pharmacological screening must be unified.

Objective: *The purpose of the work is to summarize the information of methods of establishing the structure and physico-chemical properties of new biologically active substances, assess their compliance with pharmacopoeial quality requirements and formulate mandatory requirements for standardization of first synthesized substances for their transfer for primary pharmacological screening in the form of the structure of the primary "certificate of quality".*

Materials and methods. *The research uses the collection and analysis of data from modern scientific literature and regulatory documents.*

Results. *The conformity of research on the structure of the first synthesized substances to pharmacopoeial quality indicators of substances has been determined, the structure of "certificate of their quality" has been proposed, the basic principles of ensuring stable quality indicators in the synthesis of API have been highlighted.*

Discussion. *The obligatory definition for the newly synthesized substances such indicators as melting point, solubility in solvents of different polarity (lipofilicity), elemental composition and / or molecular weight is justified. From physical and chemical methods, UV, IR, and at least NMR spectroscopy are mandatory, the use of at least one of the chromatographic methods – TLC with the use of witness substances, or LC/MS (preferred, because in addition to purity allows to estimate the quantitative content of matter and the profile of impurities) is mandatory.*

Conclusions. *Approaches to the peculiarities of establishing the structure and studying the properties of a newly synthesized substance with the promising biological activity using physical, physico-chemical and chemical methods are generalized. The methods of establishing the BAS structure are unified, which fully characterize the structure, provide information on the purity and quantity of the compound at the initial stage of pharmacological tests. The main principles of ensuring stable quality indicators in the synthesis of potential API are highlighted*

Keywords: *Active substance, standardization, quality requirements, research design, analysis methods*

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STANDARDIZATION OF ORIGINAL MEDICINE ANTI-ALCOHOL ACTION ON ASSAY OF GLYCIN

p. 26-34

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Aim. *Development and validation of an accessible method for the quantitative determination of glycine in a new original drug used in condition of alcohol dependence.*
Methods. *To quantify glycine in a drug in the form of an effervescent powder for the preparation of an oral solution, a spectrophotometric method was developed and validated using a Specord 200 spectrophotometer from "Analytik Jena".*
Results. *As a result of the study, a modified sensitive method for the quantitative determination of glycine by a spectrophotometric method was developed. The optimal conditions for carrying out the glycine – ninhydrin reaction were selected in order to obtain stable analysis results: analytical wavelength – 568 nm; heating the reaction mixture is carried out in a boiling water bath for 30 minutes; the volume of the buffer solution is 4 ml, the pH of the buffer solution is 6.8, and a reducing agent – ascorbic acid was introduced. It was established that the methodology does not have a systematic error; the relative uncertainty for the probability of 95 % does not exceed the maximum allowable uncertainty of the analysis results (1.77≤2.4 %). Validation parameters such as specificity, linearity, accuracy, precision and robustness were studied for the glycine quantification procedure. It was established that all calculated validation parameters meet the acceptability criteria.*
Conclusions. *An accessible sensitive spectrophotometric technique based on the ability of the products of the interaction of glycine with ninhydrin to absorb in the visible region of the spectrum has been developed and validated. All validation parameters meet the acceptability criteria*
Keywords: *standardization, spectrophotometry, validation, glycine, anti-alcohol drug*

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STUDY OF STRUCTURAL AND MECHANICAL PROPERTIES OF BASES IN THE DEVELOPMENT OF DENTAL GEL WITH COMBINED COMPOSITION

p. 35-41

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Aim. *The development of the composition of the dental gel for the treatment of infectious and inflammatory diseases*

of the oral cavity, taking into account the physicochemical properties of the active pharmaceutical ingredients, namely the justification of the type and concentration of the gelling agent and other excipients.

***Methods**. The determination of organoleptic characteristics, uniformity of gel samples, pH of aqueous extract, and structural viscosity index was carried out according to the methods of the State Pharmacopoeia of Ukraine. Rheological studies were carried out using a rotational viscometer of the rotating type BROOKFIELD DV-II + PRO (USA) with a coaxial cylinder system.*

***Results**. In order to choose the optimal composition of the gel base, experimental samples with various gelling agents were developed (Carbopol 974P, Carbopol 934P, Carbopol Ultrez 10, xanthan gum, sodium alginate, sodium carmellose) and their organoleptic characteristics, structural viscosity and colloidal stability were studied. The physicochemical and rheological studies that were carried out, allowed us to conclude that it is rational to use the Carbopol Ultrez 10 gel former at a concentration of 1.1 %. When choosing neutralizing agents, sodium hydroxide and trometamol were used in the studies. According to the results of studies, sodium hydroxide at a concentration of 0.32 % was selected as a neutralizer, which provides maximum, stable viscosity in the pH range from 5.0 to 7.0.*

***Concusions**. The composition of the basis of a dental gel for the treatment of infectious and inflammatory diseases of the oral cavity has been developed: Carbopol Ultrez 10 – 1.1 %, sodium hydroxide solution 10–0.32 %*

***Keywords:** gel, gelling agent, carbomer, rheology, viscosity, dental drug*

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STUDIES OF PHYSICO-CHEMICAL AND PHARMACO-TECHNOLOGICAL PARAMETERS OF BIOFLAVONOIDS DIOSMIN AND HESPERIDIN

p. 42-46

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The use of medicinal substances of herbal origin are perspective direction for the development sector of the pharmaceutical industry of healthcare in Ukraine, even though increased demand for synthetic medicines. The natural substances that have a wide range of therapeutic effects, low toxicity and can be used in therapy of anorectal diseases is diosmin and hesperidin. In the pharmaceutical market of Ukraine the substances of diosmin and hesperidin are presented as solid dosage forms, which can be used for treatment of chronic venous insufficiency. It is appropriate to development composition and technology of new combination dosage form, which can purposefully release active substances in the places of progressing pathological process. The definition of substance properties is based on a comprehensive research, which results will have a significant impact on the technology of obtaining a new drug.

The aim of the work *was physic-chemical and pharmaco-technological researches of substances diosmin and hesperidin.*

Results. *The result of our work were carrying out a microscopic research, which is confirming results a differential curve of particle distribution, studied derivatographic characteristics of the substances, moisture absorption and solubility. Based on the research it can be concluded about insufficient solubility of diosmin and hesperidin, their high hygroscopicity and high critical degradation of substances. According to the results of microscopic analysis, diosmin has a few fractions with different distributions of particles and hesperidin has capable of agglomeration.*

Conclusions*. On the basis of research it can be concluded for the feasibility of further research, which can improve properties of the substances diosmin and hesperidin. The results of research can be concluded, that conducted results will have impact on development of the composition and technology of the new dosage form with diosmin and hesperidin*

Keywords*: diosmin, hesperidin, pharmaco-technological study, microscopically researches, moisture absorption, solubility, derivatographic characteristics*

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