ABSTRACT&REFERENCES

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ALGORITHM FOR CARRYING OUT A PROCEDURE FOR VERIFICATION OF A SPECTROPHOTOMETRIC METHOD FOR ANALYSIS OF SOLID-DOSED DOSAGE FORMS ACCORDING TO THE REQUIREMENTS OF SPHU 2.0

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Aim. *The increase in the pharmaceutical market of Ukraine of the range of medicines leads to stricter requirements for their quality. According to the requirements of international standards ISO, ICH, GMP, current legislation of Ukraine and the State Pharmacopoeia of Ukraine, generic drugs must be equivalent, and the analytical methods used for quality control, validated or verified.*

One of the available methods of analysis used both in pharmacy conditions and in quality control laboratories at enterprises and in independent control and analytical laboratories is absorption spectrophotometry in the ultraviolet and visible areas.

Materials and methods. *The method of absorption spectrophotometry in the ultraviolet and visible areas is used to quantify the active pharmaceutical ingredients in finished tablet dosage forms when the quantitative determination performed and when conducting pharmaco-technological tests, such as "Dissolution" and Uniformity of dosage units".*

Results. *To use the method of absorption spectrophotometry for the quantitative evaluation of active pharmaceutical ingredients in finished drugs, it is necessary to verify the proposed methods and examine such validation characteristics as specificity, linearity, accuracy and precision of the proposed methods.*

At the same time, the uncertainty of the results of the analysis Δ_{As}, expressed as a one-sided confidence interval for the probability of 95 %, and which consists of the uncertainty of sample preparation (Δ_{Sp}) and the uncertainty of the final analytical operation (Δ_{FAO}), must not exceed the maximum permissible total uncertainty of the analysis ($max\Delta_{As}$).

Conclusions. *The approaches of the State Pharmacopoeia of Ukraine to the methods for determining the quantitative content of active ingredients in tablets during the tests "Quantitative determination", "Dissolution", Uniformity of dosage units" were studied. The procedure has been proposed for verifying methods for quantitative determination of manufactured drugs using absorption spectrophotometry according to the requirements of the 2nd edition of the State Pharmacopoeia of Ukraine*

Keywords: *validation, verification, absorption spectrophotometry, manufactured drugs, tablets, statistical analysis*

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INVESTIGATIONS WITH THE AIM OF OBTAINING A MASS FOR PRESSING MEDICATED CHEWING GUMS "LYSODENT C"

p. 11-16

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The design of high quality compressed medicated chewing gum "Lysodent C" with lysozyme hydrochloride and ascorbic acid as active pharmaceutical ingredients and the composition Health in Gum® PWD-01 as a chewable gum base involves obtaining a homogeneous mass for pressing. In order to prevent the segregation of the mass for pressing due to its polydispersity, it was necessary to carry out a preliminary granulation of the substance of lysozyme hydrochloride, which is characterized by fine dispersion, hygroscopicity and insufficient pharmacotechnological properties for direct compression method.

***Aim of the work** – to carry out physicochemical and pharmacotechnological studies in order to obtain a homogeneous mass for pressing medicated chewing gums "Lysodent C".*

***Materials and methods.** The objects of study are granulate of lysozyme hydrochloride (Bouwhuis Enthoven, the Netherlands) with an intensive sweetener sucralose (Solo Sucralose-Non Micronised NF, VB Medicare PVT. LTD., India) and a flavoring agent (Nat Apple Flavor Wonf, Kerry Inc., Malaysia), and also a mass for pressing, obtained by mixing the granulate, the composition Health in Gum® PWD-01 (Cafosa, Spain) and ascorbic acid (Foodchem, China). As a granulating liquid ethanol 96 % was used. During the experiment, physicochemical (moisture absorption capacity), pharmacotechnological (optical microscopy, flowability, bulk density and tapped density, determination of particle size by analytical sieving) and statistical studies in accordance with the requirements of SPhU 2.0 were used.*

***Results.** Crystallographic analysis revealed similarity in size and shape of the obtained lysozyme hydrochloride granulates with the granules of Health in Gum® PWD-01, which was also confirmed by the study of the fractional composition – particles with a size of 1.0>n≥0.7 are their main fraction. In addition, the conversion of lysozyme hydrochloride powder to granules improved its pharmacotechnological characteristics. However, granulate, like the pure substance of lysozyme hydrochloride, is hygroscopic, which requires, respectively, a decrease in its moisture absorption capacity. Crystallographic analysis of the mixture obtained by mixing the granulate and Health in Gum® PWD-01 with premixing of ascorbic acid, established its dispersion homogeneity, and the study of its technological characteristics – good flowability, which will ensure high-quality compressed gums. The moisture absorption capacity of the formed mass for pressing did not decrease, but on the contrary increased, due to the presence in the mixture of such hygroscopic components as lysozyme hydrochloride and chewing gum base.*

***Conclusions.** It was established that the use of pre-granulation of lysozyme hydrochloride led to the homogeneity of the resulting mass for pressing. However, the hygroscopicity of the mixture requires the introduction of moisture-absorbing agents in its composition or compliance with 40 % of the relative humidity of the environment during the preparation of the drug*

