DANYLO HALYTSY LVIV NATIONAL MEDICAL UNIVERSITY
PHARMACEUTICAL FACULTY

ANNALS OF PHARMACEUTICAL FACULTY

DANYLO HALYTSKY LVIV NATIONAL MEDICAL UNIVERSITY

Volume 7 **2021**

CONTENTS

MISSION STATEMENT

Students and young scientist (PhD students) participation in research projects is one of the important ways to improve the quality of education and to enhance graduates competitive ability on the labor market and, thereof, rating of a particular university.

Student scientific work is the shortest way to self-affirmation, raisings self-esteem, and gaining authority in the student society.

This issue contains abstracts of original papers of PhD students and abstracts of master projects defended in 2021 at pharmaceutical faculty of Danylo Halytsky Lviv National Medical University and thus represent the scientific interests of pharmacy students.

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PhD STUDENT ABSTRACTS

(APRIL 2021)

CLINICAL AND PHARMACEUTICAL SUBSTANTIATION OF THE MODEL OF ACTIVITY OF THE CLINICAL PHARMACIST AT THE AIDS CENTER

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Keywords: clinical pharmacy, clinical pharmacist, HIV/AIDS, pharmacotherapy, drug interaction,

Introduction: The availability of a wide range of antiretroviral drugs and the need to prescribe them to patients with HIV / AIDS require a comprehensive approach and special attention on the part of medical staff to prevent and eliminate their side effects, including those resulting from the inevitable polypragmasism, interactions as antiretroviral drugs with drugs of pathogenetic and symptomatic action. This raises the question of whether there is a specialist in health care facilities who treat patients with HIV / infection / AIDS who would combine two extremely important areas - medical and pharmaceutical. Such a specialist is a clinical pharmacist. The main place of work of a clinical pharmacist should be, first of all, a medical institution. It is here that the issue of pharmacotherapy is difficult to solve without a qualified specialist. Despite the above, in Ukraine only a small number of health care facilities have the position of a clinical pharmacist in the staff list, which is held by a properly trained specialist.

Materials and methods: - bibliosemantic method – to study the state of use of clinical pharmacy in the field of HIV / AIDS on the basis of scientific literature sources, electronic resources; - clinical-pharmaceutical method – for the analysis of drugs used in the field of infectious diseases; - pharmacoeconomic method – for economic evaluation of the use of drugs in the inpatient department of the AIDS Center according to the prescriptions (form № 003-4 / 0)

Results and discussion: According to the work plan for the reporting period the following tasks of dissertation work are executed:

- developed criteria for assessing the quality of medical care with the participation of a clinical pharmacist at the AIDS Center;
- the Local Form of the AIDS Center has been updated;
- the normative-legal documentation which creates a basis for practical activity of the clinical pharmacist in the AIDS Center is analyzed;
- work is underway to assess the quality of pharmacotherapy of patients in the inpatient department of the AIDS Center based on the analysis of prescriptions (Form № 003-4/0, which includes patients with Covid-19 and patients with HIV / AIDS) (n = 300).

According to the curriculum of the 2nd year of postgraduate training, the following disciplines were passed:

- Methods of statistical processing of the obtained results
- Computer programs for scientific work
- Laboratory methods of experiment construction
- Innovations in healthcare.
- Psychological aspects of personnel management and professional growth of the scientist.
- Foreign language for academic purposes.

Academic integrity. Antiplagiarism.

SCIENTIFIC JUSTIFICATION OF THE PROFESSIONAL ROLE OF PHARMACEUTICAL SPECIALIST ON THE BASIS OF PROVISIONS THE WORLD HEALTH ORGANIZATION AND THE INTERNATIONAL PHARMACEUTICAL FEDERATION IN THE CONDITIONS OF TRANSFORMATION OF UKRAINIAN SOCIETY

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Keywords: *pharmacist; the World Health Organization; the International Pharmaceutical Federation; professional roles; material and moral incentives*

Introduction: The dissertation was scheduled for October 29, 2019, at a meeting of the Scientific Council of the Faculty of Pharmacy Danylo Halytsky Lviv National Medical University.

Materials and methods: The research materials were sources of periodical literature and obtained personal data. Methods used: analysis of bibliographic references to identify the main sources of periodicals, questionnaires, mathematical statistics, generalization and interpretation of results.

Results and discussion: During the reporting period, the data of scientific sources on the selected topic of the dissertation research were analyzed. A questionnaire was developed for an anonymous survey of pharmaceutical specialists on the level of satisfaction with the material and moral side of their work. Data were collected and analyzed. The data of an anonymous questionnaire survey of pharmaceutical specialists, students of higher educational institutions of pharmaceutical orientation, as well as visitors of pharmacies in different cities of Ukraine on awareness of professional roles of a pharmaceutical specialist in accordance with WHO and FIP regulations were analyzed. An article was published in the domestic scientific professional

publication Acta Medica Leopoliensia (2020, Volume 26, №2-3. P.89-93), abstracts in two foreign conferences and five domestic ones. She took part in two foreign conferences and one domestic one.Performance of disciplines was credited, according to the curriculum of the second year of postgraduate study.

Conclusions: The amount of dissertation work is 50%.

CLINICAL AND PHARMACEUTICAL SUBSTANTIATION OF THE MODEL OF ACTIVITY OF THE CLINICAL PHARMACIST AT THE IN THE DENTAL MEDICAL UNIVERSITY CENTER

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Keywords: clinical pharmacy, clinical pharmacist, the dental university center, pharmaceutical dental care, pharmacotherapy.

Introduction: A specialist who is called to improve the quality of medical care - is a clinical pharmacist who reduces the cost of pharmacotherapy through the rational use of drugs provides pharmaceutical care to the patient and the doctor when prescribing drugs to the patient.

There are three dental medical university centers in Ukraine: University Dental Center of Kharkiv National Medical University, Dental Medical Center of the Bogomolets National Medical University, Dental Medical Center of the Danylo Halytskyi Lviv National Medical University is the first and only university center where the activities of a clinical pharmacist are implemented today.

The need for specialists in clinical pharmacy, rational pharmacotherapy and pharmacovigilance, and especially in the dental medical university center, remains relevant.

Materials and methods: - Sociological method - a questionnaire was developed to interview dentists in order to study the opinion of dentists, their attitudes and behavior towards patients with socially dangerous infectious diseases, as well as to improve the infectious safety of dental care. - Clinical-pharmaceutical method – In the analysis of drugs used in the performance of dental manipulations (anesthetics, drugs for general anesthesia).The pharmacotherapy of general anesthesia in the preoperative and operative period during dental manipulations in 2019 was evaluated. - Pharmaco-economic method – in the economic evaluation of the purchase and use in dentistry of filling, endodontic materials, materials for dental prosthetics, as well as disinfectants and medicines.

Results and discussion: Completed 40% of the dissertation, namely:

- preoperative examination by an anesthesiologist and general anesthesia protocol (n = 120) were analyzed, according to the primary accounting documentation № 003-3 / 0;
- the legal framework (n = 250) was studied and the role of the clinical pharmacist in the preparation for the accreditation of the dental medical university center was analyzed;
- a new version of the Quality Guidelines for certification of quality management system for services in the field of medical and dental practice, carried out at the Dental Medical Center of Lviv National Medical University named after Danylo Halytsky, in accordance with DSTU ISO 9001: 2015 "Quality Management System. Requirements (ISO 9001: 2015, IDT)";
- the list and features of application of extemporaneous medicines at the dental medical university center (n = 16) are investigated.

According to the curriculum of the 2nd year of postgraduate training, the following disciplines were passed:

- Methods of statistical processing of the obtained results
- Computer programs for scientific work
- Laboratory methods of experiment construction
- Innovations in healthcare.
- Psychological aspects of personnel management and professional growth of the scientist.
- Foreign language for academic purposes.

Academic integrity. Antiplagiarism.

SYNTHESIS OF 5-ENE-(5-METHYLISOXAZOL-3-YLIMINO)-4-THIAZOLIDINONES AS POTENTIAL BIOLOGICALLY ACTIVE COMPOUNDS

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Key words: synthesis, 4-thiazolidinone, isoxazole, biological activity

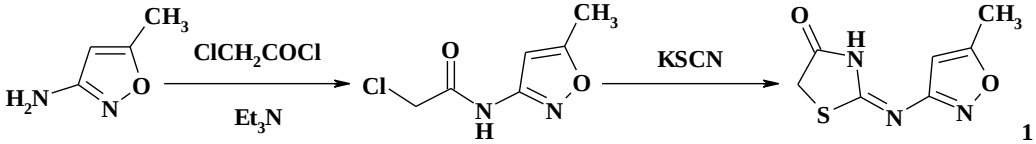
Introduction. 2-Amino/imino-4-thiazolidinone derivatives are a known group of biologically active compounds as potential drugs. Various 5-substituted 2-amino/imino-4-thiazolidinone derivatives possess anti-inflammatory activity (dual COX-2/LOX-5 inhibitors, highly selective of COX-2 inhibitors), antioxidant activity and inhibitory activity of metalloproteinases (MMP), antitumor properties (of cyclin-dependent kinase 1 (CDK1) inhibitors, inhibitors of dynamin I, antagonists of integrin αvβ3), antimicrobial effect (penicillin-binding protein (PBP) inhibitors, antiarrhythmic

and antihypertensive activity. Mentioned derivatives are selective agonists of b3-adrenoceptors (b3-AR), potential drugs for the treatment of frequent urination, type II diabetes, obesity and comorbidities [1].

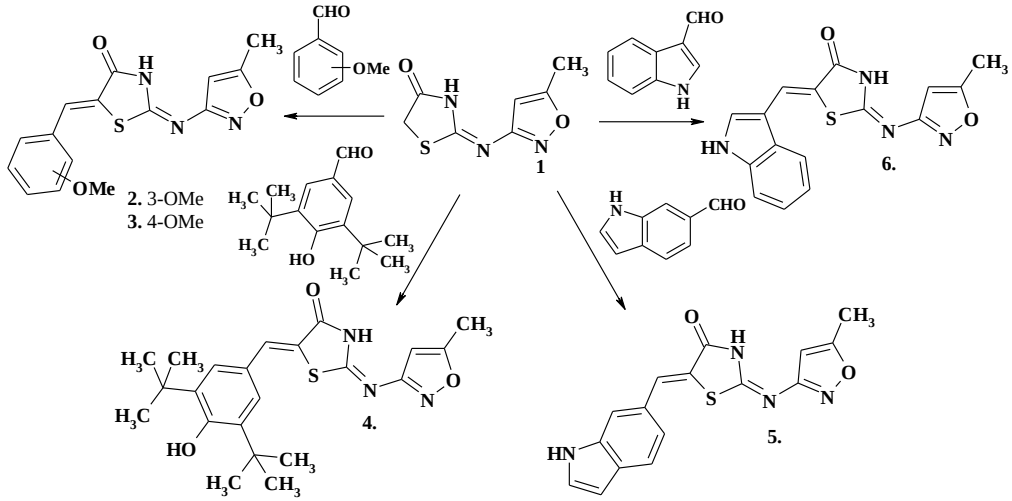
Compounds based on aminoisoxazole show a wide range of biological activities, in particular: hypoglycemic, anti-inflammatory, antibacterial. Heterocyclic systems containing isooxazole moiety are selective antagonists of γ-aminobutyric acid and selective agonists of cloned human dopamine D4 receptors, exhibit antifungal antimicrobial properties, inhibit cyclooxygenase (COX-2), show antitumor activity. Due to the strong fungicidal, herbicidal and insecticidal properties, compounds based on aminoisooxazole have become widely used in agrochemistry[2].

Materials and methods. Organic synthesis, ^{1}H NMR spectroscopy, LCMS.

Results. The starting 2-(5-methylisoxazol-3-ylimino)-4-thiazolidinone **1** were synthesized based on known approaches *via* [2+3]-cylocondensation and Dimroth rearrangement of 2-chloro-*N*-(5-methylisooxazol-3-yl)acetamide and potassium thiocyanate [3,4].

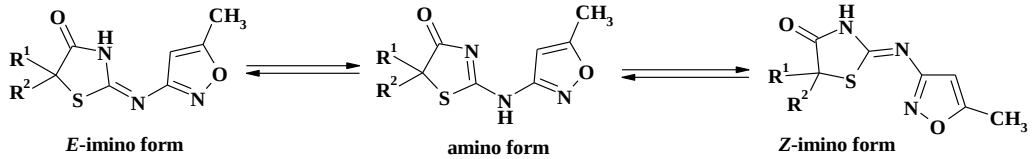


Target 5-ene derivatives **2**–**5** were obtained in the Knoevenagel reaction condition (medium – ethanol, catalyst - monoethanolamine). Some aromatic and indole-substituted aldehydes were used as oxo compounds.



Synthesized 2-(5-methylisoxazol-3-ylimino)-4-thiazolidinones can exist in the three tautomeric forms: imino-4-thiazolidinones (exocyclic C=N bond,

Z- and E-structures) and 2-amino-4-thiazolidinones (endocyclic C=N bond) [4]. The imino form presentation of structures was argued by previous data [5].



The structures of compounds have been determined by ^{1}H NMR and LCMS. A *Z*-configuration of the exocyclic C=C bond in the 5-ene derivatives **2-6** was confirmed by the signal of a methine proton, which observed at higher chemical shift (δ 7.66-7.97 ppm) as a singlet [1]

Experimental part

2-Chloro-N-(5-methylisooxazol-3-yl)acetamide. Chloroacetyl chloride (0.062 mol) was added dropwise to a mixture of 3-amino-5-methylisooxazole (0.061 mol) and triethylamine (0.062 mol) in anhydrous dioxane (20 ml). The resulting mixture was kept for 15 minutes at 130 °C. After cooling, the reaction mixture was precipitated with water, filtered and recrystallized from ethanol.

2-(5-Methylisoxazol-3-ylimino)-4-thiazolidinone (**1).** The mixture of obtained 2-chloro-*N*-(5-methylisooxazol-3-yl)acetamide (0.02 mol) and potassium thiocyanate (0.042 mol) was heated at reflux for 4 hours in acetone (20 ml). After vacuum distillation of the solvent from the reaction mixture, a clear, yellow oily product remains in the flask, which crystallizes rapidly. The obtained product was recrystallized from ethanol. Yield 68%, mp 230-232ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.37 (s, 3H, CH_3), 4.04 (s, 2H, CH_2), 6.09 (s, 1H, $CH_{isoxazole}$), 12.00 (s, 1H, NH). LCMS: m/z 198.0 (100%, $[M+H]^+$).

General procedure for the 5-ene-2-(5-methylisoxazol-3-ylimino)-4-thiazolidinone synthesis (2-6). A mixture of 2-(5-methylisoxazol-3-ylimino)-4-thiazolidinone (5 mmol), appropriate aldehyde (5 mmol), 2-3 drops of monoethanolamine in ethanol (20 mL) was heated under reflux for 4 h. Precipitate obtained after cooling was filtered off, washed with methanol and recrystallized with acetic acid or dioxane.

(Z)-5-(3-Methoxybenzylidene)-2-(5-methylisoxazol-3-ylimino)-4-thiazolidinone **(2).** Yield 95%, mp 220-222ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.41 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 6.23 (s, 1H, $CH_{isoxazole}$), 7.06 (d, 1H, *J* = 7.9 Hz, arom.), 7.19 (br.s, 2H, arom.), 7.48 (t, 1H, *J* = 8.2 Hz, arom.), 7.69 (s, 1H, =CH), 12.66 (s, 1H, NH). LCMS: m/z 316.2 (100%, $[M+H]^+$).

(Z)-5-(4-Methoxybenzylidene)-2-(5-methylisoxazol-3-ylimino)-4-thiazolidinone **(3).** Yield 78%, mp >256ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.40 (s, 3H, CH_3), 3.82 (s, 3H, OCH_3), 6.21 (s, 1H, $CH_{isoxazole}$), 7.12 (d, 2H, *J* = 8.6 Hz, arom.), 7.58 (d, 2H, *J* = 8.6 Hz, arom.), 7.66 (s, 1H, =CH), 12.55 (s, 1H, NH). LCMS: m/z 316.0 (100%, $[M+H]^+$).

***(Z)-5-(3,5-Di-tert-butyl-4-hydoxybenzylidene)-2-(5-methylisoxazol-3-ylimino)-4-thiazolidinone* (4).** Yield 30%, mp 238-240ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.41 (s, 18H, 2*$(CH_3)_3C$), 2.40 (s, 3H, CH_3), 6.19 (s, 1H, $CH_{isoxazole}$), 7.41 (c, 2H, arom.), 7.66 (s, 1H, =CH), 7.74 (br.s, 1H, OH), 12.47 (br.s, 1H, NH). LCMS: m/z 414.2 (100%, $[M+H]^+$).

***(Z)-5-(1H-Indol-6-ylmethylene)-2-(5-methylisoxazol-3-ylimino)-4-thiazolidinone* (5).** Yield 73%, mp >252ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.42 (s, 3H, CH_3), 6.22 (s, 1H, $CH_{isoxazole}$), 6.52 (s, 1H, CH_{indole}), 7.27 (d, 1H, J = 8.2 Hz, arom.), 7.55 (m, 1H, CH_{indole}), 7.69 (d, 1H, J = 8.2 Hz, arom.), 7.71 (s, 1H, arom.), 7.82 (s, 1H, =CH), 11.54 (s, 1H, NH_{indole}), 12.53 (s, 1H, NH). LCMS: m/z 325.2 (100%, $[M+H]^+$).

***(Z)-5-(1H-Indol-3-ylmethylene)-2-(5-methylisoxazol-3-ylimino)-4-thiazolidinone* (6).** Yield 14%, mp 239-241ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.41 (s, 3H, CH_3), 6.22 (s, 1H, $CH_{isoxazole}$), 7.19 (t, 1H, J = 7.7 Hz, arom), 7.25 (t, 1H, J = 7.7 Hz, arom), 7.52 (d, 1H, J = 7.9 Hz, arom.), 7.55 (s, 1H, CH_{indole}), 7.88 (d, 1H, J = 7.7 Hz, arom.), 7.97 (s, 1H, =CH), 12.06 (s, 1H, NH_{indole}), 12.35 (br.s, 1H, NH). LCMS: m/z 325.0 (87.7%, $[M+H]^+$).

Conclusions. A number of biologically active derivatives of 5-substituted 2R - (5-methyl-self-oxazol-3-yl) aminothiazol-4-one were synthesized. Studies of anti-protective and anticonvulsant activity are in porgress.

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SYNTHESIS OF 5-(3-METHYL-1-PHENYL-4,5-DIHYDRO-1*H*-PYRAZOL-4-YLMETHYLENE)-2-THIOXOTHIAZOLIDIN-4-ONES AS POTENTIAL BIOLOGICALLY ACTIVE COMPOUNDS

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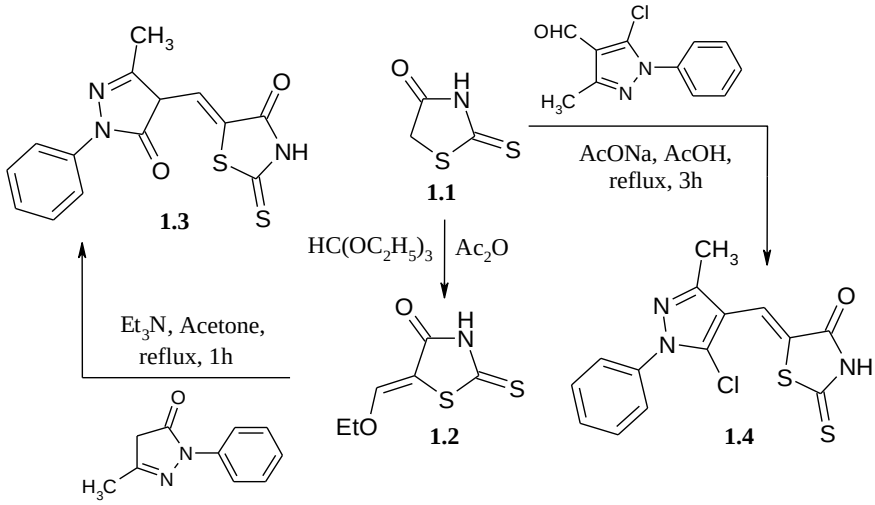
Keywords: organic synthesis, 4-thiazolidinone, pyrazole, biological activity

Introduction. The thiazolidine core is one of the various attractive fragment in modern pharmaceutical and medicinal chemistry [1]. 4-Thiazolidinone derivatives have shown a wide range of biological activities, such as anticancer [2], antimicrobial [3], anti-inflammatory [4], antitrypanosomal [5]. It is worth noting that the combination thiazolidine fragment with other heterocycles is a justified way to create drug-like molecules in the context of a hybrid pharmacophore approach that allows to achieve new pharmacological profile, potentiation of action and reduction of toxicity [6]. In continuation of this theme, we designed and synthesized novel non-condensed heterocyclic compounds containing 4-thiazolidinone and pharmacologically attractive pyrazole and pyrazoline moieties. Thus, the non-condensed systems have received considerable attention recently due to their diverse biological activity and clinical applications. The mechanisms of biological activity among pyrazoline-thiazolidinone conjugates can be associated with their affinity to JNK stimulating phosphatase-1 (JSP-1), tumor necrosis factor TNFα, cyclin-dependent kinase, heat shock proteins and P-glycoprotein [7].

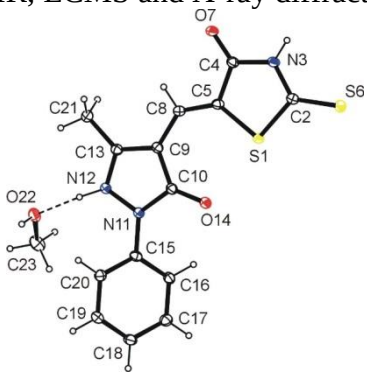
Materials and methods: organic synthesis, ^{1}H NMR spectroscopy, LCMS, X-ray crystallography.

Results and discussion: Startings 2-thioxothiazolidin-4-one **1.1** and 5-ethoxymethylene-2-thioxothiazolidin-4-one **1.2** were obtained according to the methods described previously [1,8]. The efficient method for pyrazoline(pyrazole)-thiazolidinones synthesis starting from 5-ethoxymethylene-2-thioxothiazolidin-4-one **1.2** via reaction with the appropriate methylene active 5-methyl-2-phenyl-2,4-dihydropyrazol-3-one was accomplished in 5-(3-5-ethyl-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-4-ylmethylene)-2-thioxothiazolidin-4-one **1.3**.



Target 5-ene derivative **1.4** was obtained in the Knoevenagel reaction condition 2-thioxothiazolidin-4-one **1.1** with 5-chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde.

The structures of compounds **1.3** and **1.4** have been determined by ^{1}H NMR, LCMS and X-ray diffraction method (Figures 1,2).



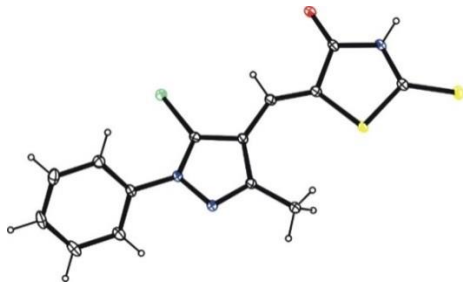


Fig. 1. Ortep view of the molecule **1.3** **Fig.2.** Ortep view of the molecule **1.4**

Experimental part

5-(3-5-Ethyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-ylmethylene)-2-thioxothiazolidin-4-one **(1.3).** A mixture of 5-ethoxymethylene-2-thioxothiazolidin-4-one (0.0026 mol), 5-methyl-2-phenyl-2,4-dihydropyrazol-3-one (0.0020 mol) and triethylamine (0.8 ml) in acetone (12 ml) was heated under reflux for 1 hour. After cooling acetone was evaporated using rotary evaporator. The residue was diluted by addition of H_2O (30 ml) and the solution was acidified to pH 5 with AcOH. After standing at room tempetature for 2 days the red coloured precipitate was collected by filtration, washed with H_2O, dried and recrystallized from ethanol. Yield 55 %, mp > 240 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): 2.36 (s, 3H, CH_3), 7.20-7.32 (m, 2H, arom.), 7.42-7.54 (m, 2H, arom., =CH), 7.66 (d, 2H, J = 7.0 Hz, arom.), 13.18 (s, 1H, NH). ^{13}C

NMR (100 MHz, DMSO-d_6): 11.4 (CH3), 100.7, 116.6, 120.4, 125.3, 126.2, 129.5, 136.2, 150.5, 160.0 (C=O), 170.2 (C=O), 197.9 (C=S). LCMS: m/z 318.0 (100%, $[M+H]^+$).

5-(5-Chloro-3-methyl-1-phenyl-1H-pyrazol-4-ylmethylene)-2-thioxothiazolidin-4-one (1.4). A mixture of 2-thioxothiazolidin-4-one (0.0067 mol), 5-chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde (0.0067 mol), sodium acetate (0.0135 mol) in acetic acid (6 ml) was heated under reflux for 3 hours. Red coloured precipitate obtained after cooling was filtered off, washed with H_2O and and recrystallized from acetic acid. Yield 65 %, mp 198 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): 2.37 (s, 3H, CH_3), 7.42 (s, 1H, =CH), 7.50-7.63 (m, 5H, arom.), 13.81 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6): 13.9 (CH_3), 113.4, 121.8, 125.6, 126.5, 127.3, 129.5, 129.8, 137.5, 149.8, 169.4 (C=O), 195.7 (C=S). LCMS: m/z 336.0/338.0 (100%, $[M+H]^+$).

Conclusions. We have achieved a convenient protocol for the synthesis of novel pyrazoline-thiazolidinone conjugates via one-pot two component methodology. A library of new thiazole-pyrazoline systems was synthesized based on a hybrid-pharmacophore approach to further investigations anticancer activity within the DTP NCI protocol and anti-inflammatory pharmacological profile.

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СИНТЕЗ ТА БІОЛОГІЧНА АКТИВНІСТЬ ПОХІДНИХ ФУРАНКАРБОНОВИХ КИСЛОТ

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Ключові слова: фуран, ацилювання, антимікробна активність, протипухлинна активність, протизапальна активність, ^{1}H ЯМР спектроскопія, елементний аналіз.

