

ABSTRACT&REFERENCES

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**RATIONALE OF THE METHODOLOGY
CLASSIFICATION OF MEDICATION RELATED
ERRORS DURING THE RETAIL SALES OF
DRUGS IN UKRAINE**

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The aim. Rationale of methodology for classification of medication related errors during retail sale of medicines in Ukraine.

Materials and methods. With the help of system-analytical, statistical, comparative methods of analysis, as well as descriptive and abstract modulation and generalization, we investigated domestic and foreign scientific publications and legal framework.

Results. An analysis of the current state of the domestic pharmacovigilance system showed that it provided reports of adverse drug reactions, their lack of efficacy, but no categories characterizing medication errors, in particular during retail sales in pharmacies and self-medication. However, despite the lack of a unified classification of medication errors, it is possible to distinguish the main categories of medication errors and group them by stages of occurrence: error; that occur during the prescribing of medication, the use of drugs during inpatient treatment, and in the release of drugs by pharmacist. The results of the comparative analysis of international classification and medication errors monitoring systems have determined that most of them include error that related to the dose, conditions and duration of medication administration, compliance of the medication with the patient, compliance with the prescribed/recommended pharmacotherapy and adapted accordingly to the conditions of development of health care of different countries.

Conclusions. Approaches to the classification of medication errors are generalized and substantiated by the global and national trends in the development of the pharmaceutical sector; the medication error classification model, which can be applied during the retail sale of drugs in Ukraine. The proposed methodology for the classification of medication errors during the retail sale of medications includes 44 cate-

gories of errors, which are divided into three levels depending on the stage of providing pharmaceutical assistance: errors in the selection of OTC drugs in the course of consulting by pharmacist, errors in the release of drugs by a pharmacist and errors at the stage of medication use by the patient

Keywords: medical error; pharmacovigilance; classification methodology; pharmaceutical assistance

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TECHNOLOGICAL ASPECTS OF OBTAINING LIQUID EXTRACTS OF BLACK KIDNEY BUDS AND DETERMINING THE STRATEGY FOR THEIR STANDARDIZATION AT THE PHARMACEUTICAL DEVELOPMENT STAGE

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The aim. Conducting research on the development of technology for obtaining liquid extract of poplar black buds, their standardization and determining the optimal parameters of the technological process of extraction, which should provide the required content of biologically active substances and pharmacological activity of the drug.

Methods. The production of liquid extracts was carried out by the method of percolation. The quantitative determination of the amount of hydroxycinnamic acid derivatives was carried out by the unified spectrophotometric method recommended by the State Pharmacopoeia of Ukraine, in terms of coffee acid, at an analytical wavelength of 509 ± 3 nm. To determine the quantitative content of the sum of flavonoids was used the method of differential spectrophotometry, flavonoids were calculated in terms of luteolin, by the reaction of flavonoids with a 2 % solution of aluminium chloride in ethanol (96 %) R at an analytical wavelength of 398 ± 3 nm.

Results. The research on the technology of obtaining liquid extracts of black poplar buds was carried out. The technological parameters of the crushed medicinal plant raw material of the black poplar buds (bulk, the coefficient of filling of the dry raw material) were determined and the extraction parameters were calculated. It is established that the process requires the use of 2nd and 3rd discharges, and returns them to the process at the first stage of the process for the series that follows. To increase the absolute content of biologically active substances, it is rational to change the extraction regimes (infusion time, extractant flow rate, temperature). The quantitative determination of extractive substances and spectrophotometric determination of the amount of hydroxycinnamic acid derivatives in terms of coffee acid, as well as the amount of flavonoids in terms of luteolin at all stages of the process of obtaining liquid extracts was done. The influence of the concentration of the extractant on the qualitative composition of the obtained extract was established. The optimal extraction conditions were selected and the technology for ethanol extracts based on ethanol (96 %) R and ethanol (70 %) R was developed from medicinal plant material of black poplar buds. To increase the absolute content of biologically active substances in liquid extracts experimentally argued to increase the infusion time to 24 hours. The liquid extracts of black poplar buds have been developed for their further screening studies.

