ABSTRACT&REFERENCES

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FEATURES OF STANDARDIZATION AND REGISTRATION OF DIETARY SUPPLEMENTS COMPARED TO DRUGS

p. 4-10

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The constant increase in the number of dietary supplements and the demand for them, as well as the progression of self-medication with the use of over-the-counter medicines, raises questions about their effectiveness, safety and bioequivalence. There are also questions about the criteria for ingredients, production, standardization and registration of finished medicines and dietary supplements.

The aim. *The aim of the work is to summarize information on the features of standardization, certification and registration of dietary supplements in comparison with drugs in the territory of Ukraine.*

Materials and methods. *Data were collected and analyzed from the current scientific literature and regulatory documents to perform the research.*

Results. *Production, standardization and circulation of finished medicines and dietary supplements is carried out in accordance with the current legislation of Ukraine, international standards (ISO, ICH, GxP) and the requirements of the State Pharmacopoeia of Ukraine. According to these documents, the requirements for the quality of medicines and dietary supplements differ, but unlike ten years ago, today there can be increased regulation and control on the part of the state and law enforcement agencies to eliminate cases of falsification and circulation of unregistered means.*

The current legislation of Ukraine regulating the production, quality and circulation of finished medicines harmonized with the EU puts forward requirements for providing the population with quality imported/domestic medicines. Regarding dietary supplements, the procedure of harmonization of the legislation of Ukraine with the EU has started, which in the future should lead to improvement of the quality of these remedies and increase of control from the state.

Discussion. *We generalized requirements for the features of standardization and registration of dietary supplements in the territory of Ukraine, which must be observed in the manufacture, quality control, registration and sale of dietary supplements.*

Conclusions. *Simpler registration, implementation and wider market conditions (multi-level marketing system, Internet) lead to a rapid increase in the production of dietary supplements in Ukraine and their imports. We generalized information about the requirements for the quality of dietary supplements in comparison with finished medicines, and the features of their registration in the territory of Ukraine according to the current legislation*

Keywords: *standardization, registration, quality, finished medicines, dietary supplements, Ukrainian legislation*

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NANOBIOTECHNOLOGICAL OBTAINING OF LIPOSOMAL FORMS OF ANTIOXIDANT PREPARATIONS BASED ON BIOFLAVONOIDS

p. 11-15

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Most pathological conditions are accompanied by lipid peroxidation and accumulation of oxidative stress products. The antioxidant action of natural hydrophobic compounds, such as quercetin, ubiquinone, curcumin, vitamin E, etc. is established. It is also known that these biologically active compounds act on different parts of antioxidant system. However, their use in parenteral drugs is difficult taking into account their hydrophobicity. Nanoparticles, such as liposomes, are used to increase the bioavailability of lipophilic antioxidants and to create water-soluble form of them.

The aim of the work *is to develop the liposomal preparation with co-encapsulation of two hydrophobic antioxidants, namely curcumin and quercetin.*

Methods. *Technological methods of obtaining liposomes and analytical physicochemical, chromatographic (HPLC, TLC, GLC), methods of determination of particle size, pH were used.*

Results. *As a result of the study, the formulation and technology of obtaining the liposomal form of curcumin and its composition with quercetin were proposed. The effect of fatty acid composition of lipids, the ratio "lipid: active substance" and the technological conditions on the liposomes formation and the level of encapsulation of active pharmaceutical ingredients were studied. The dependence of nanoparticle sizes on the pressure value and the number of homogenization cycles was investigated. The lyophilized product with a level of encapsulation of hydrophobic antioxidants at least 85 % was obtained. The physicochemical properties of the samples were observed.*

Conclusions. *The technological scheme for obtaining of complex preparation containing curcumin and quercetin, involving the obtaining of lipid film, hydration of components, high-pressure homogenization, sterile filtration and lyophilization is proposed*

Keywords: *hydrophobic antioxidants, bioflavonoids, curcumin, quercetin, nanobiotechnology, liposomes, method for obtaining liposomes*

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THE INFLUENCE OF LIFESTYLE FACTORS ON CONSTIPATION – SHOULD THE PHARMACIST BE AWARE OF THIS?

p. 16-23

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Aim *of this study was to analyze the influence of lifestyle (nutrition and physical activity) on constipation and evaluate the respondents' attitude to this disorder.*

Methods. *Pharmacy visitors who agreed to answer questions were included in the study. Data from respondents based on age (18–45 years old; 46–65 years old; above 65 years old) and body mass index ("normal", "overweight", "obese") was analyzed. Nutrition and physical activity were analyzed for the purpose of identifying risk factors for constipation. Descriptive and comparative statistics were used – the respondents' responses are presented in frequencies and percentages, Chi-square test was executed to measure association with knowledge, responses and gender, age, BMI.*