Вступ. Завдяки унікальним фізико-хімічним, хімічним і біологічним властивостям похідні фурану знайшли застосування в різних областях хімії і технології і, зокрема, у фармації. Перш за все, слід зазначити широкий спектр біологічної активності природних і синтетичних похідних фурану, а також його конденсованих аналогів (бензо[b]фурану, нафтофуранів, антрафуранів та ін.). Серед зазначених сполук знайдено цілу низку високоактивних агентів з широким спектром біологічної дії. Було ідентифіковано сполуки-лідери з антимікробною, протитуберкульозною, противірусною, антидіабетичною, протизапальною, протипухлинною, антиконвульсивною та іншими активностями. Все це обумовлює значний інтерес науковців до використання цього гетероциклу як важливого "будівельного блоку" при створенні лікарських препаратів.

Матеріали і методи: органічний синтез, ^{1}H ЯМР спектроскопія, елементний аналіз, фармакологічний скринінг.

Результати й обговорення. *Синтез і біологічна активність 2,4-диметил-N-арил-3-фурамідів.* На першому етапі нашого дослідження здійснено синтез та вивчено біологічні властивості 2,4-диметил-*N*-арил-3-фурамідів. Необхідний для цього вихідний 2,4-диметилфуран-3-карбоніл

хлорид **5** отримували згідно наведеної нижче схеми 1. На першій стадії диметилпропаргілсульфоній бромід **2** реагує з ацетооцтовим естером **1**, утворюючи етил 2,4-диметил-3-фуроат **3**, який гідролізував у водному розчині натрій гідроксиду. Далі реакцією 2,4-диметилфуран-3-карбонової кислоти з тіонілхлоридом отримано 2,4-диметилфуран-3-карбоніл хлорид **5**. Взаємодією 2,4-диметилфуран-3-карбоніл хлориду **5** з ароматичними амінами в безводному діоксані у присутності триетиламіну синтезовано 2,4-диметил-*N*-арил-3-фураміди з виходом 84–92 % (**схема 2**).

Схема 1

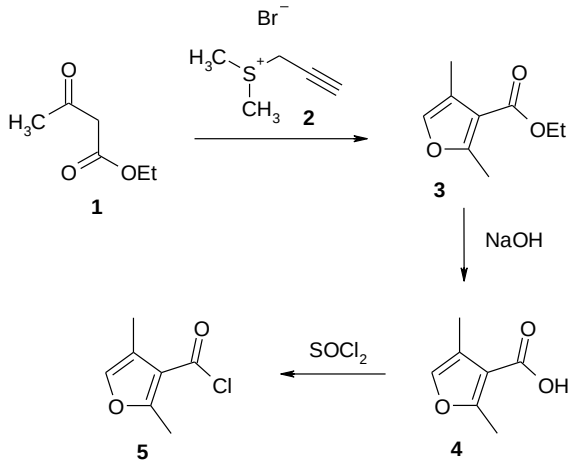
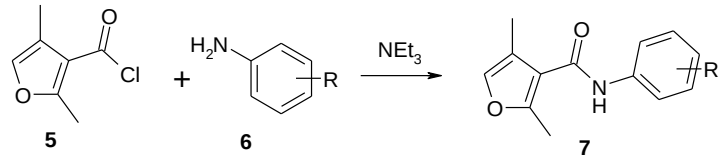
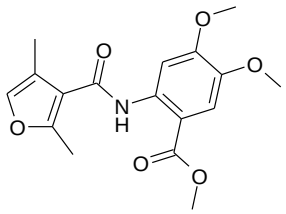


Схема 2



Для синтезованих сполук проведено дослідження протизапальної активності з використанням карагенінової моделі набряку лапи щура. За його результатами ідентифіковано сполуку-хіт протизапальної дії, яка за своєю активністю переважала препарат порівняння ібупрофен.



Показник пригнічення протизапальної реакції 45,4%

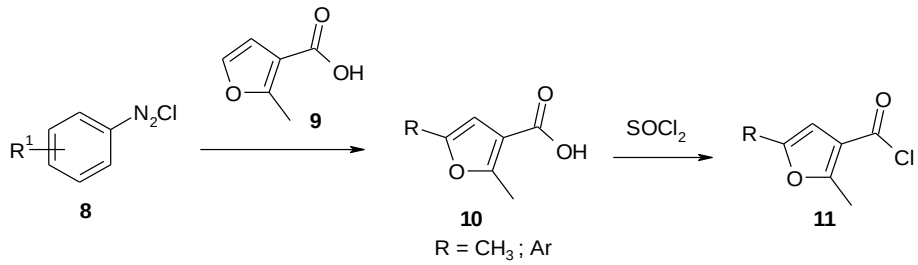
Ібупрофен 40,2%

Синтез і біологічна активність похідних 2,5-диметил-3-фурамідів та 5-арил-2-метил-3-фурамідів.

Як вихідні сполуки для синтезу 2,5- диметил-3-фуранкарбо-диметил-3-фурамідів і 5-арил-2-метил-3- фурамідів було використано хлорангідриди 2,5-нової та 5-арил-2-метил-3-фуранкарбонових кислот **11** і ароматичні аміни.

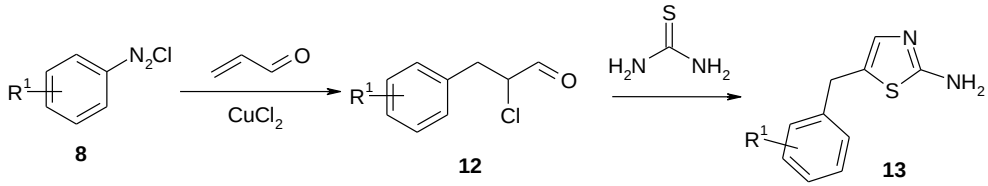
Вихідні 5-арил-2-метил-3-фуранкарбонові кислоти **10** отримували шляхом арилювання 2-метил-3-фуранкарбонової кислоти **9** з діазонієвими солями **8** в умовах реакції Меєрвейна. Кислоти **10** дією хлористого тіонілу перетворено в ацилхлориди **11** (**схема 3**).

Схема 3



Вихідні ароматичні аміни, зокрема 2-аміно-5-арилметилтіазоли, одержували за **схемою 4**. Діазонієві солі **8** взаємодією з акролеїном в умовах реакції Меєрвейна утворюють 3-арил-2-хлоропропаналі **12**. Ці альдегіди реакцією з тіосечовиною були перетворені в 2-аміно-5-арилметилтіазоли **13** з високими виходами.

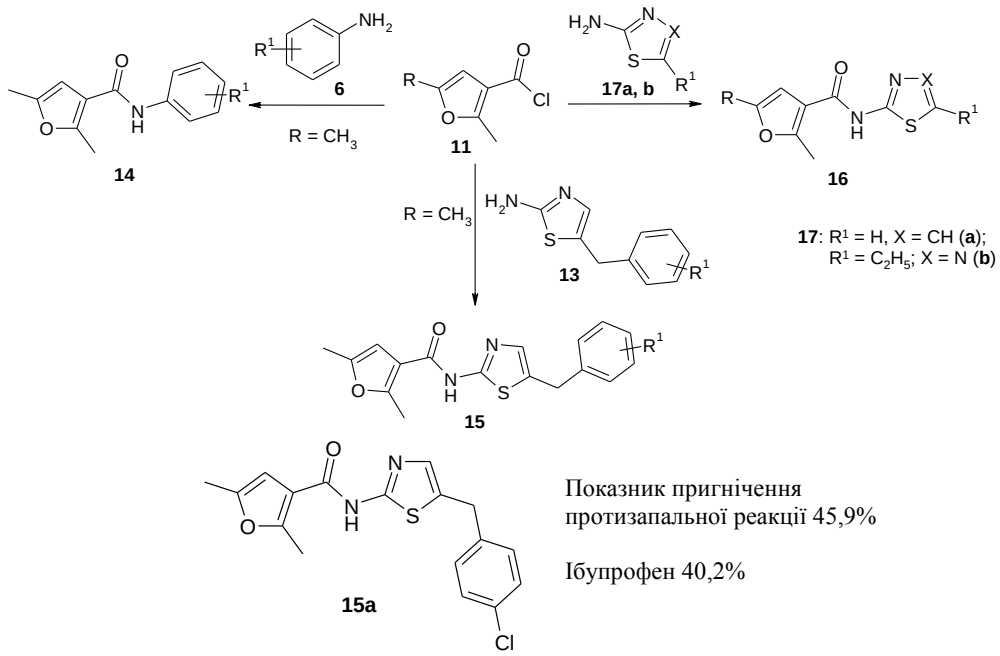
Схема 4



Цільові аміди **14-16** синтезували ацилюванням за допомогою хлорангідридів 2,5-диметил-3-фуранкарбонової та 5-арил-2-метил-3-фуранкарбонових кислот **11** та отриманих нами 2-аміно-5-арилметилтіазолів **13**, а також комерційно доступних ароматичних амінів **6**, 2-амінотіазолу **17a** та 2-аміно-5-етилтіадіазолу **17b** (**схема 5**). Реакція відбувалася в безводному діоксані при кімнатній температурі в присутності триетиламіну.

Для отриманих сполук було здійснено тестування протизапальної активності, найкращу дію, що переважала препарат ібупрофен, показав *N*-[5-(4-хлоробензил)-1,3-тіазол-2-іл]-2,4-диметил-3-фурамід **15a**:

Схема 5



Для амідів була досліджена також протипухлинна активність. Встановлено, що отримані сполуки проявляють активність різнопланового рівня із середніми значеннями GP 29.05–67.36%. Серед цих речовин найкращу активність проявила вищезгадана сполука **15a.** Для неї середнє значення GI_{50} становило 4.22 μM. Найбільш чутливою була лінія T-47D раку молочної залози зі значенням GI_{50} = 0.088 μM.

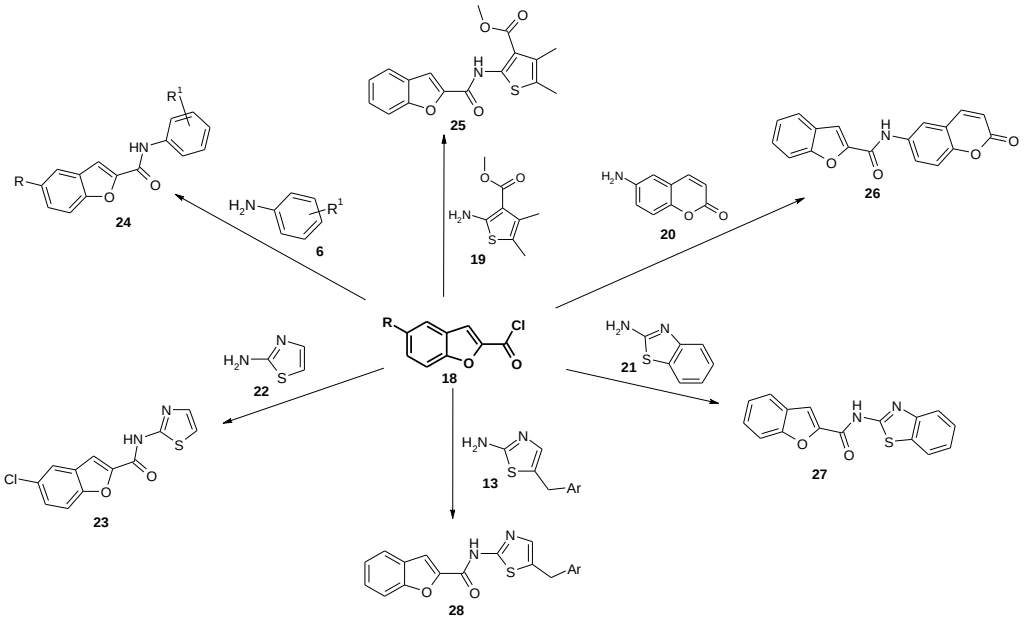
Mean growth inhibitory concentration (GI_{50}, μM) of compound 15a in comparison with 5-FU, Cisplatin and Curcumin

	Subpanel tumor cell lines									
	L	NSCLC	ColC	CNSC	M	OV	RC	PC	BC	MG-MID
15a	3.17	6.16	2.53	5.62	3.13	5.44	3.98	4.57	3.41	4.22
5-FU	15.1	>100	8.4	72.1	70.6	61.4	45.6	22.7	76.4	52.5
Cisplatin	6.3	9.4	21.0	4.7	8.5	6.3	10.2	5.6	13.3	9.48
Curcumin	3.7	9.2	4.7	5.8	7.1	8.9	10.2	11.2	5.9	7.41

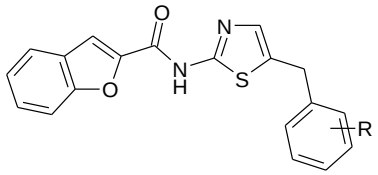
Синтез і біологічна активність похідних бензофуранкарбоксамідів. Цільові бензофуранкарбоксаміди було синтезовано з хлороангідридів комерційно доступних бензофуран-2-карбонових кислот **18** і ариламінів **6**, аміну Гевальда **19**, 6-амінокумарину **20**, 2-амінотіазолу **21**, 2-амінобензотіазолу **22**, і 2-аміно-5-арилметилтіазолів **12**. 2-Аміно-5-арилметилтіазоли **12** були отримані згідно описаної вище **схеми 4**.

Реакція ацилювання хлороангідридів бензофуран-2-карбонових кислот та відповідних ароматичних амінів проходила в безводному діоксані при кімнатній температурі в присутності триетиламіну (**схема 6**).

Схема 6



Для отриманих сполук здійснено дослідження протипухлинної дії. Було ідентифіковано сполуки-хіти, які за своєю дією переважали препарати порівняння.



28: R = 2-CH_3 (**a**), 2,3-Cl_2 (**b**), 4-Cl-3-CF_3 (**c**)

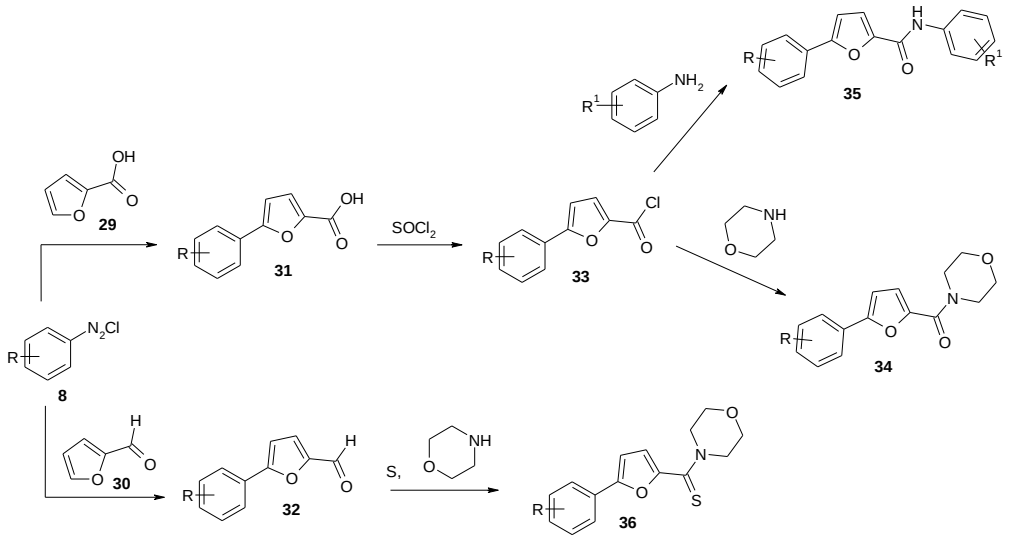
Mean growth inhibitory concentration (GI50, μM) of compound **28a-c** in comparison with 5-FU, Cisplatin, and Curcumin.

	Subpanel tumor cell lines									
Cpd	L	NSCLC	ColC	CNSC	M	OV	RC	PC	BC	MG-MID
28a	1.01	2.23	0.87	3.80	1.18	2.68	2.33	2.78	1.36	2.03
28b	14.15	1.85	0.84	1.73	1.51	1.37	2.06	3.56	2.31	3.26
28c	41.23	4.96	4.29	2.68	4.95	5.96	4.81	5.67	6.01	8.95
5-FU	15.1	>100	8.4	72.1	70.6	61.4	45.6	22.7	76.4	52.5
Cisplatin	6.3	9.4	21.0	4.7	8.5	6.3	10.2	5.6	13.3	9.48
Curcumin	3.7	9.2	4.7	5.8	7.1	8.9	10.2	11.2	5.9	7.41

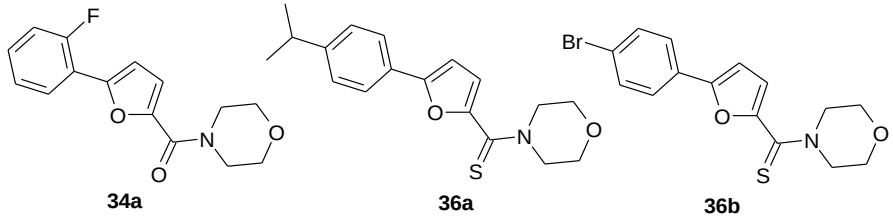
Синтез і біологічна активність 4-(5-арил-2-фуроїл)морфолінів, 5-арил-2-фуроїланілінів та 4-[(5-арил-2-фурил)карбонотіоїл]морфолінів. Синтез розпочинався з ароматичних солей діазонію **8** та фуран-2-карбонових кислот **29** або фурфуролу **30**. На першій стадії фуранові похідні зазнають ацилювання в умовах реакції Меєрвейна, згідно методів описаних у літературі. У результаті синтезовано 5-арилфуран-2-карбонові кислоти **31** і 5-арилфуран-2-карбальдегіди **32**. Щоб отримати цільові морфоліди **34**, 5-арилфуран-2-карбонові кислоти **31** перетворено

хлористим тіонілом у відповідні ацилхлориди **33**. Ці хлорангідриди далі були використані в ацилюванні морфоліну і комерційно доступних ароматичних амінів в діоксані при кімнатній температурі. Тіоморфоліди **36** синтезували використовуючи відому реакцію Вілгеродта-Кіндлера. Усі перетворення представлені на **схемі 7**.

Схема 7



У більшості випадків тестовані сполуки проявили низьку антимікробну активність. Проте сполуки **34a**, **36a,b**, структури яких наведено нижче, проявили високу активність проти *Staphylococcus aureus* ATCC 43300 зі значеннями MIC = 4–16 мкг/мл. Також було здійснено визначення цитотоксичності (CC_{50} та HC_{10}) щодо ембріональних клітин нирок людини (Human embryonic kidney cells) та еритроцитів людини (Human red blood cells). Як було встановлено, ці сполуки виявились нетоксичними. Значення $HkCC_{50}$ і $HmHC_{10}$ становило > 32 мкг/мл.



Compound	MIC	$HkCC_{50}$	$HmHC_{10}$	SI = HC_{10} / MIC
34a	8; 8	>32; >32	>32; >32	>4; >4
35a	4; 4	>32; >32	>32; >32	>8; >8
35b	16; 16	>32; >32	>32; >32	>2; >2

Висновки: 1. Отримано комбінаторні бібліотеки сполук фуранового ряду. 2. Ідентифіковано сполуки, які за своєю активністю переважають препарати порівняння.

THESIS OF THE

MASTER PROJECTS

(JUNE 2021)

DEPARTMENT OF CLINICAL PHARMACY, PHARMACOTHERAPY AND MEDICAL STANDARDIZATION

(Head of the department – prof. **Andriy Zimenkovsky**)

PHARMACEUTICAL CARE OF PATIENTS WITH MYOCARDIAL INFARCTION

Yuliia Bychuk
Scientific supervisor: assoc. prof. **Myroslava Sekh**, PhD

Keywords: myocardial infarction, pharmaceutical care, drug behavior, adherence

Introduction. According to the WHO, more than 7 million people worldwide experience acute myocardial infarction (MI) each year. Despite the fact that in recent decades there has been a decrease in mortality from this pathology, the one-year mortality rate after MI still remains at 10%, and varies depending on the individual characteristics of the patient. The medical and social burden of this pathology is that the duration and quality of life of the patient are significantly reduced, which is reflected in significant socio-economic losses of the country's vital potential. That is why the main tasks of the health care systems (HCS) of all countries without exception are to find the optimal algorithms for improving the quality of care and pharmaceutical care (PhH) for patients with MI at the stage of secondary prevention. The purpose of the study is to develop an algorithm for the evidence-based PhT of patients with myocardial infarction.

Materials and methods. The object of the study were the protocols of questionnaires of patients with a diagnosis of MI (n = 54), the relevant set of terms and concepts related to the problem; international clinical recommendations on the studied problem (n = 6); information flows on the rational choice of drugs for patients with MI; systematic reviews and meta-analysis regarding the role of pharmacists in pharmacotherapy (PhT) of patients with MI (n = 34). Subjects of research - PhT, PhC. Methods: questionnaire, system analysis, bibliographic, structural-logical analytical, clinical-pharmaceutical, comparative-analytical.

Results. A study of patients registered with a family doctor in two outpatient departments of Lviv with a diagnosis of coronary heart disease (n = 347). A questionnaire survey of patients with a history of MI was conducted to study the level of adherence (n = 54). According to the gender distribution of respondents: 83.3% were men aged 50 to 79 and 16.7% were women aged 63 to 76. The mean age of patients was 63.4 years (mean sample deviation ± 5.59 years). The majority of respondents (66.7%) have been taking medication for more than 5 years, 13% for 4 to 5 years, 11.1% for 4 to 3 years and 9.2% for 2 to 3 years. All respondents were aware of, accepted and agreed with the fact that their PhT should be for life. At the same time, it was found that 68.5% of respondents "sometimes" stopped using one or more drugs from their own PhT regimen, the answer "yes" was given by 22.2% of respondents, and only 9.3% of patients never missed the prescribed medication. Among the most common

reasons for discontinuation of PhT, respondents note: 74.1% - forgetfulness, 44.9% - the presence of adverse reactions to drugs, 36.7% - the high cost of a particular drug, 24.5% - improvement. The average level of adherence among the surveyed respondents tended to decrease over time and was: during the first 6 months - 91.8%; within 6-12 months - 81.6%; from 1 year to 2 years - 51; from 2 to 3 years - 46.9% and after 3 years - 40.8%. In case of any changes in the state of health during PhT, the surveyed respondents seek advice from their family doctor in 68% (n = 37); with the help of a pharmacist in 31% (n = 15) or decide to correct your own PhT 3.7% (n = 2).

We have developed 34 science-based reports on pharmaceutical care aimed at health care professionals and patients, in order to raise their awareness of drug management, and as a result, can improve the quality of PhT and the commitment of patients with MI to the future.

Conclusions. To reduce the medical, socio-economic burden on the HCS system, it is necessary to develop a scientifically sound successful management of MI, especially at the stage of secondary prevention, including with the participation of a pharmacist and a clinical pharmacist. The development and dissemination of evidence-based PhT messages aimed at clinicians and patients will, in our opinion, improve the quality of medical care and PhT for this category of patients in the future.

SEROTONIN SYNDROME CLINICAL AND PHARMACEUTICAL

Yuliya Batashchuk
Scientific supervisor: assist. prof. **Oxana Lopatynska**, PhD

Keywords: serotonergic pharmacotherapy, drug-related problems.

Introduction: For the first time in Ukraine, the risks of using serotonergic pharmacotherapy from the point of view of clinical pharmacy have been studied by analyzing the prescriptions of drugs, as well as the study of instructions for medical use of drugs. However, the problem of rational use of serotonergic drugs in patients remains open, which determined the purpose and objectives of this study. The aim of the study: To study the possibilities of providing qualified clinical and pharmaceutical care to patients with the use of drugs with direct or indirect serotonergic effects. Assess the quality of pharmacotherapy in patients using serotonergic drugs in real clinical practice. Identify potentially undesirable consequences of irrational pharmacotherapy with serotonergic drugs in patients and methods of prevention of drug-related problems (DRPs), complications under the influence of drugs.

Research methods: bibliographic, content analysis, method of evidence search, clinical-pharmaceutical, clinical-pharmacological, comparison, standardization, descriptive statistics, modeling.

Result: The results of the analysis of drugs with serotonergic activity allowed to establish the problems of pharmacotherapy in modern domestic clinical practice is insufficient awareness of neurologists and nurses about the potential interactions of drugs, in particular in pharmacotherapy comorbidities. We analyzed 2 medical prescriptions for drug-related problems. Of the 34 drug-related problems, 12 drug selection problems, 2 dosing problems, 6 drug interactions, and 14 domestic drug-related problems were identified.

Conclusions: The results of clinical and pharmaceutical evaluation of drugs with serotonergic activity in patients showed that these drugs in combination are associated with a number of drug-related problems that can lead to hyperthermia, muscle rigidity, hyperreflaxation, insomnia, mental disorders, and even death. According to numerous scientific studies, the risk of these problems can be prevented or minimized by rational use of drugs with serotonergic activity.

PHARMACEUTICAL CARE FEATURES IN ANTIPYRETICS ADMINISTRATION FOR CHILDREN

Tetiana Hnativ
Scientific supervisor: assist. prof. **Olga Boretska**, PhD

Keywords: pharmaceutical care, antipyretics, fever in children

Introduction. Fever is one of the most common complains parents address to doctors but it is also one of the most common conditionals that parents can manage. However due to the «fever phobia» that is widespread today in the whole world we can see exaggerated worries about fever and excessive consumption of children's antipyretics. Therefore, increase the level of awareness of parents to relief the child's condition with fever is important. The purpose of the study. Study of features of pharmaceutical care in order to use antipyretics for children.

Results. Only 61,4% of parents who were surveyed gave the correct statement about fever. This indicator ranges from 57,5% to 66,2% in different groups of respondents according to the age of their children. Thus a great number of parents have misjudgments and, in our opinion, need further classification from medical/pharmaceutical professionals.

It is established that in situations when due to the use of drugs the expected effect is not occurs, part of the parents 15,7% for some time give the same drug in the same dosage, 2,6% of respondents give a higher dose of the same drug and 1,3% – use the same drug but in different dosage form. In our mind, such situations pharmaceutical care should be directed to the issue of appropriate dosage and frequency of antipyretics for prevention of potential overdoses.

The great majority of respondents (90,8%) indicated that anxiety about fever during Covid-19 pandemic intensified. When analyzing the answers of the respondents, according to the age of their children it was found that the anxiety about fever during the pandemic period increased significantly within parents who have children younger 5 years. They are in more cases when choosing antipyretics consult a doctor, it is also very important for them to advice with pharmacist.