Conclusions. As a result of the study was developed the technology of obtaining liquid extracts of poplar black buds, their standardization was carried out, the optimal parameters of the technological extraction process were determined, ethanol extracts were developed for their further screening studies

Keywords: extraction, technological process, liquid extract of black poplar buds, standardization, spectrophotometry

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COMPARATIVE CYTOTOXIC ANALYSIS OF EXTRACTS OBTAINED FROM LEAVES AND ROOTS OF SWEET FLAG (*ACORUS CALAMUS* L.) ON RAT BONE MARROW CELLS IN VITRO

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*The aim of this study was to identify cytotoxic activity and to compare severity of cytotoxic activity of de-alcoholized alcohol-water extracts obtained from the leaves and roots of Sweet Flag (*Acorus Calamus* L.) on rat bone marrow cells in vitro. Rat bone marrow cells were isolated from the femoral diaphysis of the animals under cold temperatures.*

To obtain various concentrations of extract from the leaves (LEA) and roots REA, the initial extracts (concentration 1.0 g/mL) were immunologically titrated by rolling method. A quantitative assessment of cytotoxicity was made by testing plasma membrane damage in the Trypan Blue dye exclusion test.

It was found that the cytotoxicity of a substance obtained from the roots of Sweet Flag (REA) depends on the dose and time of contact with rat bone marrow. REA has a cytotoxic effect at concentrations of 0.03–1.65 g/mL. When in contact with rat bone marrow cells for 15 minutes it causes an increase in the number of dead cells by $0.48–1.56 \times 10^6$ per milliliter ($p < 0.05$). For REA in all studied concentrations, an increase in the effect of cytotoxicity is shown as the time of contact of cells with the active substance increases from 15 to 90 minutes ($p < 0.05$).

The substance obtained from the leaves of Sweet Flag (LEA) does not cause cell membrane destruction and does not have a significant effect on the viability of rat bone marrow cells in all studied concentrations

Keywords: cytotoxicity, red bone marrow, rats, leaf extract of *Acorus Calamus*, root extract of *Acorus Calamus*

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PHYTOCHEMICAL STUDY OF SALVIA GRANDIFLORA AND SALVIA OFFICINALIS LEAVES FOR ESTABLISHING PROSPECTS FOR USE IN MEDICAL AND PHARMACEUTICAL PRACTICE

p. 23-28

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The raw material base of medicinal plants in Ukraine is sufficient only for half of the pharmacopoeial species. Most part of the medicinal plants is growing in insufficient quantities and there is a need for their import. In conditions of import dependence and a shortage of domestic plant materials, the search for new sources of biologically active substances among the representatives of the flora of Ukraine is an urgent task of modern pharmaceutical science.

The aim of the work – conduct a comparative phytochemical study of the leaves of S. grandiflora and S. officinalis to establish the possibility of using the non-pharmacopoeia species in pharmaceutical and medical practice.

Materials and methods. The objects of the study are the leaves of S. grandiflora and S. officinalis, which was harvested in the botanical garden of the Lviv National University named after I. Franko. The study of macro- and microelement composition in the leaves of S. officinalis and S. grandiflora was carried out by atomic emission spectrographic method. Determination of the qualitative composition and quantitative content of the main groups of biologically active substances was carried out by HPLC. Quantitative determination of phenolic compounds was also carried out by spectrophotometric method.

Results. The content of 15 micro and macro elements was found in both studied species. In the leaves of S. officinalis

and *S. grandiflora*, 15 amino acids and 8 saponins were identified. Using HPLC, the qualitative composition and quantitative content of phenolic substances in the leaves of *S. officinalis* and *S. grandiflora* (13 and 9 compounds, respectively) was established.

Discussion. The dominant macro and micro elements in the studied species were silicon, phosphorus, magnesium, calcium, sodium, and potassium. The total content of trace elements in the leaves of *S. grandiflora* is 1.67 times greater than in the pharmacopeia plant *S. officinalis*. The dominant amino acids in the leaves of both species are glutamic acid, aspartic acid, valine and leucine.