Results. *The study identified a 12.8 % constant constipation rate in the study group with no significant differences between genders, however more males had no constipation problem (50.5 % vs 39.9 %). The age and body mass index had association with constipation ($p<0.05$). The consumption of coffee and/or tea was not related to constipation in the study group, however, the respondents' motionless lifestyle was related to constant and occasional constipation (75.0 % and 41.1 %, respectively) ($p<0.05$).*

Conclusions. *The consumption of carbohydrates, inadequate intake of fluids and motionless lifestyle were identified as risk factors for constipation in this study. Lifestyle modification recommendations might be included in the pharmacists' consultation*

Keywords: *constipation frequency, nutrition, physical activity, body mass index*

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RESEARCH ON THE DEVELOPMENT OF DENTAL GEL TECHNOLOGY WITH METRONIDAZOLE BENZOATE AND HYALURONIC ACID

p. 24-29

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Aim. *Development of technology of dental gel with combined composition, establishment of optimal technological parameters for the introduction of active and auxiliary substances.*

Methods. *After production of experimental gel, we determined homogeneity for the samples with the method of SPhU 1.1, section 511. The particle size of the suspension was studied using a XY-B2TLED microscope under polarized light according to SPhU 2.9.37. The quantitative determination of metronidazole benzoate and the accompanying impurities A, B, C, miramistin, sodium hyaluronate was performed by liquid chromatography, according to SPhU section 2.2.29, section 2.2.46.*

Results. *According to the results of chemical and microscopic studies, the optimal method of introducing metronidazole benzoate into the gel base is the suspension method. To ensure the best distribution of metronidazole benzoate, a micronized substance was used and the technological parameters of pre-homogenization of metronidazole benzoate in propylene glycol at 20–25 °C were determined. Microphotographs of the gel samples showed that homogenization of metronidazole benzoate with propylene glycol at a speed of 3000 to 4000 rpm provides a homogeneous translucent gel of white colour. Selected methods of dissolution and technological parameters allow to obtain a stable gel without degradation products of active substances.*

Conclusions. *The optimal way of introducing into the gel base the combination of active substances: metronidazole benzoate, myramistine, hyaluronate sodium is substantiated. The rational technology of production of the combined dental gel is developed. Critical stages and parameters of technological process are defined, criteria of their acceptability are established*

Keywords: *technology, solubility, suspension, homogenization, gel, dentistry*

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RESULTS OF STRUCTURAL ANALYSIS OF MEDICAL APPOINTMENTS OF QUERCETIN DRUGS AND ITS DERIVATIVES IN UKRAINE

p. 30-37

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The aim*: to analyze the structure of medical prescriptions for quercetin and its derivatives in Ukraine*

Materials and methods. *We used data from an expert survey of doctors from 25 cities of Ukraine, which was conducted during 2017–2018. The survey involved doctors of various specialties who had «very high» (k≥0.91), «high» (k=0.71–0.90) and «satisfactory» (k=0.51–0.70) level of competence. This indicator was determined using five coefficients (k_{1+n}), which characterized the level of theoretical and applied training of specialists in the organization of the medical and diagnostic process for patients suffering from various types of angiopathies. We used the historical, analytical, comparative, systemic, logical, hypothetical-deductive, mathematical and statistical methods, as well as the expert survey method.*

Results. *It was found that the largest number of appointments (51.82 %) was made by therapists/family doctors, and the smallest – by endocrinologists (3.6 %). The vast majority of respondents (except for allergologists and endocrinologists) prescribed these drugs in treatment according to the main diagnosis of the patient. At the same time, only therapists/family doctors and cardiologists prescribed quercetin and its derivatives in a wide range of development of the clinical picture of the pathology, namely the main diagnosis, with its complications and associated diseases. Doctors of all specialties, except for otolaryngologists noted the use of quercetin and its derivatives in the treatment of concomitant pathologies of sick patients. The first position in the structure of medical appointments (1st level of ICD-10) was taken by appointments in the treatment of I-diseases of the circulatory system (78.97 %), the second – by J-diseases of the respiratory system (11.30 %), and the third – K-digestive system diseases (6.04 %). In the structure of prescriptions for patients with cardiovascular pathologies, the largest share was made in the treatment of angina pectoris (49.60 %), in the second position – chronic ischemic heart disease (21.61 %), and in the third – other cerebrovascular diseases (10.60 %).*

Conclusions. *It was proved that the highest prescribing rates of quercetin and its derivatives were carried out by therapists/family doctors in the treatment of diseases of the cardiovascular system according to the main diagnosis, its complications and associated pathologies. The low level or lack of prescription of drugs of this group in doctors of other specialties requires further research in the indicated direction*

Keywords: *angiopathy, angioprotectors; quercetin; medical prescribing; frequency of medical prescriptions*