Conclusions. We believe that in situation of overload of doctors during pandemic, clarification of the proper use of antipyretics, increasing the awareness of parents about fever and ways of relieving their children's conditional is possible, in particular, through the pharmaceutical care at pharmacies.

CLINICAL AND PHARMACEUTICAL APPROACHES TO THE USE OF ABTIBIOTICS IN CHILDHOOD

Nataliya Eliyashevska
Scientific supervisor: assist. prof. **Oksana Horodnycha**, PhD

Keywords: antibiotic (ABs), pharmacotherapy

Introduction: A number of studies on the use of antibiotics (ABs) in patients under 18 have been conducted in Ukraine. However, the analysis of the rationality of prescribing ABs for pharmacotherapy (PhT) of infectious diseases in outpatient settings has not been conducted so far, the fact that determined the purpose and the objectives of this study. The aim of the study consists in conducting a clinical and pharmaceutical evaluation of pediatric antibiotics therapy (ABsT) and identifying typical drug-related problems of prescribing ABs in pediatrics.

Research methods: bibliographic, clinical-pharmaceutical, clinical-pharmacological, comparison, method of standardization, comparative method.

Result. The results of the analysis of the Standard list of vital medicines (M) for children allowed establishing the nomenclature of ABs and their number, which belong to the groups of access (Access), watching (Watch) and reserve (Reserve). 42 prescriptions of ABs were collected, analyzed, and drug-related problems were identified. The study identified 28 ABs-associated drug-related problems. A total of 20 technical problems related to the appointment of ABs were identified in 42 PhT schemes. Most of them were connected with the absence of instructions on the duration of ABs use (n = 19) in written prescriptions. Besides, 8 clinical problems related to the use of ABs were identified. The most common remarks were on the duration of ABs (n = 4). Drug-related problems in this section were related to azithromycin in most cases.

Conclusions. The results of clinical and pharmaceutical evaluation of the use of ABs in pediatric patients showed that ABs for the use in pediatrics are associated with a number of drug-related problems that can lead to resistance, decreased effectiveness, allergic reactions, antibiotic-associated diarrhea and others. According to numerous scientific studies, it is possible to prevent or minimize the risk of these problems through the rational use of ABs.

DRUGS FOR ACID RELATED DISORDERS OF THE GASTROINTESTINAL TRACT: ASPECTS OF PHARMACEUTICAL CARE

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Scientific supervisor: assoc. prof. **Yu.S. Nastyukha**, PhD

Keywords: pharmaceutical care, proton pump inhibitors, H_2-histamine antagonists, antacids.

Introduction. Among the drugs for acid related disorders of the gastrointestinal tract, proton pump inhibitors (PPIs), demonstrating their effectiveness, have supplanted antacids and H_2-antagonists of histamine. However, there is growing concern about the overuse of PPIs. Drugs in this group have been given the status of over-the-counter medications in many countries to relieve heartburn symptoms. In addition, PPIs are among the most widely prescribed drugs in the world. However, up to 70% of their prescriptions are made without clear indications for use. The results of the studies indicate the absence of documented indications for PPIs in 40-55% cases of long-term pharmacotherapy of patients in primary care in the United States and the United Kingdom and 40-65% cases of pharmacotherapy of hospitalized patients in the United States and Australia. The issue of efficacy and safety of drugs for the treatment of acid related disorders of the gastrointestinal tract is being reviewed in the context of the COVID-19 pandemic. Some studies show a higher risk of SARS-CoV-2 infection in patients taking PPIs and a more severe COVID-19, which is not observed with H_2-histamine receptor antagonists. These issues need further research.

Materials and methods. system approach, bibliographic, clinical-pharmaceutical and comparative analysis. Objects of research: available information flows; instructions for medical use of drugs for acid related disorders of the gastrointestinal tract from the State Register of Drugs of Ukraine (December 2020): antacids (n = 20), prostaglandins (n = 2), H_2-histamine receptor antagonists (n = 17), PPIs (n = 126); Pharmacist's protocols for dispensing over-the-counter drugs (Order of the Ministry of Health of Ukraine №875, 11.10.2013); State drug formulary (issue 12-13, 2020-2021); FDA Pregnancy category of drugs (Medscape); LactMed database; geriatric

instruments: Beers criteria, STOPP / START criteria, EU(7)-PIM list. Subject of research: modern aspects of pharmaceutical care for the drugs for acid related disorders of the gastrointestinal tract treatment.

Results. The basic pharmaceutical care statements for the use of drugs for the treatment of acid related disorders of the gastrointestinal tract are presented in the Pharmacist's protocols and the State drug formulary. The results of comparative analysis of over-the-counter drugs for the treatment of acid related disorders of the gastrointestinal tract from the State Register of Drugs of Ukraine with a list of drugs recommended by the Pharmacist's protocol for symptomatic treatment of heartburn indicate the possibility of expanding the latter, including PPIs (omeprazole, pantoprazole). The basic information for pharmaceutical care of certain categories of patients (pregnancy, lactation, elderly) needs to be supplemented by date of special resources and tools (FDA Pregnancy category of drugs; LactMed database; geriatric instruments: Beers criteria, STOPP / START criteria, EU(7)-PIM list). Pharmaceutical care concerns drugs for the treatment of acid related disorders of the gastrointestinal tract in a pandemic COVID-19 should be developed.

Conclusion. The results of the conducted studies show that basic pharmaceutical care statements for the use of drugs for the treatment of acid related disorders of the gastrointestinal tract should be updated and supplemented.

CLINICAL-AND-PHARMACEUTICAL ASPECTS OF DRUGS-INDUCED GASTROPATHY

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Keywords: drugs-induced gastropathy, side effect, pharmaceutical care.

Introduction. The use of any drug aims to cause certain reactions of the body and change the functions of organs and systems. However, these reactions can be not only therapeutic, which contribute to the positive effect, but also side effects (SE) – adverse, harmful to the body. SE of medicines impair the patients quality of life, make it difficult to conduct long courses of pharmacotherapy, cause secondary diseases, etc. Thus, prevention and in case of occurrence – elimination of SE of medicines is a necessary condition for rational pharmacotherapy. The aim of the research: the study and analysis of problematic issues concerning development, detection, prophylactic and treatment of drugs induced gastropathy.

Materials and methods. The research objects were the information on drugs using (n=125), foreign information databases containing evidence of rational drug use (Drugs.com, DrugBank, Drugsdb.com), patient survey results

(n=66), whose questions are focused on the clinical and pharmaceutical aspects of the detection, prophylactic and treatment of drugs induced gastropathy. Used methods: informative, search, analytical, comparative, questionnaire survey.

Results. It was established that the detection of risk factors for drug-induced gastropathies and the implementation of appropriate preventive measures helps to reduce the incidence of gastrointestinal complications by 40%. In the treatment of drug-induced gastropathies, the use of proton pump inhibitors, histamine H2-receptor blockers and synthetic prostaglandin analogues is pathogenetically justified. The clinical-and-pharmacological and clinical-andpharmaceutical characteristics of medicines are analyzed and the list of medicines (n=125) which according to evidentiary sources can cause development of gastropathies is formed. The results of the questionnaire disclosed the main clinical and pharmaceutical problems of druginduced gastropathies. It was found that 71.2% of respondents systematically use drugs that have gastrotoxic effects (nonsteroidal anti-inflammatory drugs, glucocorticosteroids, antiplatelet agents, iron and potassium-containing drugs, tetracycline antibiotics). Almost 70% of respondents have a causal relationship between the occurrence of SE on the gastrointestinal tract and the use of drugs that have a potential gastrotoxic effect. The key elements of pharmaceutical care aimed at timely detection, effective prevention and treatment of druginduced gastropathies have been developed.

Conclusions: It was established that the detection, effective prevention and treatment of druginduced gastropathies is based on the supplying of modern, qualified and evidentiary information for all participants in the treatment process that can be successfully implemented through the components of pharmaceutical care.

ADHERENCE TO PROTOCOLS FOR PROVIDING PHARMACEUTICAL CARE

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Scientific supervisor: assist. prof. **Olga Boretska**, PhD

Keywords: pharmaceutical care, protocols for providing pharmaceutical care, adherence to protocols

Introduction. The results of studies conducted around the world show that there is still a gap between recommended care and actual clinical/pharmaceutical practice, which is described as «adherence to clinical guidelines» and is often used as a indicator of quality of patient care. In order to reduce the difference in pharmaceutical practice, a standard of pharmaceutical care is created and implemented, in particular in the form of Protocols for providing pharmaceutical care. The purpose of the study. Study

of adherence to the protocols for providing pharmaceutical care and assessment of factors influencing the degree of adherence with the recommendations.

Materials and methods. The anonymous survey of pharmacists (n=136) were conducted from 11.03.21 to 10.04.21. Methods used: systematic analysis, bibliographical, standardization method, questionnaire method.

Results. The vast majority (83.8%) of pharmacists define pharmaceutical care as an important component of their professional activity, considering its main directions to promote the proper implementation of the instructions of medical professionals on drugs and provide recommendations for the use of over-the-counter drugs. The most important factors in promoting the provision of drugs in pharmacies are the educational component (72.1%), as well as the possibility of using the protocols for providing pharmaceutical care in their practice (61.0%). Instead, the main obstacle is the lack of time to serve one visitor/patient (82.4%). The financial component, according to result of our study, is not a significant incentive (22.8%) or obstacle (22.1%) in the process of providing drugs in the pharmacy. The results of survey of pharmacists showed that 94.9% of pharmacists use the recommendations of the protocols, and 95.6% consider the standard of pharmaceutical care provision necessary. It is proved that the share of pharmaceutical specialists who are guided by the protocols in the provision of pharmaceutical care is lower in the age category of 18-25 years 92.3% vs 100% in all other older age groups. We believe that further research is needed in this direction, to determine the causes and, accordingly, the formation of factors of influence to improve the implementation of pharmaceutical care in pharmacies.

Conclusions. In our opinion, long-term support of adherence of pharmaceutical specialists to the protocols requires taking into account the factors of positive impact on their implementation and the obstacles faced by pharmacists in providing pharmaceutical care in the pharmacy.

CLINICAL, PHARMACEUTICAL AND NUTRITIONAL ASPECTS OF LACTOSEINTOLERANCE

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Keywords: lactose, lactase, lactose intolerance, nutrition support, pharmacotherapy.

Introduction. Lactose intolerance (lactase deficiency) is one of the most common causes of metabolic disorders in both children and adults. According to statistics, lactose intolerance is observed in 65-70% of adults. This indicator depends on age, race, lifestyle, place of residence, and in some regions can reach 90%. This problem is the most important for newborns and young

children because at this age period dairy products are the basis of nutrition. Symptoms of lactose intolerance are common in gastroenterology, so they are often not detected and diagnosed in time by a physician, which is a serious clinical, pharmaceutical and medical, and social problem. The aim of research: the study and analysis of problematic issues concerning development, detection and treatment of lactose intolerance.

Materials and methods. The research objects were the patient survey results (n=54), whose questions are focused on the clinical and pharmaceutical aspects of the detection, treatment and rational management of lactose intolerance; the information on drugs and biological active additives using (n=35), foreign information databases containing evidence of rational drug use (Drugs.com, DrugBank, Drugsdb.com), clinical guidelines on lactode intolerance treatment. Used methods: informative, search, analytical, comparative, questionnaire survey.

Results of investigation summarizes the physiological role of lactose and lactase.The literature information on the mechanisms of development of lactase deficiency and its clinical signs were analyzed. The role of etiological factors in the occurrence of secondary lactose intolerance is showed. The main clinical, pharmaceutical and nutritional problems of lactase deficiency were identified based on the questionnaire survey. It was found that more than half of the respondents are prone to the development of functional disorders of the gastrointestinal tract, which is one of the specific signs of lactose intolerance. Almost a third of respondent's associate gastrointestinal disorders with the use of dairy products, but lactase deficiency was not detected by physicians in any cases. It is established that the planning, organization and implementation of preventive and treatment measures for lactase deficiency should be carried out with due regard to the diet. 150 components of the nutritional diet were analyzed and divided into groups of recommended and inappropriate foods for lactose intolerance. It was found that 58.5% of the analyzed foods are inappropriate or prohibited for use in various types of lactase deficiency.

Conclusions: It was established that the rational management of patients with lactose intolerance is based on the supplying of modern, qualified and evidentiary information for all participants in the treatment process that can be successfully implemented through the existing educational programs and components of pharmaceutical care.

CLINICAL-AND-PHARMACEUTICAL APPROACHES TO THE PREVENTION AND TREATMENT OF DRY EYE SYNDROME

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Keywords: Dry eye syndrome, pharmacotherapy.

Introduction. Dry eye syndrome (DES) is a fairly common disease, “disease civilization", associated with scientific and technological progress. According to various estimates, from 10 to 30% of the adult population suffer from DES, and about 75% of complaints patients during a visit to an ophthalmologist are associated with symptoms of dryness keratoconjunctivitis. DES reduces a person's visual performance, causes discomfort, impairs quality of life, and if ignored for a long time manifestations, can lead to severe eye diseases that cause persistent decreased and even vision loss.

Results. The patient population includes people of any age who have symptoms and signs of dry eyes, such as eye irritation, redness, mucus secretion, visual fluctuations and reduction of the lacrimal meniscus or obstruction meibomian glands. Dry eyes, both alone and in combination with other conditions, are common cause eye irritation, prompting patients to seek out ophthalmic care. Although these symptoms are common improve with treatment, the disease is usually incurable, which can cause frustration for the patient and the doctor. It is important to note that dry eyes are also the cause of decreased visual function and can jeopardize the results of corneal surgery, cataracts and correction refraction.

CLINICAL-AND-PHARMACEUTICAL ASPECTS OF THE ANALGIN SAFE USE

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Keywords: questionnaire, drugs of metamizole sodium, self-treatment.

Introduction. Metamizole is a nonsteroidal anti-inflammatory drug that has analgesic, antipyretic, antispasmodic and weak anti-inflammatory properties. Its use is still controversial, mainly due to the agranulocytosis that it causes with prolonged use. According to the state expert Center for 2019, when using Analgin, 86 reports of adverse reactions (ARs) were received. Of these, 72 were reported when using mono – agents, 14 – when using combined ones (8 of them in combination with psycholeptics). At the same time, 79 – ARs were not seriously provided for, and 7 – serious provided for by ARs.

Materials and methods. The research covered 100 respondents of different ages and areas who carried a sample questionnaire specially formed protocol with regard to problem issues relating to the Analgin safe use. The standardized poll algorithm was used, what allowed to achieve equality of conditions within the study group. The system approach, sociological (questionnaire), statistical, clinical-and-pharmaceutical methods are used.

Results. The age range of respondents is quite wide: from 17 to 52 years, the average age: 31.8 ± 9.9 years. Gender distribution of respondents: 70.0% are women and 30% are men. By place of residence: 83.0% of urban residents; 17.0% of rural residents. The results of the study showed that 19.0% of respondents consider Analgin to be the safest painkiller. At the same time, 40.0% of respondents use it for pain relief, 32.0% – ibuprofen and 10.0% – paracetamol. It is noteworthy that 77.0% of respondents take analgesics for headaches and 71.0% for toothache, 39.0% - when choosing painkillers rely on their own experience, 13.0% – use painkillers for more than 5-6 days, 61.0% – use Analgin 500 mg more than 2 times per day (risk of hematotoxicity), 23.0% of respondents developed adverse reactions when using it. In connection with the above, we consider the role of a pharmacist in the production of over-the-counter metamizol-containing drugs as a priority, since the quality standard of Pharmaceutical Care is a tool for achieving a positive result of pharmacotherapy and responsible self-medication.

Conclusions. Analgin is usually considered an absolutely safe and harmless over-the-counter drug by patients, so they often neglect the warnings indicated in the instructions for medical use, so we consider the pharmacist's recommendations regarding the potential risks and complications associated with its improper use extremely important.

CLINICAL-AND-PHARMACEUTICAL FEATURES OF THE MEDICINES USE IN PEDIATRIC PRACTICE (BASED ON THE EXAMPLE OF SYRUPS)

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Keywords: children, syrups, pharmacotherapy, dosage forms.

Results. According to the results of the data analysis of modern information flows on the problem, it was shown that the treatment of children and adolescents remains a difficult task, which requires a comprehensive approach when choosing a drug, its medical form, dosage and safety. Analyzing the pharmaceutical market of Ukraine, it was found out that 465 trade names of medicinal products in the dosage form of syrup were registered. Among them 374 are allowed to be used in pediatric practice, 141 of which are

nonprescription drugs. Adherence to the dosage regimen in treatment of children is not always possible, because many drugs do not have a special form of release. Only 10% of the total number of existing medicines is produced in medical forms for children. In Ukraine, such dosage forms as caramels, lozenges, and balms are rarely produced and used in treatment of children. Only in recent years suspensions, syrups, suppositories containing highly effective pharmaceutical ingredients have become more widely used.

Conclusions. The clinical and pharmaceutical evaluation was conducted, and clinical and pharmaceutical features of the use of drugs in pediatric practice (for example, syrups) were developed, and the elements of pharmaceutical care aimed at patients, in our opinion, will improve the quality of medical and pharmaceutical care for children.

PARTICIPATION OF A PHARMACIST AND A CLINICAL PHARMACIST IN THE ACTIVITY OF THE PHARMACOVIGILANCE SYSTEM

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Scientific advisor: assoc. prof. **Yu.S. Nastyukha,** PhD

Keywords: pharmacovigilance, pharmacist, clinical pharmacist, adverse drug reactions.

Introduction. Worldwide, adverse drug reactions remain one of the leading causes of morbidity and mortality. In Europe, about 3.5% of hospitalizations are caused by adverse drug reactions. One in ten hospitalized patients has adverse drug reactions experienced. In the USA, adverse drug reactions occupy a 4-6 position among the causes of death. The process involved in detecting, collecting, evaluating, studying, and preventing adverse drug reactions is called pharmacovigilance. One of the most widely used in pharmacovigilance is the spontaneous reporting method. An important role in the implementation of pharmacovigilance belongs to pharmacists, who are experts on drugs.

Materials and methods. systematic approach, bibliographic, questionnaire and comparative analysis. An anonymous online survey using the Google form was conducted from April 10 to 21, 2021. The developed questionnaire included a passport part and 7 questions. The criterion for including the questionnaires in the study was the pharmaceutical education of the respondents. Objects of research: available information flows; approaches aimed at supporting the implementation of pharmacovigilance; questionnaires of pharmaceutical professionals (n = 123). The subject of research: pharmacovigilance in the professional activity of pharmacists and clinical pharmacists.

Results. The results of the analysis of available information flow show the positive experience of pharmacists' involvement in pharmacovigilance in many countries of the world. However, there is a need to support this area of professional activity in order to more widely implement it in practice. The effectiveness of teaching methods, reminders, financial incentives, and the use of warning symbols indicate the feasibility of their use to facilitate the implementation of pharmacovigilance with the participation of pharmaceutical professionals. According to the results of the conducted survey, pharmaceutical professionals provide advice on the safety of vaccination against COVID19 (56.1%) and the elimination of clinical manifestations of adverse drug reactions after immunization (23.6%).

Conclusion. The results of comparing the number of sent messages obtained in our study (4.1%) with the number of requests due to adverse drug reactions after immunization against COVID-19 (31.7%) show the potential for greater involvement of pharmaceutical professionals in the pharmacovigilance system.

CLINICAL-AND-PHARMACEUTICAL APPROACHES TO THE RATIONAL USE OF TOPICAL ANTIFUNGAL DRUGS IN GYNECOLOGY

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Keywords: Candida albicans, vulvovaginal candidiasis, antifungal drugs, topical administration, pharmaceutical care.

Introduction. Vulvovaginal candidiasis (VVC) is one of the most common causes of complex gynecological diseases in women of reproductive age. Its frequency remains consistently high. About 70% of women at least once in their lives have signs of VVC In 50% of cases, candidiasis is recurrent. The incidence of VVC has almost doubled in the last 10 years. As usual, VVC is not life-threatening. However, its prevalence, impact on the quality of life of patients, and potential negative consequences determine the great social significance of this problem. The aim of the research: the study and analysis of problematic issues of rational use of topical antifungal drugs (TAD) in gynecological practice.

Materials and methods. The research objects were the information on drugs using (n=232), foreign information databases containing evidence of rational drug use (Drugs.com, DrugBank, Drugsdb.com), international guidelines on candidiasis treatment in gynecological practice; patient survey results (n=78), whose questions are focused on the clinical and pharmaceutical

aspects of the rational use of TAD in gynecology. Used methods: informative, search, analytical, comparative, questionnaire survey.

Results. It was established that a number of factors should be taken into account when choosing an antifungal drug for topical use in gynecology. The most important among them: the general condition of the body, the course of the disease, the effectiveness of previous treatment, its safety, and patient convenience. Analysis of international guidelines on the diagnosis and treatment of VCC has confirmed the feasibility of using TAD in different dosage forms as the first-line therapy. It has been established that the assignment of TAD is an unalterable option for the treatment of pregnant women with VVC. Features of formation of the Ukrainian pharmaceutical market of TAD in gynecology are established. The total number of TAD in gynecology at the pharmaceutical market of Ukraine numbered 59 medicines, which are represented by 14 international nonproprietary names. The stable range of this segment of the pharmaceutical market indicates their high efficiency and importance in gynecological practice. The main clinical and pharmaceutical problems of TAD in gynecological practice have been revealed based on the results of the questionnaire. It was established that VVC can occur at any age, but the women of reproductive age are the group at highest risk in whom the incidence of this pathology is about 70%. Almost a third of the surveyed women are guided by the principles of self-appointment and self-medication when choosing TAD. More than 12% of respondents in the treatment of VVC causeless take an excessive amount of drugs at the same time, which is considered drug-related problems. Almost 70% of respondents have a causal relationship between the occurrence of adverse reactions and the use of local antifungal drugs. In 5 of respondents, such reactions occurred quite often. Almost a third of respondents do not follow or do not always follow the recommendations for the rational use of TAD. It is due, in most cases, to the insufficiency of evidence and accessible information for patients. As a result of the investigation, the 18 massages of patient-centered pharmaceutical care as a guide to the safe and effective use of TAD have been elaborated

Conclusions: It was established that the rational use of TAD is based on the supplying of modern, qualified and evidentiary information for all participants in the treatment process that can be successfully implemented through the components of pharmaceutical care

PHARMACEUTICAL CARE OF ELDERLY PATIENTS WITH ARTERIAL HYPERTENSION AND CONCOMITANT PATHOLOGY

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Keywords: arterial hypertension, concomitant disorders, pharmacotherapy, side effects.

Introduction. The arterial hypertension develops among 60% the total population aged over 60 years, and having reached the age of 70 years this disease affects 65% of males and 75% of females. The delayed course of the disease, presence of a various concomitant disorders, low educational level of elderly patients and non-systematic control of blood pressure significantly impedes the therapeutic process and increases the risk of cardiovascular complications. In Ukraine, this problem is particularly acute, which leads to the unification of the efforts of family doctors, cardiologists and pharmacists in order to optimally solve it.

Materials and methods. The analysis of medical regimens of 38 elderly or senile patients and 24 young or middle-aged patients who applied for the purchase of medicines to the pharmacy at Rivne 1st City Hospital. All patients had arterial hypertension, majority of them had an additional cardiac and concomitant disorders. Methods used: system approach, bibliographic information, comparative-analytical, clinical-pharmaceutical, clinical-pharmacological analyzes.

Results. The socio-demographic and clinical features of the elderly patients with hypertension who visited pharmacy at Rivne 1st City Hospital with prescriptions of cardiologists or family therapists were revealed. The men (52.63%) slightly dominated over women (47.37%). There were more married people (52,63%) than other groups in terms of marital status: divorced (18.42%), widows / widowers (15.79%) and single (13.16%). Most elderly individuals were normal (39.48%) or overweight (26.31%), although some of them had grade I obesity (23.68%) or grade II obesity (7.90%). In terms of social and labor status, pensioners predominated over workers (73.68% vs 23.68%), and 1 person had a disability (2.63%).

The consideration of bad habits and additional risk factors in a cohort of elderly and senile patients (60-95 years) had found that as the main adverse health factors, they had noted: the difficult economic situation that negatively affects the mood and well-being) and sedentary lifestyle (39.47%). The main complaints related to hypertension were: shortness of breath during exercises (44.73%), swelling of the legs (42.11%) and feeling of fatigue (36.84%). Our respondents also had complained of rapid heartbeat (31.58%), forgetfulness and distraction (28.95%) and sleep disturbances (26.32%). Other unpleasant symptoms were less common, but the average frequency of complaints was 4.2

per person. Regarding the prevalence of concomitant pathology among elderly respondents: the most commonly diagnosed diseases were of the musculoskeletal system (36,84% of patients) and genitourinary system (31,58%). Also doctors had often diagnosed transferred COVID-19 (23,68%), coronary heart disease and pathologies of the gastrointestinal tract (each in 21,05%). The prevalence of bronchial or pulmonary diseases (10,53%) and cerebrovascular pathology (7,89%) was lower. Analysis of the group of elderly people according to the FINDRISC scale had revealed a significant proportion of patients at high risk of developing diabetes (15 - 19 points; 39.47%). A significant percentage of respondents with the very high risk was also diagnosed (20 - 26 points; 13.16%). That is, the total share of people with high or very high risk had exceeded half of our respondents (15 - 26 points; 52.63%). The shares of people with moderate (12 - 14 points; 32.68%), slightly elevated (7 - 11 points; 18.42%) and low risk (0 - 6 points; 5.27%) were significantly lower. Regarding the prescribing of cardiac drugs, we found that most often our respondents went to the pharmacy to buy ACE inhibitors (71.05%) and antithrombotic drugs (47.37%). Other common pharmacotherapeutic groups included beta-blockers and dihydropyridine calcium channel blockers (31.58% each), as well as thiazide diuretics and statins (28.95% each), and anticoagulants (23.68%). The average frequency of cardiac drugs was 3.11% per person. We watched that the pharmacotherapeutic regimens presented in prescriptions, copies of recipes and records of medical recommendations revealed their compliance with generally accepted modern standards. The vast majority of patients received a rational, fairly effective and safe treatment. At the same time, in some cases, patients during the purchase of drugs in the pharmacy at the Rivne 1st City Hospital noted a number of unpleasant symptoms, which were regarded by the next pharmacist as side effects. Consideration of 2 such specific situational cases, which clearly demonstrated the importance and applied significance of pharmaceutical care , was also presented in the thesis.