The dominant saponins in the leaf of *S. officinalis* were ursolic and oleanolic acids, the total content of which is 75.82 %. In the leaves of *S. grandiflora*, ursolic and euskapic acids were dominant, with a total content of 63.25 %.

The total flavonoid content is higher in *S. officinalis* leaf and is 4.90 mg/g. The total content of hydroxycinnamic acids is highest in the leaf of *S. grandiflora* and is 4.49 mg/g, which is 221.18 % (2.21 times) higher than in the pharmacopeia plant *S. officinalis* (2.03 mg/g). The total highest content of caffeic acid derivatives prevails in the *Salvia officinalis* leaf (0.77 mg/g). The highest content of the sum of all detected phenolic compounds is specified for *S. officinalis* leaves and amounts to 6.93 mg/g.

Conclusions. As a result of a comparative phytochemical study of the leaves of *S. grandiflora* and *S. officinalis*, it was established that *S. grandiflora* is a promising species for introduction into medical and pharmaceutical practice, namely, as a source of phenolic compounds

Keywords: *Salvia* genus, non-pharmacopeia species, leaves, chemical composition, phenolic compounds

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RESEARCH OF MEDICAL TREATMENT INFLUENCE OF «MELANIZOL» SUPPOSITORIES ON BACKGROUND OF “MECHANICAL” VAGINITIS IN RATS

p. 29-33

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The aim. To study the therapeutic effect of new vaginal suppositories “Melanizol” based on metronidazole and tea tree oil on a model of “mechanical” vaginitis in female rats.

Methods. The therapeutic effect of suppositories of “Melanizol” has been studied in female rats on the model of “mechanical” vaginitis, which is a secondary insemination of vaginal. On the background of vaginitis the general condition of the animals, the dynamics of body weight, the morphological composition of peripheral blood, the rate of erythrocyte sedimentation, changes in pH and temperature in the vagina were examined, and macroscopic evaluation of vaginal mucosa was evaluated.

Results. The results of studies show that, on the background of pathology, there were shifts that were manifested by a clear swelling of the tissues around the vagina, a decrease in body weight, a shift in the pH to the alkaline side, an increase in the temperature in the vagina, leukocytosis, a shift of the leukocyte formula toward an increase in the number of neutrophils, increasing the erythrocyte sedimentation rate. In the vaginal mucosa were observed lesions, manifested by edema, hyperemia, and numerous hemorrhages. Under conditions of treatment with suppositories «Melanizol» a reliable restoration of the pH and decrease in the temperature of the vagina of animals, a decrease in the rate of sedimentation of erythrocytes, the total number of leukocytes and the restoration of the level of neutrophils to indicators of the group of intact animals were observed. Macroscopic studies of the vaginal mucosa showed a therapeutic effect of vaginal suppositories «Melanizol», it was manifested by a significant

reduction in the area of the affected area of the vagina and its manifestations. The effectiveness of the suppositories of «Melanizol» significantly surpassed the comparison drug of «Gravagin» and were practically of the same efficiency as the reference drug «Hippophaes oleum suppositories».

Conclusions. The therapeutic effect of new vaginal suppositories of «Melanizol» based on metronidazole and tea tree oil on the model of «mechanical» vaginitis in female rats has been proved. Studied suppositories «Melanizol» is a perspective drug for the treatment of non-specific vaginitis caused by mechanical irritants and need further research in this direction.

Keywords: experimental vaginitis, vaginal suppositories, metronidazole, tea tree oil, rats.

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ANALYSIS OF CLINICAL EFFICACY AND SAFETY OF INTRAVENOUS USE OF DICLOFENAC FOR THE PREVENTION OF POSTOPERATIVE PAIN: CURRENT STATUS AND STRATEGIC ASPECT

p. 34-38

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The aim of the work is to analyze and systematize the literature data regarding the current state and strategic aspect of intravenous use of diclofenac for the prevention of postoperative pain, namely clinical efficacy and safety.