***Keywords:** medicated chewing gums, granulate of lysozyme hydrochloride, mass for pressing, physicochemical and pharmacotechnological studies*

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RISK ASSESSMENT OF LOGISTIC ACTIVITIES IN FOREIGN ECONOMIC ACTIVITY AS A COMPONENT OF EFFICIENT MANAGEMENT BY A PHARMACEUTICAL COMPANY

p. 17-21

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Aim. *The aim of the study is to develop a methodology for assessing the level of risk of the logistic component of foreign economic activity (FEA) of the pharmaceutical company (PhCo).*

Materials and methods. *The study used methods of synthesis, analysis and synthesis, content analysis. To determine the risks of logistics in the foreign trade of pharmaceutical companies, an expert survey method was used. The survey was attended by leading specialists of departments of PhCo, whose functional responsibilities are related to the implementation of FEA. The total number of experts was 50 people. 100 % of respondents have a higher education, they are divided into the work experience: 0–10 years – 11 %, 11–20 years – 27 %, 21–25 years – 53 %, over 25 years – 8 %. According to the gender, 83 % of women and 17 % of men participated in the survey. Experts' conclusions are grounded.*

Results. *It is determined that under the risk of logistics in the field of foreign trade of pharmaceutical companies it is appropriate to understand the likelihood of occurrence of events in the field of foreign trade of PhCo in relation to the management of all types of flows when they pass through the country's borders, which leads to certain consequences in space and time, namely, loss of part of the company's income, foreign partners, delays in fulfilling obligations to other partners in the untimely delivery of active pharmaceutical ingredients (API), fines, penalties, etc. It is proved that the risks of logistic activity in the field of foreign economic activity on the basis of the species include the following subspecies: the risk of partnership, information, transport, innovation, organization, procurement of imported API, main and auxiliary materials, sale (export) of finished medicines, storage and loss of profit.*

Conclusions. *The conducted research has led to the conclusion that the effectiveness of the functioning of PhCo is also influenced by the risks of logistics in the field of FEA*

Keywords: *pharmaceutical enterprise, risk, logistics, management, evaluation, drugs*

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SYNTHESIS OF POTENTIAL ANTIEXUDATIVE PREPARATIONS FOR 2-((4-AMINO-5-(FURAN-2-IL)-1,2,4-TRIAZOLE-(4H)-3-YL)-SULFANYL)-N-ACETAMIDE SERIES

p. 22-29

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Aim. *Conduct the purposeful synthesis of new potential biologically active substances of derivatives of 2-((4-amino-5-(furan-2-yl)-1,2,4-triazol (4H)-3-yl)-sulfanyl)-N-acetamides and evaluate their anti-exudative activity on the model of formalin edema in rats.*

Materials and methods. *In this work, standard methods of organic synthesis, physical and chemical methods of proofing the structure of synthesized compounds, elemental analysis, ^{1}H NMR spectroscopy, chromatographic mass spectrometry, and antiexudative activity were studied on the model of formalin edema in rats using a digital plethysmometer.*

Results. *By alkylation of 2-((4-amino-5-(furan-2-yl))-4H-1,2,4-triazole-3-thione with N-aryl-substituted α-chloroacetamides in ethanol in an alkaline medium, (4-amino-5-(furan-2-yl)-1,2,4-triazole(4H)-3-yl)-sulfanyl)-N-acetamide. After crystallization we obtained white or light yellow crystalline substances with clear melting temperatures. On the model of formalin edema in rats, the antiexudative activity of the newly synthesized 2-((4-amino-5-(furan-2-yl)-1,2,4-triazole(4H)-3-yl)-sulfanil)-N-acetamides was studied. According to the results of the research, a dependence between "chemical structure – antiexudative activity" of the first synthesized compounds was established. The results of experimental studies showed that fifteen out of twenty one compounds showed anti-exudative activity, eight of which exceeded this activity or were at the reference level of sodium diclofenac.*

Conclusions. *Synthesis of twenty one compounds of 2-((4-amino-5-(furan-2-yl)-1,2,4-triazole(4H)-3-yl)-sulfanyl)-N-acetamide derivatives was carried out and an evaluation of antiexudative activity, the dependence "chemical structure - antiexudative activity" was established. Leading compounds for antiexudative activity were found*

Keywords: *synthesis, 4-amino-3-thio-5-(furan-2-yl)-1,2,4-triazole, acetamides, alkylation, antiexudative activity, formalin edema*