Conclusions. Given the deteriorating health that occurs in the vast majority of people when they reach old or senile age, the diagnosis and treatment of hypertension is one of the key problems of modern gerontology. In the conditions of real pharmaceutical activity, pharmacists have the opportunity to observe numerous patients with this dangerous disease, which is characterized by a wide range of clinical manifestations and is combined with various forms of concomitant pathology. Their communication with pharmacy visitors is not limited to the issuance of drugs, but is complemented by the clarification of complaints and attempts to provide assistance in resolving health problems.

ASPECTS OF PHARMACEUTICAL CARE IN THE ELDERLY

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Scientific advisor: assoc. prof. **Yu.S. Nastyukha**, PhD

Keywords: pharmaceutical care, elderly patients.

Introduction. Geriatrics is the branch of the subspecialty that mainly consists of different aspects of illness like experimental, curative, supportive, and social features of diseases in elder people. The specialty focuses on the health care of elderly people and aims to promote health to prevent and treat diseases in older adults. By 2050, one in six people in the world will be over age 65 (16%), up from one in 11 in 2019 (9%). By 2050, one in four persons living in Europe and Northern America could be aged 65 or over. In 2018, for the first time in history, persons aged 65 or above outnumbered children under five years of age globally. The number of persons aged 80 years or over is projected to triple, from 143 million in 2019 to 426 million in 2050. In Egypt, the 2006 census showed that the elderly population (≥60 years old) represents 7.2% of the total population. At the last census in 2017, adults ≥60 years old numbered 94.8 million, which is a 2.56% increase from the 2006 census. As the world's population ages, increasing numbers of older patients are potentially vulnerable to multi-morbidity, polypharmacy, and various psychosocial problems including lack of social support, which further exacerbates physical manifestations of their disease state. In recent clinical practice, information about the prescribing in elderly patients, clinical knowledge in pharmacology and therapeutics, and clinical pharmacy are important due to the increased number of elderly people and their comorbidities.

Materials and methods: system approach, bibliographic, online survey, clinical-pharmaceutical, and comparative analysis. The questionnaire was created in English and translated into Arabic and Ukrainian languages with translation verification by native speakers. The online survey was conducted during the period 13-22 of April 2021 in Egypt and during the period 10-21 of April 2021 in Ukraine by using Google form. Objects of the research: available information flows; geriatric tools (Beers criteria, STOPP / START criteria, EU(7)-PIM list, FORTA list, etc.); pharmaceutical care programs; questionnaires of pharmaceutical professionals in Egypt (n = 82) and in Ukraine (n = 113).

Results. The results of the analysis of available information flow show that age-related pharmacokinetic, pharmacodynamic changes, and polypharmacy are a reason for applying special approaches to providing rational pharmacotherapy to elderly patients. Special communication needs, geriatric tools, and the usefulness of programs should be taken into account by pharmacists for providing pharmaceutical care to elderly patients. The results

of the conducted survey show that the highest awareness among geriatric tools with Beers' criteria: 50.0% of pharmaceutical professionals in Egypt and 30.1% in Ukraine. The pharmaceutical professionals in Egypt and in Ukraine supported the necessity to find out how many comorbidities the patient aged 65+ has (93.9% and 92.0%), how many drugs the patient takes in total (85.4% and 92.9%), about potentially inappropriate medications prescriptions (90.2% and 77.9%) and about drug dose appropriateness for patient's age (90.2% and 88.5%). However, in real pharmaceutical care practice pharmaceutical professionals do less than they think is necessary.

Conclusion. The pharmaceutical professionals in Egypt (90.2%) and in Ukraine (100.0%) accept the special needs of elderly patients in pharmaceutical care. However, the implementation of pharmaceutical care in practice could be improved.

CLINICAL-AND-PHARMACEUTICAL ASPECTS OF TOPICAL CORTICOSTEROIDS USING

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Scientific supervisor: assoc. prof. **Oksana Lopatynska**, PhD.

Keywords: topical corticosteroids, dermatology, safety, efficacy, pharmaceutical care.

Introduction. Topical corticosteroids (TC), play a major role in the treatment of a large number of inflammatory skin diseases. Available for dermatologic therapy since 1952, TC sare by far the most commonly prescribed medication in an out-patient dermatology setting. TCs exhibit potent anti-inflammatory and antiproliferative effects responsible for their efficacy in skin. However, inappropriate use of TCs can lead either to local adverse effects (AE) or to systemic AE. Moreover, TCs are the cornerstone of treatment for many chronic inflammatory skin conditions and addiction to therapy and withdrawal are common situations that healthcare practitioners need to face. Bearing all that in mind, comprehensive knowledge of TCs is essential in order to optimize therapeutic outcomes, avoid improper prescriptions and minimize the risk of AE.

The aim of research: lies in the investigation of the main problems of the rational use of TC and in the formulation of practical advice on the choice of TC for particular dermatological disorders..

Materials and methods. Current evidence-based literature and online data materials (adopted from Cochrane, EMBASE, PubMed, Google Scholar, and Research Gate). Clinical guidelines (AAN, ECTRIMS/EAN, NICE, SIGN, ABN, EFNS); information on drugs using (n=125), results of a cross-sectional survey in Ukraine (n=74) and in Egypt (n=101). Used methods: literature and online data search, content analysis, clinical-and-pharmaceutical, analytical, comparative, model development, questionnaire survey targeting patients..

Results. Analyzing the discovered information that reveals the mechanism of action, pharmacological properties, indications, and contraindications, we concluded, that TCs are valuable in the management of many dermatological diseases. The results of the investigation have shown that the problem of rational use of TCs has many unresolved issues of clinical and pharmaceutical nature, among which the most important are the issues of clinical efficacy and safety of TCs. It is established that when choosing topically applied corticosteroids should take into account several factors, among which are important: the potency of TCs, type of dosage forms, dose and duration of application, limitation, contraindications, and occurrence of side effects (SE), the effectiveness of previous treatment, safety and comfort for the patient. The results of the questionnaire survey revealed the certain patterns and trends in clinical and pharmaceutical problems associated with TCs use in Egypt and Ukraine. It was established, that the patients younger 30 years belongs to the key group of people, who the most often use TCs both in Egypt and in Ukraine (78.7% vs 48.9%), indicating the likelihood of developing relevant dermatological problems at a fairly young age. Almost 1/5 of surveyed patients in Egypt and in Ukraine when choosing TCs are guided by the principles of self-appointment and self-medication, which is a serious clinical and pharmaceutical problem. Almost 25% of respondents in Egypt and in Ukraine violate the duration of TCs using, which can be considered as a drug-related problem. Almost 25% of respondents in Egypt and in Ukraine have a causal relationship between the occurrence of SE and the application of TCs. The incidence of side effects after the application of TCs in groups of respondents, who were disposed to self-medication was higher compared to those, who apply to medical care or consult with a pharmacist in a pharmacy (74.8% vs 41.7% in Egypt and 69.2% vs 35.9% in Ukraine). Almost 1/3 of the respondents in Egypt and in Ukraine do not follow or do not always follow the recommendations on the rational use of TCs, which is due, in most cases, to the insufficient provision of patients with evidence and available information. The key elements of pharmaceutical care directed on the patient, which contain 15 massages to the safe and effective use of TCs was developed. A TCs leaflet as a tool of patient education on the rational use of medicines was designed.

Conclusions: It was established that the rational use of TCs is based on the supplying of modern, qualified and evidentiary information for all participants in the treatment process that can be successfully implemented through the components of pharmaceutical care.

DEPARTMENT OF DRUG TECHNOLOGY AND BIOPHARMACY

(Head of the department – accoc. prof. **Svitlana Bilous**)

JUSTIFICATION OF THE COMPOSITION AND TECHNOLOGY OF MEANS IN THE FORM OF PATCHES

Sofiia Bilous
Scientific supervisor: assist. **Tetiana Shostak**, PhD.

Keywords: patches, skin burns, age-related skin changes, hyaluronic acid, D-panthenol, echinacea extract, snail extract.

Introduction. In modern dermatology and cosmetology are becoming increasingly popular means to achieve the desired results faster and easier, without injuring the skin, but not inferior to the effectiveness of other means, especially important in the treatment of skin burns and correction of age-related skin changes. Patches (hydrogel plasters) are becoming popular among cosmetics and medicines as a highly effective and convenient method of skin treatment and care.

Materials and methods. The object of the study is patches for the treatment of skin burns and correction of age-related skin changes. The subject of research: development of composition and technology of patches. The paper uses methods of information retrieval, analysis of literature data, marketing research, and technological methods.

Results. Patches belong to innovative forms of release, the main advantages of which are ease and convenience of application, efficiency, and speed of action, absence of side effects, simplicity of the technology, and the possibility of inclusion in their structure of substances with various properties. An analysis of the range of medicines and cosmetics in the form of patches and plasters on the Ukrainian market has been found that medicines and medical devices of this form are registered as patches, and patches are found only among cosmetics. All patches on the domestic market are foreign-made.

Based on the analysis and generalization of data on the composition of medical and cosmetic skin products for the treatment of skin burns and correction of age-related skin changes, it was found that cosmetic patches for the skin around the eyes care include moisturizing, emollient, restorative ingredients, and medicinal hydrogel patches include anti-inflammatory, moisturizing and wound-healing substances.

The composition and technology of the basis of hydrogel patches, for the development of which gelatin and sodium alginate were used, are proposed. The base also contains polyvinylpyrrolidone as a prolongator and lamina-forming agent, guar gum as a thickener, and glycerin as an additional moisturizing component and to ensure the better release of the active substance. Given that the studied hydrogel bases have a high content of the aqueous phase, an antimicrobial preservative - phenoxyethanol was introduced into their composition to prevent microbial contamination of the finished product during storage and use. Panthenol and hyaluronic acid have been

selected as active ingredients in the medicinal hydrogel patches for the treatment of skin burns, and echinacea and snail extracts have been selected as active ingredients for hydrogel patches for the skin around the eyes care.

The technology of patches is substantiated following modern normative documents and the block diagram of production is offered. The study of hydrogel patches on organoleptic, physicochemical, consumer properties, and microbiological indicators; patches are stable for 9 months.

Conclusions. The developed hydrogel patches will help to expand the range of medicines and cosmetics for the skin around the eyes care and skin burns treatment in convenient and effective forms.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF SEDATIVE PASTILLES

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Keywords: sedatives pharmaceutical products,raw herbal substances, pastille, botanicals extracts, hop plant, rotten nettle, passiflora, essential oil of brandy mint, acacia gum.

Introduction. Neurological diseases are among one of the most widespread today, primarily due to the current pace of life, the prevalence of stress and the impact of adverse environmental factors on the human body. The spread of these diseases has prompted pharmacists to create sedatives that help to normalize the body's biological rhythm. Due to the means of such practices which are used for a long time, their effectiveness and safety are of particular importance. These requiements are met by phytomedicines that have a mild effect and can be used without the risk of side effects. Therefore, it is important to develop a sedative drug based on raw herbal substances in the form of pastilles.

Materials and methods. Herbal raw materials, plant extracts, peppermint essential oil, acacia gum, pastilles; information retrieval, monitoring of data references, pooling and systematization of data, logical analysis, physico-chemical, pharmaco-technological.

Results. The current state of production and development of sedative drugs, phytotherapy of diseases of the nervous system have been studied. The nomenclature of the sedative market goods according to the State register of medicines of Ukraine on the basis of the analysis of group N05C "Hypnotics and sedatives" was investigated. It is established that a total of 164 such drugs are registered in Ukraine, of which 88 (over 50%) drugs based on natural raw materials, 30 combined drugs, the rest - of synthetic origin. Moreover, the majority of sedative drugs are of domestic production - more than 80%.

It is noted that for the effective treatment of psycho-emotional disorders it is advisable to use complex herbal medicines. taking into account the advantages of pastilles as a solid oromucosal dosage form and the lack of registered sedative pastilles, it is important to develop a sedative phytomedicine in this dosage form. The results of the studied literature sources (references) have shown that it is advisable to use such medicinal plants as hops, rotten nettle, passionflower, mint as part of sedative herbal remedies.

The selection of dosage form - pastilles is theoretically substantiated. Dry extracts of hops, passionflower, liquid extract of rotten nettle and essential oil of peppermint were introduced into the pastilles as biologically active components, the synergistic effect of which will help reduce excitation processes, eliminating the effects of stress. Acacia gum is used as a base and gelling agent; The following excipients were also added to the pastilles: stevia extract and erythritol - as sweeteners, sorbitol - as a plasticizer and citric acid - a pH regulator and antimicrobial preservative. On the basis of the conducted experimental researches the technology of pastilles with plant extracts and essential oil of peppermint in laboratory conditions is developed and the technological block diagram of production of pastilles in industrial conditions is offered. The technological process of pastille production consists of 11 technological stages. The quality control of the developed drug was carried out.

Conclusions. It is established that complex herbal preparations are optimal for effective therapy of the nervous system disorders. Based on experimental research, the composition and technology of a new sedative phytomedicine in the form of pastilles with plant extracts of hops, rotten nettle, passionflower and peppermint essential oil have been developed.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF REPELLENT COSMETIC PRODUCT

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Keywords: repellent, spray, essential oils, geranium, lemongrass, peppermint, dexpanthenol.

Introduction. Mosquitoes are the insect that causes the most insect bites worldwide. Mosquitoes are responsible for many vector-borne diseases, and represent a large burden for health systems, cause economic issues. Not all mosquitoes transmit diseases, but they they can all be a nuisance. Ppreventing mosquito bites, therefore, is an important issue. The aim of this work was to develop repellent cosmetic product.

Materials and methods. Research object is spray with essential oils of geranium, lemongrass, peppermint, and dexpanthenol. Research subject:

development of cosmetic product in the form of spray. Methods: informative, physical, physical-chemical, and mathematical ones.

Results. The contact rate between mosquitoes and human is the outcome of a complex sequence of mosquito behaviours, including flight activation, attraction, landing and probing. It is known that mosquitoes can vary in their host preferences and that levels of attractiveness differ among human hosts. Olfaction is a major component of mosquito feeding behaviour. Considering this, affecting the odor of host, it is possible to vary mosquito behaviour.

Repellents applied to skin and clothing are of great importance in protecting human beings from mosquito attack. Repellents are products that discourage arthropods from landing or biting human skin by providing a vapor barrier. Having analyzed pros and cons, it was decided to develop topical repellent in the liquid form packed in spray bottle. Many recent studied have showed that plant-based repellents are alternatives to synthetic chemicals. Among the natural products, essential oils are effective, eco-friendly and available to many parts in the world. Geranium, lemongrass and peppermint essential oils were selected as active ingredients for the new anti-mosquito spray. Besides high repellent effectiveness against mosquitoes, the all chosen oils have antimicrobial activity and other therapeutic properties. Since spray will be applied to skin, dexpanthenol was added to preparation as skin moisturizer/skin barrier restorer. The following excipients were used to develop the cosmetic product: water purified, ethyl acohol and polysorbate-80.

The spray can be prepared both in laboratory and industrial conditions. Manufacturing process of the spray with essential oils and dexpanthenol consists of 7 stages. Process flow diagram for the manufacture of the product in industrial conditions was elaborated.

Quality of the developed cosmetic product was evaluated by the following parameters: appearance, color, odor, relative density, pH value, dyeing and unctuous mark, colloidal and thermal stability. Stability of the spray at room temperature storage for 3 months (observation time) was proven.

Conclusions. The composition and technology of repellent spray with geranium, lemongrass, peppermint essential oils and dexpanthenol were developed. Quality and stability of the cosmetic product were evaluated. Due to the properties of the added ingredients, it can be considered that the preparation will provide effective protection against mosquitoes for up to 2 hours, not drying the skin, and giving a feeling of freshness and coolness.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF PREPARATION FOR FACE PEELING

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Keywords: face care, peeling, gel, lactic acid, green tea extract, vitamin E.

Introduction. The face skin is constantly affected by different internal and external factors and therefore requires special and proper care. Cleansing is the first and the most important step of any good skincare routine. Deep facial cleansing can be performed by peeling. Considering that chemical peels are among the most popular aesthetic minimally-invasive procedures because of the sheer number of benefits they provide, the development of a new preparation for face peeling is a timely task.

Materials and methods. Research object is gel with lactic acid, green tea extract, and vitamin E. Research subject: development of cosmetic product in the form of gel. Methods: informative, physical, physical-chemical, and mathematical ones.

Results. Chemical peeling is a cosmetic procedure / cosmetic preparation for targeted cutaneous ablation with a desired depth using specific caustic agents. The general goal of chemical peels is to improve the appearance of skin by reducing redness, dyspigmentation, scarring, inflammatory lesions etc. and making the face smoother, softer, brighter and younger-looking. There are distinguished in-office and home peels that differed by the depth of action.

In order to develop a new preparation for face peeling at home hydrophilic gel was chosen as an optimal form. Hydrogels are hydrophilic systems capable of imbibing large amounts of water, they are easily applied and washed out, and can hold the active ingredients due to the porous nature. Lactic acid, green tea extract, and vitamin E were selected as active ingredients. Lactic acid gently exfoliates dead skin cells, hydrates, encourages cell turnover, and also helps lighten dark spots. Green tea extract and vitamin E have a strong antioxidant effect and can help to delay collagen aging. The following excipients were used to develop the gel: glycerin, methylcellulose, polysorbate-80, volatile lemongrass oil, and water purified.

The developed gel can be prepared both in laboratory and industrial conditions. Manufacturing process of the gel with lactic acid, green tea extract, and vitamin E consists of 7 stages. Process flow diagram for the manufacture of the gel in industrial conditions was elaborated.

Quality of the gel was evaluated by the following parameters: appearance, color, odor, consistency, and pH value. Stability of the developed cosmetic product at room temperature storage for 3 months (observation time) was proven.

Conclusions. The composition and technology of gel for home face peeling were developed. Quality and stability of the developed cosmetic product were evaluated. Due to the properties of the added ingredients, it can be considered that developed gel with lactic acid, green tea extract, and vitamin E will provide gentle exfoliation without irritation, hydration and regeneration of the skin.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF MEANS FOR LOCAL TREATMENT OF TRICHOCLASIA

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Keywords: trichoclasia, treatment, hair balm, technology.

Introduction. Recently, the number of patients who turn to specialists for dryness, lack of shine, increased fragility of hair has significantly increased. All these changes are due to hair damage. Trichoclasia, a longitudinal splitting of the hair ends into pieces, is quite common among hair lesions. Treatment of trichoclasia is aimed at the complete elimination of factors that adversely affect the condition of the hair or caused the disease, as well as the appointment for the treatment of cosmetics or medicines. The most optimal means for the local treatment of trichoclasia are balms, because their use allows you to simultaneously with effective treatment to make hair soft and shiny, to preserve the natural moisture of the hair. However, the range of tools in this form is limited, so it is important to develop new tools in the form of balm-mask for implementation in domestic production.

Materials and methods. The object of study hair balm. Methods: informative, physical, physical-chemical, technological and mathematical.

Results. The classification of injuries and diseases of hair, clinical characteristics of hair diseases, systematized data on means for the care and treatment of trichoclasia are considered. It is established that the most optimal means for local treatment of trichoclasia in the form of balm-mask, as they contain a high concentration of active ingredients (vitamin and mineral complexes, nutritious vegetable oils, essential oils), which have powerful restorative properties and intensive action hair.

We systematized the data on balms, considered their classification and characteristics. There are 3 types of hair balms: conditioner, conditioner and mask. Balm-masks are used for therapeutic purposes. Based on the general methodological approach to the development of cosmetics, the methodology is substantiated and a plan of experimental research on the creation of a balm-mask for the treatment of trichoclasia is made. On the basis of theoretical and experimental researches the structure of a nourishing balm-mask of a creamy

consistence is developed. The main active components of the mask are: active complex Multivit Shuttle - delivery system of active ingredients (vitamins F, B5, E, P, witch hazel extract) in the form of sediment; a complex of vegetable oils (burdock, coconut, flax) and ylang-ylang essential oil.

We have developed balm-mask technology and proposed a technological scheme of production. The technological process consists of the following stages - ancillary work; preparation of the hydrophilic phase; preparation of the hydrophobic phase; preparation of balm-mask; homogenization, deaeration; packing, marking, packing. The developed balm-mask meets the requirements of analytical and regulatory documentation on organoleptic and physicochemical parameters, stable during storage.

Conclusions. The composition and technology of balm-mask of creamy consistency for the treatment of trichoclasia have been developed. Given the properties of the introduced components, it is assumed that the balm-mask will provide anti-inflammatory, nourishing, restorative, moisturizing and emollient effect. Natural ingredients are easily absorbed by the hair, thanks to which high efficiency is achieved. The developed tool can be recommended for further research for implementation in production. Correct selection of cosmetics for hair care, early diagnosis of diseases of the scalp and pathologies of hair growth, correction of the condition of the scalp, rational treatment regimens - the key to healthy and strong hair.

DEVELOPMENT OF COMPOSITION, TECHNOLOGY AND RESEARCH OF A DRUG FOR THE TREATMENT OF UROLITHIASIS

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Keywords: urolithiasis, Aerva lanata herb, liquid extract of Aerva lanata.

Introduction: The current problem in medicine is urological diseases, namely urolithiasis. According to the literature, urolithiasis ranks second in prevalence, third - as a cause of death and fourth – as a cause of disability. This encourages the search for new highly effective drugs for the treatment and prevention of this disease.

Materials and methods. The object of the study is urolithiasis, Aerva lanata herb, Aerva lanata herb extract. Research methods - analysis of literature data, pharmaco-technological and statistical methods.

Results. Urolithiasis is a polyetiological disease that develops due to a violation of the colloidal balance of urine. Treatment of urolithiasis is long-term, so it is important to minimize side effects as well as the harmful effects of the drug on the human body as a whole. Such requirements are met by

medicines based on medicinal plant raw materials, which are widely prescribed in complex therapy for urolithiasis in order to ensure long-term remission. Given all the advantages, such as a wide range of medicinal plant raw materials, relative availability and minimal side effects on the body, the development of a new herbal medicine is promising. After analyzing the literature for the development of a tool in the treatment of urolithiasis, we chose Aerva lanata.

The next stage of our work was the development and study of a liquid extract of Aerva lanata. The main technological properties of medicinal plant raw materials - bulk volume and bulk density before and after shrinkage, fractional composition and alcohol absorption coefficient are studied. In order to choose a rational method of extraction, Aerva lanata extract was obtained by three methods - percolation, vortex extraction and remaceration. 70% ethanol was chosen as the extractant, because this concentration allows to fully precipitate the main biologically active substances of the Aerva lanata herb - flavonoids. On the basis of theoretical and experimental researches the rational technology of a liquid extract of Aerva lanata by a percolation method is developed. Developed a liquid extract of Aerva lanata which can be used as a stand-alone drug and administered in other dosage forms. Also the technological block scheme of production which consists of 10 stages is developed.

The quality control of the developed liquid extract of Aerva lanata in accordance with the requirements of the State Pharmacopea of Ukraine was carried out. As a result of physicochemical studies, it was found that the developed liquid extract meets the requirements on the main indicators and is stable during storage for 6 months (observation period). Appearance, color, odor, ethanol content and dry residue in the developed liquid extract of Aerva lanata within acceptable limits.

Conclusion: We conducted an informative analysis of the features of the treatment of urolithiasis and analysis of the range of drugs in the pharmaceutical market of Ukraine. The composition and technology of the liquid extract based on Aerva lanata herb have been developed. We have scientifically and experimentally substantiated the composition and technology of a new drug from the Aerva lanata herb in the form of a liquid extract. The liquid Aerva lanata extract developed by us meets the requirements of regulatory documentation, is stable during storage and can be recommended for further research for implementation in production.

DEVELOPMENT OF COMPOSITION, TECHNOLOGY AND INVESTIGATION OF ANTI-AGING COSMETIC PRODUCTS

Sofiia Bulbiak
Scientific supervisor: assoc. prof. **Oksana Yezerska**, PhD.

Keywords: anti-aging cream, snail secretion extract, hyaluronic acid, collagen, dexpanthenol.

Introduction. Aging of the skin involves a complex mixture of multiple biological processes that varies from one person to another based on exogenous and endogenous factors. Therefore, protection of skin, including use of anti-aging products, is an extremely important matter. Development of composition and technology of anti-aging cosmetic products, therefore, is a topical task.

Materials and methods. Research object is cream with snail secretion extract, hyaluronic acid, collagen, dexpanthenol, vitamins A and E. Research subject: elements of development of sunscreen product for children. The methods of the research are informative, physical, physical-chemical, and mathematical.

Results. Having analyzed literature data, it was decided to develop a new anti-aging cream in the form of oil-in-water cream. Snail secretion extract, hyaluronic acid, collagen, dexpanthenol, vitamins A and E were selected as active ingredients. Snail extract contributes to the increase in the production of hyaluronic acid and improves the density of the collagen network, allowing the skin to maintain its elasticity and regain its youthful appearance. Therefore, the snail secretion stimulates the epidermis to produce more collagen and consequently fights facial wrinkles and the first signs of wrinkles that occur with age, at the same time reduces the depth of wrinkles already present. Hyaluronic acid has several functions, including retaining moisture, providing cushioning, holding together the skin structural components of collagen, and creating a barrier against microorganisms. Collagen improve skin elasticity, reduce visible wrinkles, and increase blood flow to the skin. In order to increase sun protective action of cream vitamin E, that is a common antioxidant, was added into the composition.

The base of cream was formed by the following ingredients: grape seed and wheat germ oils – hydrophobic phase; emulsifier No.1 – o/w emulsifying agent; monoglycerides – w/o emulsifying agent; preservative euxyl; water purified – hydrophilic solvent. Manufacturing process of sunscreen cream anti-aging cream with snail secretion extract, hyaluronic acid, collagen, dexpanthenol, vitamins A and E in industrial conditions consists of 8 stages and was developed with regard to the physical-chemical properties of ingredients. Quality of cream was assesed on appearance, color and odor, pH value, colloidal and thermal stability. Stability of the developed product at room temperature storage for 6 months (observation time) was proven.