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PRIMARY SCREENING OF THE BIOLOGICAL ACTIVITY OF HETEROCYCLIC AMINODERIVATIVES OF 2,3-DICHLORO-1,4-NAPHTOQUINONE

p. 37-42

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The aim. *Check the antimicrobial and fungicidal activity of 2,3-dichloro-1,4-naphthoquinone aminopyrazole derivatives and predict their severity of toxicity to rats.*

Materials and methods *of the research. The antimicrobial activity of heterocyclic amino derivatives of naphthoquinone 3a-d was studied by diffusion of the substance into agar on solid nutrient medium and by serial dilution. Acute rodent toxicity was determined by the QSAR simulation method implemented in GUSAR software.*

Results. *In the work, the antimicrobial and fungicidal activities of new heterocyclic amino derivatives of naphthoquinone were studied, as well as the in silico determination of their acute toxicity for rats was carried out using four types of substance administration.*

Conclusions. *The study of aminopyrazole derivatives of naphthoquinone revealed the compounds exhibiting high antimicrobial activity against the Candida tenuis test culture, namely: 2-chloro-3-((1-methyl-1H-pyrazol-4-yl) amino) naphthalene-1,4-dione (3a) and 2-chloro-3 - ((1-methyl-1H-pyrazol-3-yl) amino) naphthalene-1,4-dione (3b). All the synthesized compounds were found to exhibit selective bacterio- and fungistatic activity. QSAR determined the non-toxic compound 3c in the intraperitoneal route of administration, as well as the non-toxic compound 3d in the subcutaneous route of administration*

Keywords: *aminopyrazole 2,3-dichloro-1,4-naphthoquinone derivatives, primary biological screening, GUSAR program*

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EXPERIMENTAL RESEARCH ON DEVELOPMENT AND VALIDATION OF METHODS OF QUANTITATIVE DETERMINATION OF FLAVONOIDS AND ESSENTIAL OIL IN SOLID MULTI-COMPONENT CAPSULES «UROHOLUM»

p. 43-49

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The aim. *Development and validation of methods for the quantification of flavonoids and essential oils in solid multi-component capsules for use in urology.*

Methods. *To quantify the amount of flavonoids, a spectrophotometric technique was developed and validated using an Evolution 60 s spectrophotometer from Thermo Fisher Scientific, USA, to determine the essential oil - gravimetric method.*

Results. *As a result of the study, a method was developed to quantify the sum of substances of the flavonoid structure of the total phytoextract in the form of capsules by spectrophotometric method and the sum of essential oils after pre-distillation with water vapour and extraction with organic solvent by gravimetry. Spectrophotometric quantification of flavonoid structure substances was performed after complexation reaction with aluminum salts (III) in acetic acid medium at an analytical wavelength of 410 nm. The calculation of the content of biologically active substances was performed by the standard method, which was used as a rutin. Validation parameters such as specificity, linearity, and precision have been studied for methods for quantifying the sum of substances of flavonoid structure and essential oils.*

Conclusions. *Available and validated methods for the quantitative determination of the amount of biologically active substances of a dry multicomponent herbal extract in solid capsules have been developed and validated. The studied validation parameters meet the eligibility criteria*

Keywords: *standardization, multicomponent composition, dry extract, spectrophotometry, validation, solid capsules*

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SOME APPROACHES TO OBTAINING INTERNAL AUDIT EVIDENCE FOR PHARMACEUTICAL QUALITY SYSTEMS

p. 50-55

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The aim *of the work is to analyse approaches and develop proposals for the selection of optimal methods for collecting evidence of internal audits of pharmaceutical quality systems.*

Materials and methods. *The study was based on the materials of the current state legislative and regulatory framework, ISO 9000 series standards, sources of foreign and domestic scientific literature, as well as the results of our previous research. The following methods were used in the study: system-analytical, sociological survey, comparative analysis, structural-logical modelling.*

Results. *According to the results of previous studies conducted on the basis of domestic pharmaceutical enterprises of various fields of activity, it was found that the main reason for the often insufficient effectiveness of internal audits is the low level of professionalism of auditors. At this stage of the study, an investigation of such an internal audit method as an interview was conducted, and approaches to its application were analysed. In particular, it was found that the interview method is used at domestic pharmaceutical enterprises as the main method of collecting audit evidence for their further assessment and interpretation. It was also proved that one of the key skills of the auditor is to pose the correct, appropriate questions for obtaining informative answers. An algorithm for posing audit questions was developed and tested, optimized to increase the completeness and meaningfulness of staff responses.*

Conclusions. *The study allowed us to propose an interview technique that is effective for collecting audit evidence, which increases the effectiveness of the internal audit process by increasing the value of the information received from the position of managerial decision-making.*

Keywords: *quality management system, pharmaceutical quality system, self-inspection, internal audit, pharmaceutical activities, GMP, ISO 9001.*

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