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INFLUENCE OF DRY EXTRACT OF BRASSICA OLEARACEA ON THE MORPHOLOGICAL STRUCTURE OF THE GASTRIC MUCOSA OF RATS DURING AN EXPERIMENTAL ULCER CAUSED BY ALCOHOL-PREDNISOLONE MIXTURE

p. 30-41

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Aim *– study of the effect of cabbage dry extract on the morphological state of the gastric mucosa of rats on the background of an experimental alcohol-prednisolone ulcerative lesion.*
Materials and methods. *Ulcerative lesions of the gastric mucosa of nonlinear white rats were reproduced by intragastric*

administration of a mixture of 80 % ethanol and prednisolone 20 mg/kg at the rate of 0.6 ml per 100 g of body weight. Dry extract of cabbage in doses of 30, 40, 50 and 60 mg/kg and the reference drug Altan at a dose of 1 mg/kg was administered intragastrically in the treatment and prophylactic mode: daily for 3 days before pathology simulation, on the day of the introduction of the alcohol-prednisolone mixture and the next day at the end of the experiment. Histologically we examined the mucous membrane of the fundus and pyloric stomach. Conducted semi-quantitative assessment of the mucous membrane by the presence of destructive changes within the entire microdrug, haemocapillar disorders, edema of mucosal stroma and productivity of mucoid secretion by mucous-forming cells of the pathogenic epithelium outside the destructive zones by the intensity of the periodic acid Schiff reaction.

Results. *The introduction of an alcohol-prednisolone mixture to rats led to the emergence of a pronounced acute ulcer-erosive process in various parts of the gastric mucosa, which was accompanied by significant hemocapillary disorders and stromal edema. In most cases, the ulcers spread to the entire depth or most of the glandular tubes. In areas outside the zones of destruction, a decrease in mucoid secretion by cells of the gastric superficial-foveolar epithelium, additional cells of its own glands, glandular cells of the pyloric glands, stimulation of pepsin production, increased acid formation were observed. Dry extract of cabbage reduced the severity of acute ulcerative-erosive process and hemocapillary disorders and edema, restriction of degradation zones occurred, processes of mucoid synthesis stabilized, severity of pepsin and acid formation decreased. The experimental data indicate pronounced gastroprotective properties of dry extract of cabbage, the most pronounced positive effect is set at a dose of 50 mg/kg*

Conclusions. *According to the activity of the gastroprotective effect of dry extract of cabbage, it prevailed in comparison with the domestic plant-based drug Altan at a dose of 1 mg / kg. The results indicate the promise of further experimental studies of the pharmacological properties of dry extract of cabbage in order to create an effective anti-ulcer phytopreparation*

Keywords: *gastric and duodenal ulcer, alcohol-prednisolone ulcer, dry extract of cabbage, gastric mucosa, histological examination*

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BIOLOGICALLY ACTIVE SUBSTANCES OF SALIX PURPUREA F. GRACILIS (GREN. & GODR.) C.K. SCHNEID. (SALICACEAE)

p. 42-48

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The medicinal raw materials of many representatives of the Salicaceae family have long been widely used both in folk medicine and in modern pharmaceuticals. Currently, some species of willow are official medicinal raw materials in some European countries. In 2014, "Salicis cortex" acquired the status of official medicinal raw material and included in the State Pharmacopoeia of Ukraine. In this regard, the study of biologically active compounds of different species, varieties and hybrid forms of willow is important, which will allow to expand the range of medicinal plant material both at the expense of local and at the expense of introduced species of willow, common in Ukraine.

Aim. *Study of qualitative and quantitative composition of biologically active substances of Salix purpurea f. Gracilis (Gren. & Godr.) C.K. Schneid., Growing in Ukraine.*

Methods of the research. *The object of the study were dry shoots of the Salix purpurea f. Gracilis (Gren. & Godr.) C.K. Schneid. Plant raw materials were collected in 2016–2017 years by the NBS named after M. M. Grishko National Academy of Sciences of Ukraine. The component composition of volatile substances was determined using the Agilent Technologies 6890 chromatograph with a mass spectrometer detector 5973. The content of the phenolic substances was determined colorimetrically by the Folin-Ciocalteau method. Component composition of phenolic substances was determined by high performance liquid chromatography (HPLC) using the Prominence LC-20 Liquid Chromatographic System Shimadzu (Japan).*

Results. *The qualitative composition and quantitative content of volatile compounds and phenolic substances of Salix purpurea f. Gracilis (Gren. & Godr.) C.K. Schneid shoots have been determined. It was established that the raw material contains rather high concentrations of volatile compounds, which are dominated by aromatic – in particular, geraniol and eugenol, among the terpenoids, squalene predominates. It was found that phenolic substances are represented by flavonoids and hydroxycinnamic acids. Among substances of phenolic nature dominated by flavanones. The conducted studies confirm the feasibility of further studies of willow species.*

Conclusions. *The qualitative composition and quantitative content of volatile compounds and phenolic substances in Salix purpurea f. Gracilis (Gren. & Godr.) C.K. Schneid shoots have been determined. The studies significantly expanded the data on the chemical composition of raw materials of plants of the genus Salix L. Data obtained from the study of Salix purpurea f. Gracilis (Gren. & Godr.) C.K. Schneid will be used for the planning of pharmacological research and development of QCM for raw materials and medicines*

Keywords: *Salicaceae, willow, shoots, biologically active substances, volatile compounds, phenolic substances*

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