Conclusions. Composition and technology of a new anti-aging cream with snail secretion extract, hyaluronic acid, collagen, dexpanthenol, vitamins A and E in the form of oil-in-water cream were scientifically and experimentally justified. The proposed cream for organoleptic and physico-chemical indicators meets the requirements of the current documentation.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF THE BALM WITH IMMUNOMODULATORY PROPERTIES

Kateryna Bryn
Supervisor: assoc. prof. **N.I. Hudz**, PhD

Introduction. In conditions of ecological and epidemic distress, a promising direction of preventive medicine is the eco-adaptive principle of disease prevention, which aims to correct maladaptation using adaptogens and immunomodulators of mild prolonged action, antioxidants that neutralize and eliminate toxic agents. The versatility of the pharmacological effects of medicinal plants in combination with high bioavailability and low toxicity expands the list of diseases for which the administration of herbal medicines is indicated. The use of balms has a historical past and is the most adequate preventive and complementary method of the treatment under unfavorite ecological and epidemic conditions. Therefore, it is advisable to develop balms with immunomodulatory, antioxidant and adaptogenic activities. The aim of our work was to develop balms with immunomodulatory properties based on the tinctures of *Echinacea purpureae radix*, *Echinacea purpureae flos*, tincture of *Schizandra chinensis folium*, tincture of *Monarda fistulosa herb*, and honey.

Materials and methods. The following methods were used: analysis, synthesis, systematization, and comparison for processing of published scientific data on the composition and application of sprays; potentiometric analysis for determining the pH value of samples of the balms.

Results. The three balms on the base of the tincture of *Echinacea purpureae radix*, *Echinacea purpureae flos*, tincture of *Schizandra chinensis folium*, tincture of *Monarda fistulosa herb* were objects of the studies. The coefficients of alcohol absorption were established: for the roots of *Echinacea purpurea* (size from 2 to 5 mm) 1.2 ml/g, flowers of *Echinacea purpurea* (size from 1 to 3 mm) 2.25 ml/g, *Schizandra chinensis* leaves (size from 1 to 5 mm) 4.1 ml/g, Monarda fistulosa herb (size from 0.5 to 3 mm). The technology of four tinctures by the method of remaceration was developed: Honey in concentration 20 % was employed in order to impart a sweet taste to the balms. The tincture of *Monarda fistulosa herb* provides a pleasant specific odour to the balms. Special features of the development of the balms were: obtaining the solution of honey (at elevated temperatures). The mixtures were thoroughly stirred until

homogeneous mass was obtained. The balms were packed into containers with a nominal content of 25 ml.

Conclusion: The developed balms were clear and yellow or greenish solutions with slight turbidity, nice strong smell of components, and a sweet taste.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF A VITAMIN SYRUP

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Scientific supervisor: assoc. prof. **Oksana Strus**, PhD.

Keywords: black currant, chokeberry, juice, vitamin syrup, technology, standardization.

Introduction. Vitamins are biological catalysts that are necessary to maintain the normal functioning of the body and without which the normal course of biochemical processes is impossible, because they are part of the molecules of many enzymes and some physiologically active substances involved in metabolism. Therefore, if vitamins do not come with food, the body does not receive the necessary substances, which is detrimental to human health. Vitamin deficiency is accompanied by disorders of biochemical and physiological processes and the emergence of specific pathology.

Medicinal syrups, which are solutions of medicinal and excipients, from a biopharmaceutical point of view are the most physiological and effective dosage forms, and medicinal substances, being dissolved in them, are absorbed faster.

The purpose of our work is to theoretically and experimentally substantiate and develop the composition and technology of vitamin syrup.

Materials and methods. Materials of the study were experimental samples of juice, vitamin syrup with juice of chokeberry and black currant. Methods of system analysis (study of literary data and the establishment of common approaches in the technology of liquid dosage forms); organoleptic (appearance, color, smell, consistency), physico-chemical (viscosity assessment, and pH of the medium) were used.

Results. The choice of chokeberry and black currant juice, which contain vitamins C, P, etc., organic acids, trace elements, flavonoids and polyphenols, is substantiated and chosen as an active pharmaceutical ingredient. The technology is developed, which consists of the following stages: grinding of raw materials, pressing of crushed raw materials, inactivation of enzymes, juice filtration, preservative introduction, juice settling, juice filtration, packing and labeling. The composition of the syrup, which contains 10 ml of chokeberry and currant juice, 0.1 sorbic acid and up to 100.0 sugar syrup, is substantiated. The technology of vitamin syrup has been developed, which contains the

following stages: preparation of sugar syrup, filtering of sugar syrup, preparation of medicinal syrup, packing of syrup into vials and sealing, labeling of vials, packing of vials in packs, packing of packs into boxes.

Conclusion. As a result of the analysis of literature data and experimental researches the structure and technology of vitamin syrup are substantiated and developed and its standardization is carried out.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF ANTIFUNGAL PRODUCT FOR FEET

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Keywords: liniment, composition, technology

Introduction. Modern experimental formulation of linear variants and includes liniments-solutions, Rosenthal liniment, capsitrin, pepper-camphor, pepper-ammonia, chloroform composition, methyl salicylate complex, turpentine complex; liniments - emulsions: ammonia, naphthalene; liniments-suspensions: balsamic according to Vishnevsky; combined liniments: chloramphenicol, streptocide, syntomycin. Significant number of linear changes in production. The connection with this problem of using the association of linear changes to calculate the export production in the pharmacy is the most urgent task.The purpose of our work was to theoretically and experimentally substantiate and develop the composition and technology of antifungal agent.

Materials and methods. Materials of the study were experimental samples of antifungal liniment. Methods of system analysis (study of literary data and the establishment of common approaches in the technology of liquid dosage forms); organoleptic (appearance, color, smell, consistency), physico-chemical (pH of the medium), physical were used.

Results. The data of the literature are generalized and the etiology of mycoses is characterized, their classification and modern methods of treatment and prevention are given. The dermatological group of antifungal drugs is represented by ointments, creams, gels, solutions, pastes, sprays and varnishes. It is determined that liniments are the optimal dosage form in which it is possible to combine components different in chemical nature, physical state, purpose, biological activity, which due to high viscosity are more stable and have high bioavailability. The results of the research substantiate the composition and technology of the liniment intended for the treatment of foot fungus, which includes 1.0 terbinafine hydrochloride, 20.0 g of corn oil, 10.0 g of tween-80 and purified water up to 100.0. Liniment technology consists of several successive stages: preparatory work, preparation of the primary

emulsion, preparation of a solution of the active substance, dilution of the primary emulsion, quality control, packaging and registration for release.

Conclusion. Developed the composition and technology of liniment, which meets the requirements of SPh of Ukraine and can be recommended for further research for individual or small-scale extemporaneous production

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF EYE DROPS WITH MOISTURIZING AND ANTIMICROBIAL ACTION

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Scientific supervisor: assoc. prof. **S.B. Bilous**, PhD

Keywords: eye drops, infectious eye diseases, «dry eye» syndrome, hydroxyethyl starch, silver nanoparticles, hyaluronic acid.

Introduction: Despite the constant improvement of methods of ophthalmic diseases treatment, treatment of infectious and inflammatory diseases of the eye, the syndrome of "dry eye" remains an actual problem in ophthalmology. An important way to solve this problem is to develop domestic original drugs with local antibacterial action that can directly affect the eye and quickly and effectively eliminate the symptoms of the disease.

Materials and methods: Methods of information search, literature data analysis and technological methods have been used.

Results: Among the most common eye diseases are infectious and inflammatory diseases - conjunctivitis, blepharitis, keratitis, uveitis, etc., as well as, in recent years, «dry eye» syndrome - a multifactorial disease manifested by symptoms of eye discomfort, tear film instability with possible damage eye surface. In the absence of adequate treatment, some of these diseases can lead to serious consequences up to vision loss. The most optimal dosage form for the treatment of ophthalmic diseases are eye drops, which are characterized by easy use and speed of onset of effect.

Because antimicrobial, moisturizing and regenerating effects are important for the treatment of infectious and inflammatory eye diseases, as well as for the elimination of «dry eyes», hydroxyethyl starch with silver nanoparticles and hyaluronic acid as active pharmaceutical ingredients are used at the development of eye drops. Considering the high medical and biological requirements to ophthalmic preparations, in particular the compliance of the drug with the normal state of lacrimal fluid - isotonicity, pH, refractive index, etc., in the composition of eye drops were used the following excipients: sodium nitrate as isotonic agent, sodium dihydrogen phosphate as pH regulator, nipagin as a preservative, and purified water as a solvent. The technology of drops was substantiated and the block-scheme of their production was

developed. The manufacture of eye drops was performed under aseptic conditions. Sterilization of the solution was performed with saturated steam under pressure at a temperature of 120 ° C for 8 minutes. The developed eye drops are stored for 3 months (observation time) and for all studied organoleptic parameters (color, transparency, absence of mechanical impurities, pH) are stable.

Conclusions. The composition and technology of eye drops, which can be effective both for the complex treatment of infectious and inflammatory eye diseases and for the elimination of «dry eye» syndrome have been developed.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF MEDICINAL COSMETICS FOR THE TREATMENT OF PARASITIC SKIN DISEASES

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Keywords: cream, parasitic skin diseases, metronidazole, silver nanoparticles, sodium hyaluronate, tea tree oil.

Introduction: Treatment of parasitic skin infections is an actual problem for modern dermatology and cosmetology. In recent decades, skin parasites have been linked not only to the development of demodicosis, but also to other dermatological diseases such as rosacea, acne and others. The range of medicines for the treatment of parasitic skin diseases in the pharmaceutical market is quite limited, what necessitates the development of new topical drugs in this direction.

Materials and methods: Methods of information search, literature data analysis and technological methods have been used.

Results: Parasitic skin infections are a significant problem in dermatology and cosmetology. The same parasite can be pathogenic for one organism and harmless for another, so there is a variety of clinical picture - from asymptomatic parasitism to severe manifestations of parasitic diseases. For the development of parasitic diseases in addition to invasion and sensitization by parasites, other endogenous and exogenous factors are important, including chronic infections, diseases of the digestive tract, immune system disorders, endocrine disorders and others. The study of modern approaches to the treatment of parasitic skin diseases has shown that special attention should be paid to the use of nitroimidazoles, in particular metronidazole, which provides antiparasitic effect against *Demodex folliculorum*, as well as bacteriostatic action against gram-negative bacteria and anti-inflammatory effect. At development of preparation for the treatment of parasitic skin diseases as a dosage form chosen hydrophilic cream type o/w,

which contains a significant content of aqueous phase and moisturizing components, as well as a low concentration of emollients. As active ingredients at the development of the cream were used - metronidazole with silver nanoparticles, which will further enhance the antimicrobial action of metronidazole; sodium hyaluronate, which will help regenerate the epidermis and protect tissues from drying out, and tea tree oil, which has antimicrobial action, eliminates itching and inflammation of the skin.

As auxiliary components in the cream were used - grape seed oil as an emollient, hostacerin as an emulsifier, carbopol as a thickener, glycerol as a humectant, ammonia solution as a pH regulator, phenoxyethanol as a preservative, and purified water as a solvent. The technology of the cream is substantiated and the block diagram of production is developed, which provides application of the following technological stages: preparation of the aqueous phase, preparation of the oil phase, emulsification, cooling, introduction of thermolabile substances, and packaging of the cream. The developed cream is stable for 3 months (observation time) for all studied indicators (color, odor, homogeneity, pH, etc.).

Conclusions. The composition and technology of the cream, which can be effective for the treatment of demodicosis and other dermatological diseases that are accompanied by acne-like dermatoses, has been developed.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF HAIR MASK WITH COCONUT OIL

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Keywords: hair, mask, coconut oil, wheat germ oil, argan oil.

Introduction. Hair is an important part of the appearance that sets the tone of your entire look, health, social individuality and even status. Hair plays so significant role in our society that its loss or too much growth can influence the self-esteem. The global hair care market, therefore, is progressive and dynamic. The awareness of various hair care procedures is continuously rising and the demand on hair care products with natural ingredients is increasing. Such data indicate that there is need for development of new effective hair care products with plant oil.

Materials and methods. Research object is mask in the cream form with coconut oil. Research subject: development of cosmetic product in the form of cream. Methods: informative, physical, physicalchemical, and mathematical.

Results. Hair is an integrated system with a peculiar chemical and physical behavior. In order to have healthy hair, you need to take care of it

considering the type of hair and its physical properties. Hair care routine includes different steps. Washing the hair with following conditioning is the most crucial one to maintain the health of your hair. The primary goal of hair conditioning is to decrease friction, detangle the hair, minimize frizz and improve combability. Conditioners, balms and masks are used for conditioning. Masks, also called deep conditioners, are cosmetic products for intensive hair care. Having more concentrated composition, hair masks provide not only conditioning and lubrication, but also can moisturize, regenerate, nourish and strengthen the hair.

Considering the hydro-lipid structure of hair cuticle, emulsion oil-in-water cream was chosen as an optimal form for the development of a new hair mask. Coconut oil was selected as the main active ingredient for the mask. Due to its polarity, low molecular weight and high affinity for hair proteins, coconut oil can penetrate into the hair cortex, nourishing the hair and protecting from damage. It helps lock in moisture giving it a gorgeous glow and shine, and acts as natural sunscreen. Wheat germ and argan oils were added in the mask to improve its cosmetic effect. Wheat germ oil is known for its antioxidant, nourishing and emollient properties. Argan oil helps to hydrate and soften hair, to reduce fizziness and boost shine; it protects against styling damage and damage caused by free radicals. The following excipients were used to develop the carrier: dimethicone, propylene glycol, cetyl alcohol, glycerol monostearate, methyl parahydroxybenzoate, flavorant, and water purified.

The developed mask can be prepared both in pharmacy and industrial conditions. Manufacturing process of the cosmetic product with plant oils consists of 8 stages. Process flow diagram for the manufacture of the mask in industrial conditions was elaborated. Quality of the mask was evaluated by the following parameters: appearance, color and odor, pH value, colloidal and thermal stability. Stability of the developed cosmetic product at room temperature storage for 3 months (observation time) was proven.

Conclusions. Composition and technology of hair mask with coconut oil were developed. Quality and stability of the developed cosmetic product were evaluated. Due to the properties of the added ingredients, besides the conditioning, the mask with coconut, wheat germ and argan oils will provide amazing results of hair health improvement.

DEVELOPMENT OF COMPOSITION, TECHNOLOGY AND INVESTIGATION OF DRUG PRODUCT IN THE FORM OF TABLETS

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Keywords: *Salvia officinalis*, ascorbic acid, orodispersible tablets, excipients

Introduction. The most common and preferred route of drug administration is through the oral route. Orodispersible tablets are gaining importance among novel oral drug-delivery system as they have improved patient compliance and have some additional advantages compared to other oral formulation. They are also solid unit dosage forms, which disintegrate in the mouth within a minute in the presence of saliva due to super disintegrants in the formulation. Thus this type of drug delivery helps a proper peroral administration in pediatric and geriatric population where swallowing is a matter of trouble. Therefore, development of orodispersible tablets is a topical task.

Materials and methods. Research object are tablets with sage leaf extract and ascorbic acid. Research methods – analysis of literature data, pharmaco-technological and statistical methods.

Results. The development of drugs in the form of orodispersible tablets suggests taking into account certain requirements for this dosage form: sufficient mechanical strength along with rapid disintegration in a small amount of liquid, pleasant tactile and taste sensations, the choice of optimal packaging. The achievement of the optimal strength and disintegration is possible by using two methods – adding excipients (first of all, fillers, binders and superdisintegrators) and selecting the pressure on a tablet machine. Orodispersible tablets are tablets that disintegrates and dissolves rapidly in the saliva, within a few seconds without the need of drinking water or chewing.

A orodispersible tablets usually dissolves in the oral cavity within to 3 min. Most of the orodispersible tablets include certain super disintegrants and taste masking agents. Investigated range medicinal products with sage, registered on pharmaceutical market of Ukraine, were held according to the State Register of Pharmaceutical Products. On the basis of theoretical and experimental studies, a composition of orodispersible tablets was developed, and sage leaf extract and ascorbic acid was introduced into the tablets as the main active pharmaceutical ingredients. Xylitol, sorbitol, microcrystalline celluloses, aerosil, croscarmellose sodium, magnesium stearate and fragrance "Orange"were used as excipients. The average mass of the proposed tablets is 0.6 g.

The technological process consists of the following stages: preparation of production and raw materials, mixing of active pharmaceutical ingredients and

excipients, compression, quality control, packaging and labeling. The technological scheme of the orodispersible tablets with sage leaf extract and ascorbic acid manufacturing has been developed . Quality control of the developed product was conducted according to the requirements of Ukrainian State Pahrmacopoeia: an average tablet weight is 0.6 ± 5%, the resistance to crushing is not less than 46 N, the erasibility degree is not more than 1%, the tablet weight uniformity – ± 2 %, decomposition takes no more than 3 minutes. Stability of tablets with sage leaf extract and ascorbic acid at room temperature storage was prove.

Conclusions. We have scientifically and experimentally proved the composition and the technology of new medicinal product with sage leaf extract and ascorbic acid in the form of orodispersible tablets. The developed medicinal product is a tablets with sage extract and ascorbic acid that meets the requirements of analytical documentation requirements, is stable in storage and can be recommended for the further research with the purpose to be implemented in production.

DEVELOPMENT OF COMPOSITION, TECHNOLOGY AND INVESTIGATION OF MEDICINAL PRODUCT FOR PSORIASIS TREATMENT

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Keywords: psoriasis, treatment, cream, salicylic acid, urea, cholecalciferol, amaranth oil.

Introduction. One of the most pressing problems in modern dermatology is the search for effective treatments for psoriasis. In recent years, there has been a significant increase in the incidence of this dermatosis, especially among children and young people; increase in the number of severe, recurrent, disabling and atypical forms of the disease resistant to therapy; appearance of forms that do not have differentiated stages, frequent absence of seasonal occurrence of the disease. The main goal of therapy is to achieve clinical remission of the process by reducing the activity of inflammation, normalization of the keratinization process and elimination of skin infiltration. The range of products for topical treatment of psoriasis is insufficient, so the development of new combined effect products for the topical treatment of psoriasis in a convenient dosage form is an urgent issue of modern medicine and pharmacy.

Materials and methods. The research object is a cream for psoriasis treatment. The methods of research include data monitoring, grouping and

systematization of information, logical analysis, physical-chemical and technological methods.

Results. The results of the analysis of information search showed that the rational therapy of patients with psoriasis is determined by etiopathogenetic factors of their origin and development, the clinical picture, the nature of the pathological process and the need for concomitant pathogenetic therapy. Treatment involves a comprehensive topical and systemic therapy, the approach of which is determined individually. When developing drugs for the topical treatment of psoriasis, it is necessary to take into account that such drugs should have anti-inflammatory activity, help normalize the keratinization process, as well as eliminate skin infiltration. The study established that the most optimal dosage form for the external treatment of psoriasis in the stationary and regressive stages are ointments or creams.

The composition of the cream for the treatment of psoriasis was theoretically and experimentally substantiated. Salicylic acid, urea, cholecalciferol, amaranth oil were introduced as the main active components. This combination of ingredients will act on different components of the pathogenesis of psoriasis and contribute to faster healing. The composition of the water-in-oil emulsion type of base was experimentally substantiated: hydrophilic phase consists of purified water; hydrophobic phase contains amaranth oil; emulsifiers consist of a mixture of glyceryl monostearate and polysorbate 80 at a concentration of 10%. Xanthan gum was used as a thickening agent, and sorbic acid was used as a preservative agent.

The technology of cream was developed and the technological scheme of production was offered. The technological process consists of the following stages: pretreatment; preparation of the hydrophilic phase; preparation of the hydrophobic phase; preparation of the cream; homogenization, deaeration; pre-packing, labeling, packing. The developed cream meets the requirements of analytical documentation for organoleptic and physicochemical parameters and it proved to have good storage stability.

Conclusions. The composition and technology of the cream for psoriasis treatment were developed. Considering the properties of the introduced ingredients, the cream is expected to provide keratolytic, anti-inflammatory, antibacterial, moisturizing and emollient effect.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF SEMI-SOLID DRUG PRODUCT WITH *HORSE CHESTNUT* EXTRACT

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Keywords: gel, horse chestnut extract, Japanese pagoda tree extract, peppermint oil, chronic venous insufficiency.

Introduction. Development of mew effective drug preparations for the treatment of social important diseases is one of the priorities of the pharmaceutical science. Chronic venous insufficiency (CVI) is among the most prevalent medical problems in the adult population: its overall prevalence is estimated to be 10-15% for men and 20-25% for women, and approximately 150.000 new patients are diagnosed with this disease each year. Medicines of plant origin play a significant role in the pharmacological treatment of CVI. The most popular ones include the horse chestnut seed extract or aescin isolated from it.

Materials and methods. Research object is gel with horse chestnut extract, Japanese pagoda tree extract, and peppermint oil. Research subject: elements of pharmaceutical development of preparation in the form of gel. Methods: informative, physical, physical-chemical, and mathematical.

Results. CVI is a common condition that typically involves lower extremity edema, pain, trophic skin changes, and discomfort secondary to venous hypertension. The initial management of CVI involves conservative approaches to reduce symptoms and prevent development of secondary complications and progression of disease. The vasoactive drugs are widely used in the treatment of CVI. Lots of in vitro and in vivo studies confirmed that horse chestnut seed extract (HCSE) and aescin – the major active principle of HSCE, possess anti-inflammatory, antiangiogenic, and antioxidant activities. HCSE may be as effective as treatment with compression stockings that is the mainstay of CVI management. However, the number of topical preparations with HSCE registered in Ukraine is a very small. In order to develop a new semi-solid preparation with HCSE, hydrogel was chosen as the most optimal dosage form. Since CVI is a complex condition with widely varied clinical manifestations, it was decided to add Japanese pagoda tree extract and peppermint oil to improve the effectiveness of the preparation. Japanese pagoda tree extract contain compounds with antihemorrhagic, antihemostatic, antioxidant, anti-inflammatory and regenerative properties, while peppermint oil will offers frosty and refreshing relief to skin and helps to reduce itching. The following excipients were used to develop the hydrogel: carbomer 934 (gel-forming agent), propylene glycol (co-solvent, penetrant and moistening agent), methyl parahydroxybenzoate (preservative agent), ammonia solution 10 % (pH-regulator), water purified (solvent). The gel with horse chestnut extract,

Japanese pagoda tree extract, and peppermint oil can be prepared both in pharmacy and industrial conditions. Manufacturing process of the gel consists of 7 stages. Process flow diagram for the manufacture of the gel in industrial conditions was developed.

Quality of the preparation was evaluated by the following parameters: appearance, color and odor, consistency, pH value. Stability of the developed gel at room temperature storage for 3 months (observation time) was proven.

Conclusions. Composition and technology of the hydrogel with horse chestnut extract, Japanese pagoda tree extract, and peppermint oil were developed. Quality and stability of the preparation were assessed. Due to the properties of the added ingredients, it can be considered that gel can be used for the management of CVI.

DEVELOPMENT OF COMPOSITION AND TECHNOLOGY OF COSMETIC ANTI-AGE FACIAL PRODUCT

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Keywords: facial care, anti-aging products, facial serum, technology

Introduction. Recently, the share of anti-aging cosmetics is increasing among cosmetic products. This trend is due to the growing number of an aging population, as well as a significant amount of various information materials and recommendations on skincare. To prevent skin aging and promote its care, a significant number of cosmetics have been proposed. However, most anti-aging products are represented by foreign manufacturers, which, accordingly, have a high cost compared to domestic ones. Therefore, the development and introduction into the production of new effective anti-aging cosmetics for facial skincare, which is affordable, is an urgent and promising task of modern cosmetology and pharmacy.

Materials and methods. The object of the study is an anti-aging facial serum. Methods included data monitoring, grouping and systematization of information, logical analysis, physical-chemical and technological tools.

Results. As a result of the study, the mechanisms of skin aging were considered; the main approaches to the prevention and correction of skin aging were analyzed; and data on cosmetics for the care of aging skin was systematized. The main finding is that careful skincare is an integral part of a comprehensive approach to the prevention of signs of aging, characterized by loss of volume and density, wrinkles, and related conditions, including dryness or sensitivity of the skin. The use of anti-aging products is essential to prevent skin aging. The optimal means of anti-aging action for facial skincare are serums, which have significant advantages: the ability to create a locally high

concentration of the active substance in the tissues at a low total dose of the drug; minimal systemic action or its absence, convenience, and ease of use. The concentration of active ingredients in the serum is several times higher than in any effective cream. Due to this finding, the effectiveness of serums is much higher compared to other products. We theoretically and experimentally substantiated the composition of the serum for the face. As active ingredients, the active Regu-Age complex based on rice germ, soy, and yeast proteins was introduced. The other components included low molecular weight hyaluronic acid; vitamin C and chamomile extract liquid as excipients used: purified water - solvent, glycerin - co-solvent, viscosity regulator, humidifier; sorbic acid - a preservative. The composition and technology of serum for the face are developed, the technological scheme of means in industrial conditions is offered. The technological process consists of 8 technological stages. As a result of physicochemical studies, it has been found that the developed serum for the face meets the requirements of analytical and regulatory documentation on the studied indicators and is stable during storage for three months (observation period).

Conclusions. The composition and technology of anti-aging serum for the face have been developed. The created product meets the requirements of analytical and regulatory documentation. It is stable during storage and can be recommended for further research for implementation in production.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF THE ANTISEPTIC WITH CHAMOMILE TINCTURE

Ivan Polokhach
Scientific supervisor: assoc. prof. **N.I. Hudz**, PhD

Introduction. The coronavirus disease 2019 pandemic greatly increased the frequency of disinfecting surfaces in public places and treating hands, causing a strain on the ability to obtain disinfectant and antiseptics solutions, respectively. Contaminated hands are the most active factor in the transmission of pathogenic microorganisms in everyday life, including virus SARS-CoV-2. Therefore, this qualification magister paper was dedicated to the problem of antiseptics development for hand treatment in order to prevent the spread of diseases that are transmitted in a contact way. The aim of the study was to develop a composition and technology, and conduct the research of the antiseptic gel with the tincture of *Matricariae flos* for topical application in everyday life.

Materials and methods. While carrying out the research the following methods were used: analysis, synthesis, systematization and comparison for processing of published scientific data on the composition and assignment of

antiseptic gels; potentiometric analysis for determining the pH value of the developed samples.