Materials and methods. Studies were conducted using databases on the Internet: PubMed; Food and Drug Administration, European Medicines Agency. It has used retrospective, logical, research methods, content analysis.

Results. Conducted clinical data analysis indicates that diclofenac sodium, when administered intravenously, has an opioid-saving effect, is effective in patients experiencing acute postoperative pain, or as part of a multimodal analgesic strategy to achieve perioperative pain control. This increases the possibility of relief of pain and promotes accelerated rehabilitation after surgery, reduces the need for opiates. The incidence of side effects with intravenous diclofenac was similar to that seen with other treatments. New opportunities of the strategic aspect of intravenous use of diclofenac is related to the use of Dyloject, Hospira Inc., USA, which has improved solubility, shorter administration time than infusion. The incidence of thrombophlebitis on treatment with Dyloject was less pronounced compared to Voltarol.

Conclusions. Thus, the experience of clinical intravenous use of diclofenac sodium for the prevention of postoperative pain has confirmed its efficacy, favorable safety profile and the ability to reduce the need for opiates. The promising strategic aspect is the creation of domestic diclofenac sodium preparations for intravenous administration, which have improved solubility, shorter administration time than infusions and have no additional safety risk

Keywords: diclofenac, postoperative pain, opioid-saving effect, intravenous injection

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MORPHOLOGICAL CHANGES IN TISSUES OF ORGANS IN RATS WITH ARTERIAL HYPERTENSION (SHR) WITH TREATMENT OF HYPOTENSIVE MEDICINES (WITH RAMIPRIL AND CANDESARTAN) IN COMBINATION WITH CORVITIN

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To date, arterial hypertension (AH) is the most common cardiovascular disease, which is the most common cause of disability in the population due to high risk of developing complications, such as heart failure, coronary heart disease, stroke. The nature of the morphological manifestations of hypertensive disease depends on the duration and its severity, but hypertension triggers a cascade of pathological changes in the lung disease and is accompanied by disruption of the structure most sensitive to fluctuations in blood pressure organs (brain, heart, kidneys). The search for new drugs that not only reduce blood pressure but also have polytropic effects is constantly in progress. In the first place is cardioprotection, which is based on the principles of continuous monitoring of myocardial oxygenation and metabolism. Recently the attention of researchers attract bioflavonoids, namely Corvutin, which has antioxidant, prediabetics, anti-inflammatory properties. The question of influence Corwin in combination therapy with antihypertensive drugs in the treatment of hypertension has been insufficiently studied, that determines the relevance and aim of our study.

Materials and methods. The study was performed on hypertensive SHR rats, which spontaneously had hypertension. Rats were divided into groups. Experienced animal groups SHR were administered ramipril at a dose of 0.5 mg/kg,

candesartan – 0.4 mg/kg, and conducted combined therapy ramipril and corvutin, candesartan and corvutin. Corvutin – 50 mg/kg. Drugs were administered 1 time per day for 7 days with food (for short-term treatment) and 21 days (for long-term therapy).

To evaluate the morphological changes of the heart, kidneys and liver, we used frozen transverse sections, 10 μm thick, which were stained by the method of Ramonovsky-Gimze..

The results of the study. Corvutin when applying with ramipril and candesartan had a protective effect on the studied structures of target organs: myocardium of the ventricles, cortex of the kidney, hepatocytes. But Corvutin cardioprotective effect observed in myocardial tissue of the left ventricle during long-term combination therapy with candesartan was more significant and is characterized by the disappearance of signs of hydropic vacuolation of cardiomyocytes. Combination therapy with hypotensive drugs corvutin reduced degree of atrophy of the glomeruli, the greatest efficiency was achieved after long-term therapy. Changes in the liver tissue with the combination of drugs also had positive dynamics.

Conclusions. Combined therapy with antihypertensive drugs and corvutin significantly improves the morphological result in the studied structures not only by reducing blood pressure, but also by the pleiotropic effects of corvutin

Keywords: hypertension, candesartan, ramipril, Corvutin

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