Results. As a result of performing research, a new composition and technology of some cosmetic gels for skin care were developed. The following excipients were used: carbopol 980 as a gelling agent, glycerin as a hydrophilic solvent and moisture keeper and purified water as a solvent. As active substances for the development of the gel, ethanol and tincture of *Matricariae flos* were used, which will provide antimicrobial and partly wound healing effect on the skin and impart yellow colour to the elaborated gel. The tincture of *Matricariae flos* was incorporated into the gels as preparations with antioxidant, anti-inflammatory,and antimicrobial properties. The tincture of *Matricariae flos* was obtained with the aid of remaceration method. It was selected that triethanolamin was optimal adjuster of pH. Trometamol is incompatible with carbopol 980 and ethanol as carbopol precipitates. Concentrations of anothercomponents were selected on the base of literature data and experimental results. The special features of the gel preparation were: a previous preparation of the tincture; previous preparation of the concentrated gel base of carbopol; adding ethanol and the tincture; packaging and quality control. The adding of the liquid components (ethanol, adjester of pH and tincture) into the concentrated neutralized gel base of carbopol was carried out gradually while stirring until homogeneous mass was obtained. Adding the tincture was carried out in the last turn. The mixture was thoroughly stirred until homogeneous mass was obtained. The antiseptic gel was packed in plastics containers of an appropriate volume.

Conclusion: The developed gel with the tincture had a yellowish colour and nice strong smell of *Matricariae flos*, pH of samples of the developed gel was in the range of 5.0-7.0.

DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF AROMATIC PRODUCT TO PREVENT PSYCHO-EMOTIONAL STRESS

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Keywords: psycho-emotional stress, aromatherapy, essential oils.

Introduction: Psycho-emotional stress, which is manifested by increased nervousness, headaches, insomnia and other symptoms, is an urgent problem today for specialists in various professions, including medical and pharmaceutical specialists. In recent years, the problem has intensified for some categories of workers because of the COVID-19 pandemic. One of the effective methods to prevent psycho-emotional stress can be aromatherapy,

which can be used alone or in combination with reflexology, physiotherapy, massage and medical treatments.

Materials and methods: Methods of information search, literature data analysis and technological methods were used.

Results: The problem of psycho-emotional stress has emerged over the past two decades as a result of changes in people's lifestyles and work activities due to the increasing role of mental work, which requires increased attention, processing a lot of information and decision-making in conditions of acute shortage of time. Aromatherapy, which helps to relieve tension, relaxation, activation of vitality and positive mood, restoring the overall balance of the body and vital energy, as well as the treatment of various psychosomatic diseases - headaches and muscle aches, loss of sleep and appetite, depression, neurosis and others, is one of the effective methods of preventing psycho-emotional stress.

At development of aroma product to prevent psycho-emotional stress, we have selected three essential oils - orange, sage and mint, which will provide a calming and relaxing effect, increase concentration and adaptive capacity of the body, improve mood and memory, and eliminate emotional exhaustion and anxiety. Taking into account that the essential oils in pure form are not recommended for application to mucous membranes, and for the skin is used only in combination with other components, in the composition of aroma product as a base oil olive oil was used/ Olive oil will provide additional positive effects on the skin. For better mixing of essential oils with water and, accordingly, to ensure slower evaporation of essential oils, in aromatherapy, in the composition of aroma product o/w emulsifier - polysorbate-80 were used. The technology of the aroma product in the form of a solution, which allows its preparation even at home, is substantiated, and the possible ways of proposed aroma product are substantiated - in the form of an aromabath, massage and aromalamp. The developed aroma product is stable during 3 months (observation time) according to the studied parameters (appearance, color and odor).

Conclusions. The developed aroma product, according to the composition, can be effective for the prevention of psycho-emotional stress as an independent means or as an effective addition to other methods.

RESEARCH OF THE COMPOSITION AND TECHNOLOGY OF DISINFECTIVE SOLUTIONS FOR APPLICATION IN PHARMACIES

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Scientific supervisor: assoc. prof. **S.B. Bilous**, PhD

Keywords: disinfection, disinfectants, disinfectant solutions

Introduction: Disinfection plays an important role in overcoming infectious diseases, as it directed on preventing the epidemiological process by destroying pathogens or vectors of infection in the environment and in the ways of their spread. Disinfection requires the use of a significant number of disinfectants, highly effective and safe for humans. Therefore, it is important to study the composition and technology of modern disinfectant solutions.

Materials and methods: Methods of information search and literature data analysis.

Results: The basis for choosing a disinfectant for specific objects is their efficiency and safety. At the choice of disinfectants should be taken into account the characteristics of the object being treated, the biological characteristics of the microorganism and the duration of its survival in the environment, the range of antimicrobial action of the disinfectant, the toxicity of the active substance and environmental impact. Important additional requirements for disinfectants are the following characteristics: to have detergent, cleaning and deodorizing properties; do not damage objects that can be disinfected; do not require rinsing. The analysis of disinfectants registered in Ukraine from 2018 to 2021 showed that with the development of the COVID-19 pandemic, the registration of disinfectants has increased in many times over. Thus, in 2018, 131 products were registered, in 2019 - 222 disinfectants, and in 2020 - 1248 products. In 2021 (until April), 201 products are allowed to be used, of which 30 products can be used for disinfection in pharmacies and other healthcare facilities. Among the manufacturers of disinfectants are dominated domestic manufacturers, which occupy more than 50% of the market, and also these products are supplied to the Ukrainian market by manufacturers from other countries, including Belgium and Germany, as well as Italy, Slovakia, Poland, Estonia and Romania.

Disinfectant solutions are the main group of disinfectants. On the market, disinfectant solutions and gels account for 95%, tablets and wipes - 2% of each, powders - 1%. Disinfectants are largely ready to use - most hand antiseptics, alcohol disinfectants for quick disinfection, as well as a large number of products are concentrates that must be diluted with water before use. The main active components of disinfectants are: ethanol, chlorine, glutaraldehyde, isopropyl alcohol, hydrogen peroxide, phenoxyethanol and quaternary ammonium compounds. The range of disinfectants is mainly provided by industrial production, which differs from the production of drugs

and has its own characteristics. Extemporaneous production of disinfectants can be a significant addition to industrial production, as it allows the urgent manufacture of products.

Conclusion. The general approaches to the choice of disinfectant solutions during disinfection depending on their composition were substantiated and the general principles of their industrial and pharmacy production were determined.

DEPARTMENT OF ORGANIZATION

AND ECONOMICS OF PHARMACY

(Head of the department – prof. **Bohdan Hromovyk**)

ANALYSIS OF THE MARKET OF DRUGS FOR THE TREATMENT OF PEPTIC ULCERDISEASE

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Scientific supervisor: assoc. prof. **Oleksandra Korniyenko**, PhD

Keywords: Peptic ulcer of the stomach and duodenum, drugs, pricing

Introduction. In Ukraine, more than 5 million patients with peptic ulcer (PU) are registered, the share of peptic ulcer disease (PUD) of the stomach and duodenum reaches 13.3% of all diseases of the gastrointestinal tract. Research of the market of medicines (drugs) for treatment of PU of stomach and of duodenum, specifics of their release from drugstores in Ukraine is relevant.

Materials and methods. The objects of the study were the clinical guideline (CG) "PU of stomach and of duodenum", the State Register of Drugs of Ukraine, as well as lists and registers governing the specifics of the release of drugs from pharmacies. Methods of information search, generalization, comparative and marketing analysis of secondary information data have been used.

Results. It has been established that as of 04.02.2021 the State Register of Drugs of Ukraine in- cludes 198 assortment items of 22 International Nonproprietary Names (INN) of monoprepara- tions recommended by the CG "PU of stomach and of duodenum". The most common are lev- ofloxacin, omeprazole, metronidazole (36, 24, 20 names respectively), clarithromycin and pantopra- zole (18 and 17 drugs, respectively), slightly less common - drotaverine (13), ranitidine and pa- paverine (10 each), the remaining drugs are presented with the range from 1 to 9 names. Almost half of the drugs are antibacterial agents (45.5%), slightly less - proton pump inhibitors (25.7%), an- tispasmodics (13.0%), blockers of histamine H_2-receptors (9.6%). Proportion of combined drugs is significantly lower, in particular: alginates and antacids (4.0% and 0.5%, respectively), as well as other drugs (1.5%). In general, 38.3% of the arsenal is provided by domestic manufacturers, but the ratio of domestic and foreign manufacturers in different pharmacological groups is heterogeneous. In particular, preparations of antacids, alginates, proton pump inhibitors and antibacterial agents aremostly supplied to the Ukrainian market by importers of pharmaceutical products (100%, 87.5%, 69.6% and 63.1% respectively), in the vast majority from India, China and Spain (43.6%, 15.8%, 12.0% respectively). The rest of the pharmacological groups are dominated by domestic manufac- turers, in particular: other drugs (gastroprotectors), antispasmodics and blockers of histamine H_2-re- ceptors (75.0%, 59.4% and 54.2%, respectively). More than half of the drugs are available in pill form (51, 5%), solutions for infusion and injection are 19.0% and 10.6%,

respectively. Almost alldrugs tested should be available on prescription, only drotaverine pills, antacids and alginate drugsare over-the-counter. It has been established that in the current National List there are 10 INN drugs for the treatment of PU, in the Register of Wholesale Prices (WP) - 186 assortment items of singledrugs of the studied groups and 4 combined drugs. Situational analysis of the price situation in the retail segment of the market of Omeprazole, in caps., 20 mg №30 showed that the level of trademargin of some producers is lower than it is limited by the regulatory lists, and the real purchase prices of OJSC "Farmak", CJSC "PC" Darnytsia "and LLC "Astrapharma" are lower than registeredWP.

Conclusions. The structure of the product range of drugs for the treatment of PU of stomachand of duodenum has been studied. As a result of the conducted situational analysis, it can be assumed that the regulatory lists mostly only declare markup restrictions, since in most cases the prices in pharmacies are regulated by the competitive environment.

PHARMACEUTICAL COMPONENT OF VACCINATION OF THE POPULATION

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Keywords: vaccines, immunization, marketing analysis, a pharmacist`s role.

Introduction: Immunization is a proven tool to fight infectious diseases. Vaccination can prevent 2to 3 million deaths each year. It is one of the most effective health care tools. Of course, all specialists take part in the immunization process: doctors, paramedics, pharmaceutical workers. Consider carefully the role of pharmacists in vaccinating the population in Ukraine.

Materials and methods: The materials of the study were: data from the state register of medicines, data on drug prices (according to the site https://compendium.com.ua/). Methods used: literature search, marketing analysis and interviews (questionnaires using google forms).

Results: The historical aspects of the origin of vaccines, trends in the development of this area of healthcare and the possibility of its use to save lives and health of the population have been studied. As a result of marketing analysis of vaccines registered in Ukraine, it was found that as of01.04.2021 in the State Register of Medicines there are 71 vaccines, 32% of them produced in Belgium, 16% - in France and in India, and 10% - in Ukraine. Leaders among vaccine companies are GlaxoSmithKline Biologics SA,

Belgium (28%), Sanofi Pasteur, France (15%), Serum Institute, India (11%) and Biolik JSC, Ukraine (10%). The study of the price situation of vaccines showed that among the bacterial vaccines the most expensive is PREVENAR (costs from 1662.14 to 2049.60 UAH), viral vaccines –VARILRIX (715.90 – 1070.00 UAH) and CERVARIX (987.90 –1172.00 UAH), combined vaccines – INFANRIX HEX (1146.80 – 1476.50 UAH). The lowest prices are for such vaccines as ADP-M-BIOLIC (10.20 – 22.10 UAH), ENGERIX (179.80 – 195.00UAH), TETRAXIM (595.90 – 716.00 UAH). As a result of an online survey of the population of Ukraine (1197 respondents from all regions of the country were interviewed on March 11, 2021), it was found that 95.1% of respondents are generally positive about vaccination, and 86% are vaccinated in a timely manner according to the current vaccination calendar. The positive attitude to vaccination is due to the opinion that it is a good way to prevent common diseases (60.4%) and the generally accepted world practice (26.8%). Negative attitude to vaccination is explained by fear of side effects of vaccines among respondents and general distrust of their safety (28.4% respectively), another 14.7% of respondents do not believe in the effectiveness of these drugs.

Regarding the role of the pharmacist in vaccination, according to 69.9% of respondents, the doctor plays a leading / important role in deciding on vaccination; while the role of the pharmacist is insignificant (61.6% consider it unimportant or irrelevant). The attitude to vaccination against COVID-19 in more than half of respondents (66.5%) is positive, the vast majority of respondents are ready to be vaccinated (90.4%), with more than half – in each case (56%), 25.2% - if necessary, 9.5% - only if it is free. As for the vaccination passport, 77.6% have a positive attitude to it (absolutely - in 58.6% of respondents and 19% - in case if such a document will not be mandatory). The role of the pharmacist in the direction of vaccination respondents see as follows: the pharmacist is a source of professional information about vaccines and can participate in educational work with the population on these issues (25% and 16.4% respectively), vaccination literature can be sold through pharmacies (16.5 %), and 15.7% of respondents do not see in this direction the work of a pharmacist.

Conclusion: The pharmaceutical aspects of population immunization in Ukraine have been studied. These are, in particular, a high level of positive attitude of the population to vaccination, readiness to be vaccinated according to the vaccination calendar, considerable trust in doctors in these matters and insignificant – in pharmacists. The role of the pharmacists on these issues in Ukraine is classic: to dispense medicines and provide information about them. Marketing and price characteristics of vaccines registered in Ukraine have been studied.

MARKET CHARACTERISTICS OF DRUGS USED TO TREAT LIVER ANDBILIARY TRACT DISEASES

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Keywords: liver, gallbladder, cholagogues, hepatotropic drugs, range, medical history

Introduction. Liver diseases remain a major public health problem worldwide. Liver diseases are currently one of the most common causes of disability and the fifth leading cause of death in manydeveloped countries. For the treatment of liver diseases are widely used drugs that help preserve and restore the structure and function of the hepatobiliary system (hepatotropic and cholagogues). Therefore, the study and analysis of their range in the modern pharmaceutical market and the establishment of the peculiarities of their use in the hospital is a topical issue today.

Materials and methods. Materials: The range of hepatotropic drugs and drugs used in the case of biliary pathology and the declared wholesale prices for them. Medical cards of inpatients of gastroenterological departments of the 5th city clinical hospital of Lviv. Methods: Information retrieval, retrospective method, content analysis and generalization.

Results. When analyzing the range of drugs containing bile acids and their derivatives (22 drugs, group A05A A according to the ATC classification) it was found that more than half of them are available in the form of capsules (54.5%). 22.7% of the range is made in Ukraine, , all drugs are released from the pharmacy on a doctor's prescription. The smallest registered wholesale price - 133.40 UAH (Ukrliv, oral suspension, 250 mg / 5 ml, 30 ml in a bottle), the largest - 1730.30 UAH (Ukrliv, tablets of 500 mg). As a result of the study of the range of drugs used in biliary pathology (33 drugs, group A05A X according to the ATC classification), it was determined that the largest share is occupied by such dosage forms as capsules and tablets (24.2% each). According to the prescription from this group, only 1 drug is released (Rovahol, enteric capsules, soft, № 50), all other drugs are over-the-counter. One third of drugs are manufactured in Ukraine (73%). The smallest registered wholesale price - UAH 43.33 (Artihol, tablets, 200 mg; № 30), the largest - UAH 179.20 (Allohol, tablets №180). As a result of the analysis of the range of hepatotropic drugs (39 drugs, group A05B A according to the ATC classification) it was found that almost half of them are available in the form of tablets (25.7%) or capsules (20.6%). Most of the range is made in Ukraine (69.3%) and is available from pharmacies without a prescription (59%). The lowest registered wholesale price is UAH 47.52 (Darsil, table № 30), the largest is UAH 1,820.00 (Hepatox, concentrate for solution for infusion № 10).

424 Medical histories of patients of gastroenterological departments of Lviv hospital were analyzed.The largest number of analyzed history cards according to the diagnosis established during hospitalization belong to the class K70-77 "Liver disease" - 48.1% (204 patients), including K.74. "Fibrosis and cirrhosis of the liver" (56 patients). As a result of studying the structure of prescriptions, it was found that most often in these departments prescribed dietary supplements to maintain liver function, biliary tract and gallbladder, less drugs from the group of bile and hepatotropic drugs.

Conclusions. The commodity situation of cholagogues and hepatotropic drugs was studied and analyzed. The case histories of 424 people built in the technological departments in terms of condition, age, employment, type of hospitalization, number of days spent in hospitals, diagnosis during administration were analyzed. Pharmacotherapy regimens of patients using the liver and biliary system have been studied.

RESEARCH ON PROBLEMATIC ISSUES OF FORGERY OF DRUGS

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Keywords: forgery of drugs

Introduction. Despite changes in domestic legislation and a number of open criminal cases for activities in the field of circulation of forged drugs, still, there are cases of circulation of forged products in the pharmaceutical market, therefore the study of this problem is relevant. The aim of the work is to establish the structure of the range of forged drugs detected in Ukraine in 2020 and tocompare the objects of forgery with the leaders of pharmacy sales.

Materials and methods. The object of the study were the orders of the State Service of Ukraine on Medicines and Drugs Control on series of forged drugs detected in 2020. The source of information on the volume of pharmacy sales was the data of the analytical market research system "PharmXplorer" / "Pharmstandard" of the company "ProximaReseach". Methods of information search, generalization, comparison and systematic analysis of secondary marketing information datahave been used.

Results. It has been established that during 2020, a total of 403 assortment items of forged drugs were detected on the Ukrainian pharmaceutical market, the largest number of orders banning their sale were issued by the State Service of Ukraine on Medicines and Drugs Control in September 2020 (83), some less - in April, October and February 2020 (62, 48 and 42 respectively). The majority of forged drugs were imported (96.03%), a significant part of the drugs was produced in Russia, Moldova and Germany (17.08%, 12.41% and 11.17%, respectively). 3.97% of the objects of forgery

were of domestic production. Drugs in the form of pills were most often forged (44.42%), and quite often - solutions for injections, solutions for internal and external use, drops and capsules (21.34%, 13.15% and 9.18%, respectively). The range of pharmacological action of forged objects has slightly expanded, compared to previous years (14, 10, 12 pharmacotherapeutic groups in 2020, 2017-18, 2015, respectively). In 2020, the most frequently forged drugs were of three pharmacotherapeutic groups: N - drugs for the treatment of diseases of the nervous system, L -antitumor drugs for systemic use and G - drugs for the treatment of diseases of the urogenital organsand sex hormones (97, 67 and 64 names respectively). There is no steady tendency in the priorities of forgery of drugs in the areas of pharmacological action, there is fluctuation in the number of forged drugs in some groups (in particular: N, G, L - increase; J, M, C — decrease).

It has been established that the majority of forged drugs in 2020 are expensive, the retail price of more than a third of banned drugs exceeds 1,000 UAH (35.48%), from 100 to 500 UAH and from 500 to 1,000 UAH is 33.5% and 24,32% of items, respectively. As a result of comparison with theleaders of pharmacy sales, it was found that 15% of brands were subject to forgery, in particular, the widely advertised antithrombotic drug xarelto, as well as nurofen and sodium chloride.

Conclusions. It has been established that most of the objects of forgery, withdrawn from circulation on the pharmaceutical market of Ukraine in 2020 are expensive imported drugs.

Tendencies in priorities in the areas of pharmacological action have not been identified, but thereare facts of forgery of pharmacy sales leaders.

MARKETING ANALYSIS OF MEDICINES AND DIETARY SUPPLEMENTSBASED ON BEEKEEPING PRODUCTS IN UKRAINE.

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Keywords: Marketing analysis, apitherapy, beekeeping products.

Introduction. Recently, the need for medicines of natural origin is growing in modern medicine, and it is bee products that can become an available raw material base for these drugs. Today, beekeeping products are used in the medical industry, cosmetics, diet in many countries. The great importance of honey, bee venom, pollen for the human body, and propolis (bee glue) and wax - for various industries.

Materials and methods. The objects of the study were the State

Register of Medicinal Products (SRMP) of Ukraine, the prices of the retailers of the medicines in Ukraine. Methods of data retrieval and generalisation, mathematical and statistical analysis were used, literature monitoring, generalization, marketing research.

Results. Interest in apitherapy is developing rapidly in industrialized countries. Recently, many research institutions in Ukraine, Russia, Romania, Poland, Germany, the United States and other countries are studying the nutritional and medicinal properties of bee products. 82% Of pharmaceuticals based on bee products are produced in Ukraine. 17 trade names and 30 dosage forms and dosages of drugs based on bee products are included in the State Register of Medicines of Ukraine in March 2021. These drugs containbee products such as propolis, royal jelly, pollen, bee venom, their combinations and combinations of other ingredients. 58.8% of all trade names analyzed by drugs include propolis. In second place are combinations of bee products (29.4%) and in third place are drugs with royal jelly (11.8%).

Studies of retail prices for medicines based on bee products have shown that the mostexpensive on the market were the Latvian drug Apilak Grindeks table. № 50 (UAH 282.0) and the domestic drug Apiprost caps. №60 (UAH 210.01). The second in the price category were Apilak Grindeks table. № 25 (UAH 178.00) and ointment (UAH 117.01) and drugs based on bee pollen Vazavital caps. № 30 (UAH 135.20). Next in the price category were ointment with bee venom and tablets, suppositories, sprays and aerosols based on propolis. Their price ranges from UAH 38.18 to UAH 98.00. The cheapest on the market were tinctures of propolis (13.44 - 20.00 UAH).

Conclusions. The results of the study can be used to improve planning the assortmentand pricing policy of manufacturers, wholesale intermediaries and pharmacies dealing with medicines and dietary supplements based on bee products.

MEDICINAL PRODUCTS ADVERTISEMENT MONITORING ON SOCIAL NETWORKS

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Keywords: medicines, advertising, social networks, Internet, monitoring

Actuality: The Internet has introduced a number of new opportunities in the field of advertising and promotion of medicines. Now the promotion and advertising of drugs and health products on the Internet is actively developing. However, there is no separate legislative regulation of such activities. Therefore, when using the Internet, it is necessary to take into

account the general regulations governing the advertising of pharmaceutical products. Thus, it is relevant to analyze medicines advertisements on the Internet (social networks) and study consumer opinions regarding such advertising.

Materials and methods: materials - the legislative framework of Ukraine regarding medicines advertising, literary sources, information materials from the Internet, information from expert assessment questionnaires of consumer attitude towards medicines advertising on the Internet. Methods: information retrieval, analysis and synthesis, logical generalization, expert assessments.

Results: An analysis of the advertising activity of pharmaceutical companies in the specialized medical Internet publication "Apteka Weekly" (March 2021) showed that in the period under review,there were placed advertisements for 30 medicines, 13 dietary supplements and 1 medical product. At the same time, advertisements for such drugs as Panangin (Gedeon Richter, Hungary), Warfarin nycomed (Takeda, Austria) and dietary supplement NUTROF® FORTE (Laborator Tea, France) were repeated twice. 2/3 of the medicines is advertised were prescription medicals. Among the studied medicines, according to the ATC- classifications, medicines from anatomical group A were most often advertised - drugs that affect the digestive system and metabolism. It was found that the format of advertising for medicines, dietary supplements or medical products affects the frequency of its viewing, because contextual advertising (9823 views) is almost 6 times higher than banner advertising (1613 views).

The peer review of the attitudes of consumers to advertising medicines on the Internet with the participation of 115 respondents showed that among the respondents 50% are at the age of 21-30. Most of the respondents are students (54%), and 56.5% are related to the field of medicine and pharmacy. Slightly more than half of the respondents (51%) do not trust medicines advertising on the Internet, since they believe that the manufacturer pursues only its own interests. They only trust the advice of a doctor and pharmacist. Almost half of the respondents (49%) do not purchase medicines under the influence of Internet advertising. 62% of respondents know that there should be warning labels in medicines advertisements. And 65% say that appear such warning labels when advertising medicines on the Internet, as: "The site contains general information about the products, which in no way replaces the doctor's advice and the content of the instructions for the use of medicines", "Self-medication can be harmful to your health". Most often the respondents (67%) met the warning label "Self-medication can be harmful to your health". 55% of respondents, after seeing an advertisement for medicines on the Internet, have a desire to close the advertising banner, as it causes irritation. Still, 64% believe that advertising for medicines on the Internet is necessary.

The majority of the respondents (90%) came across medicine advertising on the Internet. Therespondents were divided into almost identical groups: 35% of them have a negative attitude to drug advertising on the Internet, 33% positively and 30% are indifferent. Banners and videos are the most popular formats for medicines advertising on the Internet. Most often, users see such advertisements on medical websites, search engines and social networks.

Conclusion: Advertising of medicines as a phenomenon (including on the Internet) is an important component of the marketing communications system of pharmaceutical companies and has a significant impact on people's behavior. Therefore, it must be in a strictly defined legal framework and not create health risks for consumers.

THE ROLE OF THE PHARMACIST IN THE SAFE USE OF MEDICINES

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Keywords: pharmacovigilance, drug, adverse drug reactions (ADRs).

Introduction. As defined by the order of the Ministry of Health of Ukraine № 543 of25.09.2009, the safety of the drug is its characteristic, based on a comparative assessment of the benefits and potential harm that may be caused to the patient duringits use. In this direction, the role of the pharmacist as a professional in the field of medicine is unconditional.

Materials and methods. The research materials were: data from the professional literature, the results of the questionnaire. Methods of literary search and online questionnaires (google-forms) are used.

Results. As a result of the analysis of the data of the State Expert Centre of the Ministry of Health of Ukraine, it is established that for the period 2015 - 2019 received 124449 reports of drug use, with the largest number received in 2017 (28431reports, 22.8% of the total period). The largest number of ADRs reports concerns group J - Antimicrobials for systemic use (on average 56.6% for the analysed period). The ratio of non-serious and serious ADRs (for the period 2017 - 2019) is 10: 1. The largest number of ADRs characterizes oral dosage forms (68% in 2015, 67% in 2018). As for the drug manufacturers that most often caused ADRs, they are drugs of domestic production (55%).A survey of the population on the specifics of their druguse and occurrence of ADRs was conducted. 80% of respondents report a good andexcellent state of their health, and take medication as needed (82.5%), while 98% prefer oral medication. 63.7% of respondents read the instructions before using drugs,

22.5% - sometimes. 27.5% of respondents had cases of ADRs, while more than halfof them (54.5%) – on antimicrobial drugs. ADRs were mostly from the digestive tract (63.6%) and the nervous system (22.7%). 82% of respondents went to the doctor incase of ADRs. 91% of respondents consider the collection of ADRs reports to be an integral part of safe drug use. According to 74% of respondents, importance of thepharmacist'swork in this direction is obvious. Such activities, in particular, should include: informing the patient about drugs (68.8%) and the peculiarities of their use (60%),analysis of the prescription list (40%), etc.

Conclusions. The study of the reporting data of the State Expert Centre of the Ministry of Health of Ukraine showed that the number of ADRs is constantly growing, with the absolute leaders being antibacterial drugs. Collecting reports of ADRs is an important part of the safe use of medicines by the public, and the role of the pharmacist in this is very important.

DERMATOLOGICAL MEDICAMENTS MARKET MONITORING

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Keywords. Dermatological diseases, acne, market conditions, market analysis, medicaments, diseases.

Introduction. Dermatological diseases are very diverse in their types and clinical manifestations and are quite common. The most common dermatological disease is acne. Statistics indicate that from acne suffers: up to 80% of the population aged 12 to 25 years and about 30-40% of people aged over 25 years. Dermatological diseases affect the quality of life of the patient. Teenagers and adults, who suffer from acne, have higher rates of anxiety, low self-esteem and depression compared to those who do not have this problem. Among adults with severe lesions, the level of unemployment is much higher than among similarly aged groups without acne. Deterioration of quality of patients' life with acne is similar to disorders caused by asthma, epilepsy or arthritis. So it is important to conduct a marketing analysis of the market of dermatological medicaments, the results of which would make it possible to outline trends in the market of analyzed medicaments.

Materials and methods. Official legal documents, search for medical and pharmaceutical information, scientific articles and publications were used as sourcing materials. In the course of work the method of information search, statistical and graphic methods were used.

Results. On the basis of the analysis of scientific literary sources, medical and social aspects of dermatological diseases in Ukraine and the world are investigated, as well as of modern view on the impact of acne on quality of

life ware analyzed. Epidemiological characteristics of dermatological diseases are processed, their structure is analyzed. The etiological aspects of dermatological diseases, their classification, causes, methods of prevention and treatment are analyzed. The dynamic of the assortment's structure of the domestic dermatological medicaments market in 2013-2021 is analyzed; a quantitative estimation of the assortment of dermatological medicaments and acne treatment products is performed; the rating of pharmaceutical manufacturers of dermatological medicaments is established; the pricing of dermatological medicaments was analyzed and the coefficients of liquidity, adequacy of solvency and completeness of the assortment are determined for studying of the availability of these means to consumers. An analysis of strategies for the prevention and treatment of acne was conducted. Pricing aspects of acne pharmacotherapy were studied.

Conclusions. The marketing analysis of the market of dermatological medicaments and means for acne treatment was conducted. The results of the study can be used for optimization of pharmaceutical care for patients with dermatological diseases and also for patients with acne.

RESEARCH ON THE PHARMACEUTICAL SEGMENT OF THE COSMETICS MARKET

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Keywords: Technical regulations, cosmetics, pharmaceutical market.

Introduction. Cosmetics are one of the groups of pharmacy assortment. A significant amount of cosmetic products is offered by subjects of pharmaceutical industry, so the study of these products' market trends and specifics is relevant.

Materials and methods. Regulatory documents governing the circulation of cosmetics in Ukraine. Conjuncture of pharmaceutical segment of the cosmetics market. Methods: generalization, systematization, comparison.

Results. In 2021, Ukraine has introduced Technical regulations for cosmetic products, whichharmonizes the requirements for cosmetics with the requirements of EU directives. It establishes a safety assessment procedure, the need to comply with proper manufacturing practices, a ban on animal testing, and a mandatory indication of contained nanomaterials.

As of April 2021, 14 classification groups of cosmetics were presented in the section "Cosmetics" on the website of the directory compendium.com.ua. 634 items of cosmetics were included in the "Health cosmetics" section alone. Health cosmetics are produced by 163

manufacturers from 19 countries, including Ukraine. 82% of health cosmetics are made by domestic manufacturers, 18% - by foreign ones. The leaders in the number of positions are LLC "Elixir" (Dnipro), LLC "Pharmacom" (Kharkiv), PE "Euro-Plus" (Dnipro), LLC "Beauty and Health" (Kharkiv) , LLC "Botanica" (Kyiv), PJSC Chempharmfactory "Chervona zirka" (Kharkiv) and LLC "Flora-Pharm" (Kyiv). The preferred forms of health cosmetics are balms (15%), solutions (12%), creams and cream-balms (11% each). Other cosmetic products are available in the form of gel- balms (9%), sprays (8%), gels (8%), cream-gels (7%), ointments (5%) and powders for external use (5%). The presence of 9% of suppositories indicates a lack of competence of site moderators and shortcomings of mechanisms for compliance with the requirements of the law. For 94% of items of health cosmetics, listed on the information resource compendium.com.ua, medical diagnoses are indicated for which the use of cosmetics is recommended, in 26% additional references are made to the International Classification of Diseases 10th Edition (ICD-10). Only 6% of positions do not provide medical recommendations and do not specify medical diagnoses, which meets the requirements of the Law of Ukraine "On Advertising". The range of cosmetic products for health in pharmacy chains "Podorozhnyk" and "D.S." in terms of the number of product items and the average value of the retail unit price, is significantly inferior to the group of face, body and hair care products produced by the so-called "luxury" cosmetic brands.

Conclusion. 94% of health cosmetics contains declaration of therapeutic effect, which contradicts the requirements of the law.

THE USE OF NASAL PREPARATIONS FOR TOPICAL USE FROM THE POSITION OF SOCIALPHARMACY

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Keywords: Nasal preparations for topical use, diseases of the nasal cavity, physical and economic accessibility, Defined Daily Dose, liquidity ratio, availability ratio, competitiveness ratio.

Introduction. The problem of inflammatory diseases of the nasal cavity is one of the most pressing in modern medicine. The incidence of rhinosinusitis, for example, has almost doubled in the last 10 years, and the share of hospitalized in this regard is growing annually by 1.5-2.0%. Patients with rhinitis, rhinosinusitis and rhinopharyngitis make up 60-65% of outpatients of otorhinolaryngologists. The largest number of patients is between the ages of 18 and 55 years. The treatment regimen for such diseases, according to the protocol, depends on the duration of the disease, clinic,

comorbidity and other factors, and therefore requires different intranasal drugs. Nowerdays a sufficient number of drugs for the treatment of diseases of the nasal cavity has been registered in Ukraine. These were drugs from both foreign and domestic manufacturers. Their availability (physical and economic), as well as safety and rational use were the subjects of study of social pharmacy.

Materials and methods. The objects of the study were the State Register of Medicinal Products (SRMP) of Ukraine, the prices of the retailers of the medicines. Methods of data retrieval and generalisation, mathematical and statistical analysis were used.

Results. 161 analysed medicines were based on 21 active pharmaceutical ingredients and were divided into 5 subgroups of the forth level according to the ATC classification system. The biggest part of all the trade names of these medicines belonged to the subgroup R01AA "Sympathomimetics" (61.5%). It was followed by the subgroups R01AD "Corticosteroids" (11.8%), R01AB "Sympathomimetics, combinations excluding corticosteroids" (16.1%), R01AX "Other nasal preparations" (8.7%) and R01AC "Antiallergic agents, excluding corticosteroids (1.9%). The half of the all registered medicines contain only two active pharmaceutical substances (xylometazoline (32.9%), oxymetazoline (20.5%). Nasal sprays (65.2 %), drops (29.8 %) occupied the first, and the second places among all the dosage forms. 36% of them were locally manufactured. 79.5% of registered medicines belong to monocomponent drugs and 20.5% are combined medicines. Economic affordability was determined using the following indicators: liquidity ratio, affordability ratio, competitiveness ratio. The liquidity ratio was calculated for 66 drugs. Only for 4 of them this ratio was within the norm, as price fluctuations for drugs should not exceed 15%. The availability index was calculated for 52 drugs. For half of the drugs, the availability indicator was less than 1, and therefore, during the study period, the increase in their price was more significant compared to the growth of the average wage. The most competitive drug was the one with the highest competitiveness ratio. According to their importance, drugs were divided into 3 niches: low, medium and highly competitive. Half of the analyzed drugs fall into a low-competitive niche. The rest of the drugs were almost equally sought in medium and highly competitive niches.

Conclusions. The special characteristics of Ukrainian market of nasal preparations for topical use were defined due to their physical and economical availability.

ANALYSIS OF THE MARKET OF ORAL CARE PRODUCTS

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Keywords: drugs used in diseases of the oral cavity, marketing analysis.

Introduction. Oral care products include drugs for the topical treatment of oral diseases (eg, cold lozenges, local anesthetics) or for prevention and daily care (eg, rinses, toothpastes, dental floss, toothbrushes, and tooth powders). The pharmaceutical market offers a large number of these drugs, which are not always used properly by the average static patient.

Materials and methods. The objects of the study were the State Register of Medicinal Products (SRMP) of Ukraine, the assortment and ratail prices of drugs and other healcare products used in diseases of the oral cavity presented in pharmacies of Ukraine. Methods of data retrieval and generalisation, mathematical and marketing analysis were used.

Results. 65 trade names of drugs used in diseases of the oral cavity from subgroup A01A were included in the DRLZ of Ukraine. The first place was taken by drugs from subgroup A01AD11 (Others), which mainly contained drugs on medicinal plant raw materials. Second and third place beloned to drugs with benzydamide (A01A D02) and metronidazole in combination with chlorhexidine (A01A B67). Drugs with propolis (A01A B11), hexetidine (A01A B12) and clotrimazole were also included in the register. 64.6% of the studied drugs were domestically produced and the largest importers were India (9.2%) and Poland (7.7%). Most often drugs were presented in the form of solutions (23.1%), sprays (21.5%) and gels (20%). 87.6% of trade names of registered drugs could be purchased in pharmacies in Lviv. In January 2021, Lithuania registered almost half of drugs from subgroup A01A (33 trade names) used in Ukraine. In Lithuania, this subgroup included drugs with neomycin and miconazole, which were not available in Ukraine. Conversely, drugs from the subgroups of clotrimazole and metronidazole in combination with other substances were presented only in Ukrainian register. Sodium fluoride drugs for caries prevention in children and dexamethasone preparations for topical oral use in dentistry were also available on the Lithuanian market.

More than half (56.1%) of the studied drugs were in the low-cost niche with a cost of 6.59 to 68.85 UAH. The average cost niche contained 15.8% of drugs with a price ranging from UAH 68.86 to UAH 131.11. 16 drugs entered the third niche of the high-value niche. A comparative analysis of average retail prices in Lithuania and Ukraine showed that their prices are slightly higher in Lithuania, but our calculated solvency ratio indicated that these drugs are 3-4 times more affordable for patients in Lithuania. 32 mouth rinses could be bought in Lviv pharmacies. The greatest demand was for rinses against

periodontitis (31%) and with complex action (28%). Also the first places were taken by rinses with alcohol (50%), fluorine (39%), and plant components (11%). One quarter of the rinses were domestically produced. Italy (25%), Germany (18.75%) and Russia (15.63%) most often represented these products on the Ukrainian market.

Conclusions. The peculiarities of the Ukrainian market of drugs and rinses were determined due to the assortment of these drugs, the type of medical forms, the assortment dependence on imports and the peculiarities of pricing. The obtained results are important for the further formation of the assortment and pricing policy of these products.

MARKETING ANALYSIS OF THE MARKET OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

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Keywords: nonsteroidal anti-inflammatory drugs, assortment, the State Register of Medicinal Products of Ukraine and Lithuania, adequate solvency ratio.

Introductions. Nonsteroidal anti-inflammatory drugs (NSAIDs) occupy a leading position in terms of consumption. Thus, worldwide more than 30 million people are forced to take non-steroidal anti-inflammatory drugs, and 300 million consume them in short courses. NSAIDs remain the most effective means of combating pain of inflammatory origin. Moreover, while medical professionals have not found a safer and no less effective alternative, finding ways to optimize the treatment of NSAIDs is a problem of global importance.

Materials and methods. Information retrieval, analysis, generalization and marketing research.

Results: 19 active substances (international non-proprietary names (INN)) and 4 combinations of them from 6 subgroups of the fourth level according to the ATC classification system have been registered in Ukraine. On the base of them 411 drugs have been created. The largest width of the assortment belonged to the subgroup of propionic acid derivatives (9 INN) and acetic acid derivatives (7 INN). The subgroup of fenamates was the least represented is the register. The distribution of NSAIDs by countries -producer was carried out, which showed that 70.3% of the analysed drugs were imported. Analysis of NSAIDs by type of contractual form of entry into the domestic market showed that 50.6% of the NSAIDs were manufactured and declared by one manufacturer. In 45.8% of cases, manufacturers delegated the right to register (re-register) to another organization. NSAIDs were presented

in 11 different medical forms. Tablets (51.6%), injectable solutions (18.0%) and capsules (13.1%) were the most popular among them.

A comparative analysis of the assortment of NSAIDs in the State Register of Medicinal Products (SRMP) of Ukraine and the State Formulary of Ukraine showed that only half of registrated drugs were included into the Formulary. A comparative analysis of the assortment of NSAIDs in the SRMP of Ukraine and Lithuania in January 2021 showed that in Ukraine it included on 103 trade names of analysed drugs and 7 INN more than in Lithuania. The same drugs in both countries formed the top five of NSAIDs. The leader among them were medicines with ibuprofen. Our analysis of NSAID producers also indicated the same import dependence in the aalysed countries (70.3% Ukraine, 71.1% Lithuania). The results of the analysis of adequate solvency ratios showed that the prices for the NSAIDs were 2.8-6 times more affordable for patients in Lithuania in comparison to Ukraine.

Conclusions. The special characteristics of Ukrainian market of NSAIDs were defined due to the assortment of these medicines, the kind of medical forms, assortment dependence upon the import The obtained results are important for the further forming of the assortment and the price policy of NSAIDs.

PROBLEMS OF MEDICAL PROVISION OF THE POPULATION AND THE ROLE OF PHARMACIES IN THEIR SOLUTION

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Scientific supervisor: assoc. prof. **Kateryna Dorykevych**, PhD

Keywords: problems, medical supply, pharmacy, Covid-19, medicines.

Introduction: Complete, high-quality and timely medical care is a very important part of the health care system. Providing the population with effective and safe medicines is a basic function of pharmacy in society. Despite the existing legal framework, state control pharmaceutical activities and special programs for drug supply of various categories of the population (state, private company initiatives), in our country there are different kinds problematic aspects in this area.

Materials and methods: The method of system analysis is used a set of data on the state and problems of medicine provision of the population, method of literary search and method of interviewing (questionnaire using a google form).

Results: Visitors of pharmacies answered: there are enough pharmacies (91.4%) and walking distance to the nearest pharmacy does not exceed 1 km (82.7%), which has a positive effect, because when choosing a pharmacy, the most important thing is close location (86.4%). Also important low prices

(61.7%) and round-the-clock operation (51.9%). Only few consumers know about and use drug reimbursement programs (17.3%). This is actually a problem in providing medicines to the population. 70% of respondents have a positive attitude to visiting pharmacies in Ukraine, which is also a positive thing. As for the employees of pharmacies, most of which are managers, they are not satisfied with the payment of their work (78.6%). Which actually has a negative impact on the supply of medicines. In 57.1% of all pharmacies that participated in the survey, there are valid programs to reimburse the price of medicines. We believe that comfortable working conditions improve the supply of medicines in general, so we asked questions that are aimed at studying the factors that improve these conditions by the pharmacy itself. That is, 82.1% of respondents indicated the need for financial motivation, 55% chose discounts for staff, 52.9% voted for training. 89.3% of respondents believe that pharmaceutical services are available to all segments of the population without exception. 93.6% of respondents gave the maximum score for determining the number of pharmacies.

Conclusion: There are many problems in the medical supply system of Ukraine that need to be solved immediately. The government must understand the existence of these problems and prevent the emergence of new ones. Pharmacies, in turn, should also work to address these issues for the high-level functioning of the health care system.

USE OF MOTIVATIONAL THEORIES IN THE PRACTICE OF MODERN PHARACEUTICAL MANAGEMENT

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Keywords: motivational theories, pharmaceutical specialists, staff training, social projects.

Introduction. In the world's practice of personnel management the social orientation in staff's work is becoming more and more important, there is a change of accents on the account of interests of workers, increase of their motivation and other social and psychological factors of growth of labor productivity and efficiency of the enterprise. However, the changing role of the pharmaceutical worker in the XXI century poses new challenges to the pharmaceutical industry, which necessitates the search for new approaches to the realization of the personal potential of the pharmaceutical specialist.

Materials and methods. Summarization, comparison, questionnaire.

Results. Classical motivational theories, which emerged at the beginning of the last century, have not lost their significance and have received new development. The need to use motivational theories in the practice of modern

personnel management leads to their modification, the emergence of new approaches, such as flow theory, generation theory, emotional intelligence.

As a result of analysis and comparison of personnel development programs declared by leading domestic pharmaceutical manufacturers (PC "Arterium", JSC "Farmak" and PJSC RPC "Borshchahivsky CPP") it has been found that the first two companies make significant efforts to train staff and attract employees to social, humanitarian and charitable projects. The PS questionnaire, conducted via Google form, found that the main self-motivating factors of the respondents are the possibility of personal realization (58.9%), the level of salary, the opportunity to pursue a career and achieve success (45.2% each). The prestige of the profession and its humanistic orientation are important for less than a third of respondents. The main motivational tools used by employers in the pharmaceutical industry are the provision of training and professional development opportunities for their employees (64.4% of respondents); only material forms of stimulation (42.5%), a combination of material and socio-psychological forms of motivation (39.7%). 81% of respondents have attented trainings and education during their professional activities, 64.4% of PS respondents assess their effectiveness as generally positive. Professional and motivational-psychological trainings are in the lead in the rating of topics of educational projects. 92% of employers use various methods of personnel evaluation, namely: testing (in 67.1% of cases), quantitative measurements of employee performance (45.2%), rating or scores (35.6%). On the positive side, almost half (46.6%) of PS respondents did not feel any pressure from employers regarding the implementation of the sales plan, the need to sell the mandatory list of drugs and other restrictions.

Conclusions. The participation of employers in the pharmaceutical industry in social and charitable projects forms a positive attitude in the vast majority of PS respondents (84.9%), and for some of them is a motivational advantage when choosing a job (9.6%).

COMPARATIVE ANALYSIS OF THE MARKET OF DRUGS AND DIETARY SUPPLEMENTS WITH PROBIOTICS

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Keywords: assortment, dietary supplement, drug, probiotic

Introduction. Among all the drugs sold in pharmacies, a significant share is occupied by drugs that contain probiotics - living microorganisms, the use of which in adequate quantities has a healing effect on the human body.

Therefore, the study of the specifics of the market of probiotics, which are registered as drugs or dietary supplements is a relevant issue of today.

Materials and methods. Materials: legal documents regulating the requirements for the quality of dietary supplements, assortment of probiotics, price offers for probiotics in pharmacies in Lviv, instructions for medical use and leaflets-tabs for probiotics. Methods: statistical, marketing analysis, comparison, positioning, content analysis.

Results. The market of dietary supplements, including probiotics, is developing dynamically, showing significant growth rates and increasing share in the pharmaceutical market of Ukraine. This is facilitated by the following factors: an increase in sales in quantity of packages and the redistribution of consumption towards more expensive goods, an increase in the weighted average price per pack. Leading place in this group of pharmaceutical products is occupied by dietary supplements with probiotics. In Ukraine, as of January 1, 2021, 13 drugs containing probiotics were registered, which, according to the ATC classification belong to group A - Drugs that affect the digestive system and metabolism. It had been established that 175 dietary supplements with probiotics were included in the online directory "Compendium - Drugs". During 2019-2021, prices for probiotics have increased by 14%, with a larger increase in prices for probiotics registered in the form of drugs. There is a high value of Kliq indicator in most probiotics. The official source of information on drugs is the State register of Drugs. It has been established that dietary supplements lack a single unified database.

The compliance of instructions for medical use of probiotics with the requirements of the legislation of Ukraine has been established. The lack of complete necessary information for rational probiotic therapy in the instructions of some probiotics has been determined. It is also advisable to release specially adapted forms of some probiotics for children’s usage (taking into account the dose and/or release form). More than a third of the analyzed leaflets-tabs for probiotics from the group of dietary supplements does not meet the requirements of the legislation of Ukraine, as it contains information about the medicinal properties of probiotics.

Conclusions. It has been established that the characteristic features of the probiotic market are the lack of a single, unified, reliable database on dietary supplements in general and with probiotics in particular; transition of probiotics from drugs to dietary supplements; assortment of probiotics in the form of dietary supplements is much wider; higher cost of probiotics in the form of dietary supplements; there is non-compliance with legal requirements in the information materials of some probiotics in the form of dietary supplements.

RETROSPECTIVE ANALYSIS OF THE MARKET OF ANTITUBERCULOSIS DRUGS

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Keywords: tuberculosis, morbidity, mortality, market analysis, product range, market conditions, antituberculosis drugs.

Introduction. Despite the tendency to decrease in morbidity of tuberculosis, the epidemic situation of tuberculosis in Ukraine still remains difficult. Approximately 30 000 people are diagnosed with tuberculosis every year for the first time and more than 6 000 people die annually from the disease. Therefore, it is important to perform the retrospective analysis of the market of anti-TB drugs.

Materials and methods. The objects of this study were the regulatory documents from the website of the Ministry of Health and drug directories. Statistical methods, marketing analysis, methods of comparison and positioning were used.

Results. According to the analysis of the statistic of tuberculosis in the world, Ukraine is among the five countries with the highest incidence and prevalence of tuberculosis in the European region. The peculiarities of the epidemiological situation of tuberculosis in Ukraine have been studied. It was established that the deterioration of the tuberculosis epidemic situation is contributed by the deterioration of economic security of the population, destruction of material and technical base and reduction of human resources of the antituberculosis service, insufficient awareness of the population on tuberculosis prevention.

Assortment and product analysis of the market of anti-TB drugs in the dynamics from 2014 to 2020. It is established that for today in Ukraine are registered 6 subgroups of group J04A, of which 8 subgroups of level 5 are not registered and are not used in modern chemotherapy. During the data analysis, chain growth coefficients (GC) were determined for each subgroup and in the group as a whole. This segment of the pharmaceutical market is characterized by uneven growth of the commodity situation.

The analysis of the dynamics of representation in the market of antituberculosis drugs by producer countries shows that both in 2014 and in 2020 antituberculosis drugs in the market of Ukrainian are represented by domestic (26%) and imported manufacturers (74%) and have the largest share in the market inexpensive generic drugs mainly of Indian and Ukrainian origin.

Drugs for the treatment of tuberculosis are presented in various dosage forms. The predominant dosage forms are tablets (56%), capsules (22%), solutions for injection (15%) and powders for solution for injection (12,4%). Only one drug is available in the form of eye drops, one in the form of a

suspension, one in the form of syrup and none in the form of candles. This situation creates a problem in the treatment of tuberculosis in children and outside the pulmonary localization.

Conclusions. As a result of the scientific work the etiological and pharmacotherapeutic aspects of tuberculosis were studied, the dynamics of epidemiological indicators of tuberculosis was analyzed, the peculiarities of tuberculosis pathogenesis were analyzed, the structure of the assortment of the domestic market of antituberculosis drugs was studied.

RESEARCH ON THE PHARMACY SEGMENT OF THE DOMESTIC MARKET OF MEDICAL PRODUCTS

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Keywords: medical devices, classification, assortment.

Introduction. The assortment of modern medical devices (MDs) is extremely diverse, it includes tools, apparatuses, devices, means, software that are used with diagnostic or therapeutic purpose for prevention, monitoring, relief of the patient's condition in case of illness, injury, disability or its compensation. A pharmaceutical specialist must possess knowledge of the regulatory provision of their circulation and basic classification approaches to their distribution.

Materials and methods. Summarization, systematization, comparison.

Results. As a result of the analysis of the normative documents and literary sources, 12 general classification approaches to MDs have been allocated. In the work of a pharmaceutical specialist distribution by assortment groups, by storage groups and by the possibility of self-use by the patient is important.

As of March 2021 on the *Compendium.online* directory site in the rubric "Medical Devices" 22 groups of MDs are presented. The classification distribution applied is stated as intuitive, which does not meet legislative and generally accepted norms.

In the rubric "Medical Devices" on the Compendium.Online directory site, in group 13 «Other devices for treatment», there is a subgroup "Liquids", among which the products are presented, which is recommended to be used with medical purposes with the indication of the medical diagnose according to ICD-10. 43.9% of the assortment of the subgroup "Liquids" are made up by 6 manufacturers of drugs (PLC "Yuria Farm", JSC "Farmak", Jadran Galenski Lab. (Croatia), Corporation "Arterium", Delta Medical Promotions AG (Switzerland), PLC "Xantis Pharma"). In the assortment of the studied

pharmacy, the share of MDs was 13%, of which 71% - at a preferential VAT rate (7%) and 29% - at the total VAT rate (20%). The most numerous assortment group of MDs in the pharmacy were dressing change products (14% of the total number of positions). Products of compression knitwear, band-aids and patient care items each occupied 10% of the structure of the pharmacy assortment of MDs. Diapers, medical gloves, condoms, injection and infusion tools each occupied 7-8% of the MDs assortment in the pharmacy. Other assortment groups of MDs occupied 3-5%. Only 5 MDs manufacturers are presented in several assortment groups, namely: PJSC "GemoPlast" - in 5 groups: patient care items, injection and infusion tools, surgical instruments and devices, medical clothing, auxiliaries. 4 manufacturers offer MDs of two assortment groups: PLC "Ukrmedtextill" – dressing change tools and compression knitwear products; PLC "Ukrmedproduct" – medical gloves and auxiliaries; PLC "Firm Technocomplex" - medical clothing and auxiliaries; JSC "Torunsk Plant of Dressing Change Materials" (Poland) - diapers and medical gloves.

Conclusions. The problems of normative support of the turnover of MDs in Ukraine has been summarized. The pharmacy assortment of medical devices has been studied.

MARKETING ANALYSIS OF IMMUNOMODULATORS BASED ON HERBAL AND BEEKEEPING PRODUCTS

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Keywords: immunomodulators, immunostimulators, medical plants, beekeeping products.

Introduction. Traditional herbal medicine and beekeeping products has come to stay as it remains the oldest and still widely chosen choice for public use. They have also proven to show great immunomodulatory activities and it is still considered most common and widely used as immunomodulators.

Materials and methods. The objects of the study were the State Register of Medicinal Products (SRMP) of Ukraine, the assortments of the immunostimulating medicines based medical plants and beekeeping products in Ukraine. Methods of data retrieval and generalisation, mathematical and statistical analysis, literature monitoring, generalization, marketing research, questionnaire survey were used.

Results. 29 tade names of immunostimulants of plant origin were included in the SRMP of Ukraine in January 2021. 55.2% of them were based on Echinaceae purpureae. 62% of analysed immunostimulants could be bought in Ukrainian pharmacies. Tablets (38.9%) and tinctures (33.3%) were the most

popular medical forms used for production analyse of herbal immunostimulants. 56.3% of medicines with Echinacea were made from its root and rhizome and most often for producing tinctures, sypups and extractes. Dry juice of the upper part of Echinacea was most often preferred for tablets with this plant. 77.8% of analysed drugs were mono component medicines. 77.8% of herbal immunostimulants were localy produced. Germany and Slovenia were the only importes of these drugs to Ukraine. 17 trade names of drugs based on beekeeping products were included into the SRMP of Ukraine in March 2021. These drugs contained propolis, royal jelly, pollen, bee venom, their combinations and combinations with other ingredients. 58.8% of all trade names of analyzed drugs included propolis. Ointments (17.6%), sprays and aerosols (17.6% and 11.8%) were the most popular. 82% of drugs based on beekeeping products were produced in Ukraine. Germany, Estonia and Latvia were the countries importing these drugs to Ukraine. Survey of respondents about herbal immunostimulants confirmed that customers rely herbal immunostimulants and often use them.

Conclusions. The special characteristics of Ukrainian market of immunostimulating medicines based medical plants and beekeeping products were defined due to the assortment of these medicines, the kind of medical forms, assortment dependence upon the import and peculiarities. The obtained results are important for the further forming of the assortment and the price policy of these medicines and dietary supplements

DEPARTMENT OF PHARMACEUTICAL, ORGANIC AND BIOORGANIC CHEMISTRY

(Head of the department – **prof. Roman Lesyk**)

SYNTHESIS AND PROPERTIES OF RHODANINE DERIVATIVES OBTAINED ON THE BASIS OF TRYPTAMINE

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Scientific supervisor: assoc. prof. **Volodymyr Horishny**, PhD

Keywords: rhodanine, tryptamine, antiexudative activity

Introduction. Due to the unique physico-chemical, chemical and biological properties of indole derivatives have found application in various fields of chemistry, technology, medicine and pharmacy. The wide range of biological activity of natural and synthetic indole derivatives causes a significant interest of scientists in the use of this heterocycle as an important "structural block" in the development of drugs. An important representative of indoles is the biogenic amine tryptamine, which is formed from the amino acid tryptophan and plays a role in the biosynthesis of vital compounds, as well as in the synthesis of promising biologically active substances. On the other hand, at the present stage of development of medical chemistry, the rhodanine cycle is also considered to be privileged. Therefore, the aim of our study was to build a rhodanine cycle based on tryptamine, in anticipation of biosynergism and valuable pharmacological properties from such a hybrid approach.

Materials and methods. The methods of organic synthesis based on cyclization and condensation reactions and also spectral methods of structure, purity and identity confirmation (NMR spectroscopy, chromatomass spectroscopy), as well as the study of antiexudative properties are used in the work.

Results. A method for the synthesis of 3-[2-(1H-indol-3-yl) ethyl]-2-thioxothiazolidin-4-ones has been developed. The structure of the synthesized compounds was reliably confirmed by NMR spectroscopy. Signals of all protons with chemical shifts corresponding to the structure of molecules are present in the NMR spectra of target substances. Physicochemical parameters, lipophilicity, water solubility, pharmacokinetics and druglikeness of synthesized compounds were evaluated using the SwissADME Internet resource. Their bioactivity score is calculated. They have been shown to be promising for research as enzyme inhibitors. A study of the anti-exudative activity of selected substances is planning.

Conclusion. A number of new 5-ylidene-3-[2-(1H-indol-3-yl)ethyl-2-thioxothiazolidin-4-ones based on the biogenic amine tryptamine were synthesized. One of the compounds showed activity commensurate with the reference drug "Ketanov".

SYNTHESIS OF NEW THIAZOLE DERIVATIVES AS BIOLOGICALLY ACTIVE COMPOUNDS

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Scientific supervisor: prof. **Roman Lesyk**, PhD, ScD.

Keywords: thiazoles, anticancer activity and anti-inflammatory activity

Introduction. Search for new efficient and nontoxic drug-like molecules among 4-thiazolidinones and related heterocycles has been a fruitful direction in medicinal chemistry for the last decades. The study of pharmacological effects of 4-thiazolidinones proved the 5-ene-4-thiazolidinones to be one of the most promising groups of compounds with antiinflammatory, antibacterial, antiviral, as well as anticancer activity. The importance of C5-ene fragment in the thiazolidinone core for revealing their druglike properties has been proved in many studies. Among 5-ene-4-thiazolidinones, a series of active anticancer agents inhibiting the cancer cells' growth was identified *in vitro* assays. Moreover, many ligands with a high affinity toward the known anticancer targets were described, for example, integrin αvβ3 antagonists, inhibitors of CDK1/cyclinB, PPAR antagonists, estrogenrelated receptorα (ERRα) modulators, SHP-2 inhibitors, PTP1B inhibitors, DNA-binding agents, and so forth. As a result the aim of current work was to perform the synthesis of structure related analogues to 5-ene-4-thiazolidinones, namely 3-arylidene-1-[4-methyl-2-(pyridine-2/3-ylamino)thiazol-5-yl]ethanones and their further biological activity evaluation.

Materials and methods. It has been performed the synthetic procedure of obtaining of appropriate biologically active 3-arylidene-1-[4-methyl-2-(pyridine-2/3-ylamino)thiazol-5-yl]ethanones in the in the Claisen–Schmidt condensation. The synthesized compounds were evaluated for anticancer activity in NCI60 cancer cell lines and for anti-inflammatory activity via carrageenan-induced paw edema method in the rats.

Results. The novel 3-arylidene-1-[4-methyl-2-(pyridine-2/3-ylamino)thiazol-5-yl]ethanones were synthesized from 1-[4-methyl-2-(pyridine-2/3-ylamino)thiazol-5-yl]ethanones and various aromatic aldehydes in the Claisen–Schmidt condensation. As a result, the library of new pyridine-substituted thiazole derivatives for search of new anticancer and anti-inflammatory agents have been designed and synthesized. The structures of newly synthesized compounds were established by spectral data. The tested 3-arylidene-1-[4-methyl-2-(pyridine-2/3-ylamino)thiazol-5-yl]ethanones demonstrated a promising activity in the *in vitro* screen on most of the tested cell lines, as well as some distinctive patterns of selectivity. Some of synthesized compounds possess sufficient level of anti-inflammatory activity *in vivo* comparable to reference drugs Diclofenac sodium and Ketorolac.

Conclusions. The preliminary results allowed to identify the active compounds with promising anticancer and anti-inflammatory activities among novel thiazole-pyridine hybrid molecules.

SYNTHESIS AND BIOLOGICAL ACTIVITY OF PYRAZOLINE-SUBSTITUTED 4-THIAZOLIDINONES

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Scientific supervisor: prof. **Roman Lesyk**, PhD, DSc.

Keywords: synthesis, pyrazoline, 4-thiazolidinones, Knoevenagel reaction, [2+3]-cyclocondensation, spectral characteristics, pharmacological studies.

Introduction. One of the most important task of medicinal chemistry is the creation of effective, highly selective and low-toxic drugs. In the context of this, one of the promising areas is using of thiazolidine core like privileged heterocycle to create "drug-like molecules". Thus, heterocyclic systems containing thiazolidine and pyrazoline fragments in molecules have received considerable attention recently due to their diverse biological activity and clinical applications. Derivatives of this heterocyclic system are promising biologically active compounds with antitumor activity, which are confirmed by previous studies. The mechanisms of realization of biological activity among pyrazoline-thiazolidinone conjugates can be associated with their affinity to JNK stimulating phosphatase-1 (JSP-1), tumor necrosis factor TNFα, cyclin-dependent kinase, heat shock proteins and P-glycoprotein. In continuation of this theme, we designed and synthesized novel non-condensed heterocyclic compounds containing 4-thiazolidinone, and pharmacologically attractive pyrazole or pyrazoline moieties.

Materials and methods. Organic synthesis, spectral analysis, anticancer activity.

Results. A new method for the synthesis of pyrazoline-substituted 4-thiazolidinones is proposed based on the [2+3]-cyclocondensation and Knoevenagel reactions. Synthesized non-condensed (5*Z*)-5-[(1,3-diphenylpyrazol-4-yl) methylene]-2-thioxothiazolidin-4-one demonstrated the activity against Human hepatoma HepG2 cells and Human cervical adenocarcinoma HeLa cells was studied, and the parameters of drug similarity and affinity for enzymes.

For lead-compound potential drug-like parameters were investigated, which indicate compliance with the criteria of flexibility, polarity, lipophilicity, insolubility and have a molecular weight of less than 500 g / mol. The potential affinity of (5Z)-5-[(1,3-diphenylpyrazol-4-yl) methylene] -2-thioxothiazolidin-

4-one for different classes of enzymes was studied, which indicates the potential pharmacological multivectority of the synthesized compound.

Conclusions. Purposeful synthesis of new library of heterocyclic compounds was performed, among which (5Z)-5-[(1,3-diphenylpyrazol-4-yl) methylene]-2-thioxothiazolidin-4-one with antitumor activity. Drug-like parameters and affinity for biotargets were established

SYNTHESIS AND ANTICONVULSANT ACTIVITY OF SOME NEW 4-THIAZOLIDINONE DERIVATIVES

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Keywords: epilepsy, 4-thiazolidinones, anticonvulsant activity

Introduction. More than 70 million people suffer from epilepsy and seizure conditions constituting nearly 1% of the world population. The available schemes and protocols for the treatment of such pathologies are very often imperfect so research and development of innovative anticonvulsants are an unmet and an actual problem for medicinal chemists. In the aforementioned context the 4-thiazolidinone derivatives presents interest for study as a potential anticonvulsant. Thus, among this class of heterocycles as an important source of drug-like molecules with various kinds of biological activities as well as polypharmacological agents was identified. Taking into account the all above reasons, herein we present a study of 4-thiazolidinone anticonvulsant properties in subcutaneous pentylenetetrazole (scPTZ) seizure model. And as a logical continuation, the other main goal of the current work was the synthesis of some thiazole-thiazolidinone hybrids and evaluation of their anticonvulsant activity in scPTZ test.

Materials and methods: organic synthesis, spectral data, SwisAdme protocol, pentylenetetrazole (scPTZ) seizure model.

Results. In the present work, anticonvulsant activity screening study of dual COX-2/5-LOX inhibitor darbufelone methanesulfonate, as well as design, synthesis of structural analogues of dabrufelone, and their anticonvulsant properties evaluation were described. Darbufelone possesses anticonvulsant properties in the scPTZ model in mice in dose 100 mg/kg and presents interest for in-depth studies as a possible anticonvulsant multi-target agent with anti-inflammatory activity. Structure analogues/hybrids of darbufelone with thiazole moieties at position C-2 of the basic molecule demonstrate significant protection level for animals in the scPTZ model which equals or more potent than for darbufelone one.

Conclusions. Described thiazole-thiazolidinone hybrid molecules are promising compounds for the design of potential anticonvulsants with satisfactory drug-like parameters.

SYNTHESIS OF THIAZOLIDINONE-THIAZOLE CONJUGATES AND THEIR BIOLOGICAL ACTIVITY

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Scientific supervisor: prof. **Roman Lesyk**, PhD, ScD

Keywords: thiazoles, thiazolidinones, biological activity, SwisAdme.

Introduction. 4-Thiazolidinone ring system is a core structure in various synthetic compounds displaying broad spectrum of biological activities. Mechanisms of 4-thiazolidinones and related heterocycles biological activity may be associated with the affinity to various biotargets, such as COX-2/5-LOX, phosphatase of a regenerating liver (PRL-3), nonmembrane protein tyrosine phosphatase (SHP-2), PPARα and PPARγ, aldose reductase, JNK-stimulating phosphatase-1 (JSP-1), tumor necrosis factor TNFa, antiapoptotic biocomplex Bcl-XL-BH3, integrin avb3, MurD ligase etc. On the other hand thiazole ring belongs to the privilleged scaffolds in modern medicinal chemistry particularly in discovering of new anticancer and antimicrobial agents. Various thiazole derivatives were proposed as COX-2 inhibitors, serine protease urokinase (uPa) inhibitors, adenosine A1 receptor antagonists, metabotropic glutamate receptor 5 (mGluR5) antagonists. 5-arylidene derivatives were previously shown as the most active group of compounds with biological activity among large pull of 4-azolidone derivatives and analogs. During the studies presented in number investigations it was found that attachment of thiazole moiety to 5-arylidenethiazolidinone scaffold allowed as gaining of biological activity in comparison to 2/3-unsubstituted analogous. Consequently, the combination of 4-thiazolidinone template with thiazole moiety in one molecule can be considered as promising approach in drug-like molecules design. In this spirit, herein we describe the synthesis and biological activity evaluation of new 4-thiazolidinones with thiazole moiety.

Materials and methods. organic synthesis, spectral data, SwisAdme protocol, acute toxicity.

Results. The starting 2-(2-thiazolyl)imino-4-thiazolidone was synthesized from 2-chloroacetamidothiazole and ammonium thiocyanate in acetone medium. The further reaction of 2-(2-thiazolyl)imino-4-thiazolidone with various aromatic aldehydes via Knoevenagel condensation providing novel 5-substituted 3-(2-thiazolyl)-2-imino-4-thiazolidones. The structures of synthesized compounds were confirmed by their ^{1}H NMR and LCMS spectroscopic data. Study of the drug-likeness parameters of synthesized

compounds showed that mentioned compounds possess satisfactory ADME parameters, pharmacokinetic properties and medicinal chemistry friendliness according modern requirements for potential drug-like molecules. The synthesized compounds showed low acute toxicity in mice with the LD_{50} values within the range of 450-630 mg/kg.

Conclusions. The synthesized 5-arylidene-3-(2-thiazolyl)-2-imino-4-thiazolidones are a promising molecular platform for creation of new highly active potential drug candidates with a low toxicity.

SYNTHESIS AND PROPERTIES OF RHODANINE DERIVATIVES WITH AZINE SUBSTITUENTS IN MOLECULES

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Scientific supervisor: assoc. prof. **Volodymyr Horishny**, PhD

Keywords: rhodanin, phenothiazines, antimicrobial activity

Introduction. Among the large number of nitrogen-containing heterocyclic compounds, one of the most important in biological terms are monocyclic and condensed azines. Among condensed azines, an important place is given to phenothiazines as drugs. Among the N-alkyl derivatives of phenothiazine, a number of drugs of neuroleptic, antihistamine, cholinolytic, antiparkinsonian and antiemetic action are known. N-acyl derivatives of phenothiazines are represented by antidepressants (fluorocyzin) and antiarrhythmic and coronary dilators (etmosin, nonachlazine). On the other hand, at the present stage of development of medical chemistry, the rhodanine cycle is also considered to be privileged. Therefore, the aim of our study was to combine phenothiazine and rhodanine cycles in one molecule, namely the synthesis of 5-ylidenerodanine-3-acyl derivatives of the phenothiazine series.

Materials and methods. The methods of organic synthesis based on cyclization, condensation and acylation reactions and also spectral methods of structure, purity and identity confirmation (NMR spectroscopy, chromatomass spectroscopy), high-efficiency screening of antimicrobial activity are used.

Results. Condensation of 4-thiazolidone carboxylic acids with aromatic and heterocyclic aldehydes gave 5-ylidenerodanine-3-alkanecarboxylic acids, which were used to obtain the corresponding acid chlorides. Subsequently, acylation of phenothiazine and its 2-chloro-substituted 5-arylidene (heterolylidene) rhodanine-3-alkanecarboxylic acids was performed and a number of new acylphenothiazines were obtained. The structure of the synthesized compounds was reliably confirmed by NMR spectroscopy. The parameters of bioactivity of the obtained substances are calculated. It is established that they are promising for biological research as enzyme inhibitors

and have high values of druglikeness. The antimicrobial activity of the synthesized substances was studied.

Conclusion. The synthesized 5-heteroteridenrodanine-3-acyl derivatives showed pronounced antibacterial activity against the strain Staphylococcus aureus ATCC 43300, and halogen-containing 5-arylidenerodanine-3-acyl derivatives of the 2-chlorophenothiazine series showed high antifungal effect against the strain Candida albicans ATCC 90028.

SYNTHESIS AND BIOLOGICAL PROPERTIES OF 2-METHYLIDENE-4-THIAZOLIDONES

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Scientific supervisor: assoc. prof. **Volodymyr Horishny**, PhD

Keywords: 4-thiazolidones, antitumor activity

Introduction. Current trends in the intensive development of chemistry of 4-thiazolidone are associated with advances in the synthesis and study of biological activity of thiazolidinedione derivatives, rhodanine and pseudothiohydantoin. Instead, 2-methylidene-substituted 4-thiazolidones have been insufficiently studied, and little is known about their biological activity. Therefore, research aimed at obtaining new 2-methylidene-substituted 4-thiazolidone for biological screening is a scientifically sound and relevant problem.

Materials and methods. The methods of organic synthesis, reaction of cyclization, condensation and also spectral methods of structure, purity and identity confirmation (NMR spectroscopy, chromatomass spectroscopy), high-efficiency screening of antitumor activity are used.

Results. Methods of synthesis of 2-cyano-3-mercapto-3-phenylamino-N-arylacrylamides were reproduced and optimized. A method for the synthesis of 2-cyano-aryl-2-(4-oxo-3-phenylthiazolidin-2-ylidene) acetamides has been developed, and their interaction with pyridine-3 and pyridine-4-carbaldehydes under condensation reactions has been studied. A series of new 2-cyano-2-(4-oxo-3-phenyl-5-pyridin-3/4-ylmethylenethiazolidin-2-ylidene)-N-phenylacetamides was obtained. The structure of the synthesized target substances was reliably confirmed by NMR spectroscopy. In the spectra there are signals of all protons with chemical shifts corresponding to the structure of molecules. The synthesized compounds were evaluated according to the parameters of drug-likeness, which indicate the compliance of the characteristics of the investigated substances with the criteria of drug-likeness. The parameters of bioactivity of the synthesized compounds are calculated. They have been shown to be promising for research as kinase inhibitors. The antitumor activity of selected compounds was studied.

Conclusion. As a result of screening of the selected synthesized substances of the 2-methylidene-4-thiazolidone series, the hit compound N-(4-chlorophenyl)-2-cyano-2- (4-oxo-3-phenyl-5-pyridin-4-ylmethylenethiazolidine-2-ylidene) acetamide was identified, which shows high antitumor activity against VACC-62 cell lines (GI_{50} = 0,0341μM) and M14 (GI_{50} = 0,0874μM) melanoma, K-562 leukemia (GI_{50} = 0,0462μM) and SW-620 epithelial bowel cancer (GI_{50} = 0,0465μM).

FURAN-4-THIAZOLODONE CONJUGATES. SYNTHESIS AND BIOLOGICAL ACTIVITIES

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Keywords: synthesis, furan, 4-thiazolidones, conjugates, antimicrobial activity

Introduction. The 4-thiazolidone cycle is considered as a privileged structure in medical chemistry. Among the derivatives of this heterocycle, a number of highly active agents with a broad spectrum of biological action were found and leader compounds with antimicrobial, antitubercular, antiviral, antidiabetic, anti-inflammatory, antitumor, anticonvulsant and other properties were identified. On the other hand, a prominent place in medical chemistry is occupied by compounds containing the furan cycle. The wide range of biological activity of natural and synthetic derivatives of furan, as well as its condensed analogues, causes significant interest of scientists in the use of this heterocycle as an important structural unit in the synthesis of structures with high biological activity. Therefore, the appearance of valuable pharmacological properties should be expected from the combination of furan and 4-thiazolidone cycle in one molecule.

Materials and methods. The methods of organic synthesis, the reaction of condensation, acylation and also spectral methods of structure, purity and identity confirmation (NMR spectroscopy, chromatomass spectroscopy), high-efficiency screening of antimicrobial activity are used.

Results. In order to obtain the target substances, the methods of synthesis of rhodanine-3-carboxylic acids and 3-arylrodanines were reproduced and their interaction with furfural was studied. A number of 5-furan-2-ylmethylene-4-oxo-2-thioxothiazolidin-3-yl) alkanecarboxylic acid derivatives previously not described in the literature were obtained. The structure of the synthesized compounds was reliably confirmed by NMR spectroscopy. The synthesized compounds were evaluated according to the parameters of drug-likeness and bioactivity. The antimicrobial activity of the synthesized substances was studied.

Conclusion. The study of antimicrobial activity of the synthesized compounds allowed to identify a number of compounds that exhibit high antibacterial activity against the *Staphylococcus aureus* ATCC 43300 strain.

SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF THIAZOLIDINE-INDOLE CONJUGATES

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Keywords: synthesis, 2-thioxo-4-thiazolidinone, indole-carbaldehydes, spectral data, antimicrobial activity

Introduction. Among the design strategies in drug discovery, considerable interest has been paid to thiazole-based heterocycles. Thiazole/thiazolidinone derivatives constitute an important class of therapeutic agents in medicinal chemistry including antitrypanosomal, antiviral, anticancer, antioxidant, anti-inflammatory activities and also display a pivotal role as antimicrobial and antifungal agents. Thus, thiazole ring is present in several drugs, such as penicillin, monobactam, sulfathiazole, thiabendazole and nizatidine, and making this heterocyclic fragment an ideal candidate to construction more potent and safer drug candidates, especially in therapy of infectious diseases. It was envisaged, that combination of thiazolidinone with other pharmacophores, especially indole fragment would generate molecular templates with new pharmacological profile and lower toxicity. In continuation of this theme, we designed and synthesized new non condensed heterocyclic compounds containing 4-oxo-2-thioxo-thiazolidine (rhodanine), and pharmacologically attractive indole moieties. The evaluation of their antimicrobial and antifungal activity in vitro against several reference and clinical strains was carried out.

Methods: Organic synthesis, NMR spectroscopy, pharmacological screening.

Results and Discussion: The reaction between rhodanine-3-propionic/ethanesulfonic acids with indole-carbaldehydes in an acetic acid medium providing series of 5-indolylmethylene rhodanine-3-carboxylic/sulfonic acid derivatives. Based on esterification reaction with methanol in the presence of sulfuric acid, 5-indolylmethylene rhodanine-3-propionic acid was transformed into appropriate ester for further evaluation of antimicrobial activity. Antimicrobial activity screening allowed the identification of compounds with significant effect against tested microorganisms with MIC/MBC/MFC values in the range of 25-50 μg/mL.

Conclusions: The synthesized 5-indolylmethylene rhodanine-3-carboxylic/sulfonic acid derivatives are a good platform for the development of

new highly active and low-toxic agents as potential drug-like molecules with antimicrobial activity.

THIAZOLE DERIVATIVES IN MEDICINAL CHEMISTRY

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Keywords: heterocycles, thiazoles, 4-thiazolidone, biological activity.

Introduction. The use of thiazole core is an important and promising direction in medical chemistry for the search and design of new potential biologically active agents with satisfactory drug-like parameters. This is primarily due to the relatively easy synthetic availability of molecules of this class and the wide choice of starting reagents used in synthetic schemes. Nowadays, many organic compounds containing one or more thiazole rings have been identified as pharmacological agents that exhibit promising antimicrobial, antiprotozoal and antitumor properties. The development and in-depth studies of thiazole-containing compounds, the use of new and different synthetic strategies and methods of biological research are very useful and relevant tasks facing scientists working in the field of new drugs. Structural modification of thiazole core has an additional effect on biological properties and a large group of substituted thiazole-containing heterocyclic molecules have a wide range of pharmacological properties and affect a wide range of therapeutic targets thus implementing antimicrobial, antitumor, anti-inflammatory and anti-inflammatory. Compounds of this chemotype act as high-affinity ligands of estrogen receptors, and are also being actively developed as an innovative group of adenosine receptor antagonists. A number of molecules with a fragment of aminothiazole in their structure have the potential as highly active fungicides, antischistosomal and anthelmintic drugs.

Materials and methods. The objects of this work was to systematize data on the current state of methods for the synthesis of thiazole-containing molecules, as well as some aspects of their pharmacological application; synthesis of 5-aryl/heterylidene derivatives of 3-allyl-2-(thiazol-2-ylimino)thiazolidin-4-one, study of their physicochemical and spectral properties. Methods: literature monitoring, physical, physical-chemical, and mathematical.

Results. The systematic review devoted to synthetic methods for construction of some types of thiazole-bearing molecules has been presented. The main trend such as anticancer drug discovery in pharmacological application of these molecules has been described. The focused synthesis of 5-aryl/heterylidene derivatives of 3-allyl-2-(thiazol-2-ylimino)thiazolidin-4-one

in multicomponent preaction, study of their physicochemical and spectral properties have been performed.

Conclusions. The novel 5-aryl/heterylidene derivatives of 3-allyl-2-(thiazol-2-ylimino) thiazolidin-4-one were synthesized in multicomponent reaction, and evaluated *in silico* for their physicochemical descriptors for compliance with the rules of "five" Lipinsky, Weber's rules and parameters of their bioavailability as well as *in vitro* for their antitumor activity in 60 lines cell screening.

VITAMINS OF HETEROCYCLIC STRUCTURE AS DRUGS

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Keywords: vitamins, essential micronutrient, vitamer compounds, coenzymes, biological action.

Introduction. A vitamin is an organic molecule that is an essential micronutrient which an organism needs in small quantities for the proper functioning of its metabolism. Essential nutrients cannot be synthesized in the organism, either at all or not in sufficient quantities, and therefore must be obtained through the diet. The term vitamin is derived from the word vitamine, which was coined in 1912 by Polish biochemist Casimir Funk, who isolated a complex of micronutrients essential to life, all of which he presumed to be amines. Vitamins have diverse biochemical functions. Vitamin A acts as a regulator of cell and tissue growth and differentiation. Vitamin D provides a hormone-like function, regulating mineral metabolism for bones and other organs. The B complex vitamins function as enzyme cofactors or the precursors for them. Vitamins C and E function as antioxidants. Both deficient and excess intake of a vitamin can potentially cause clinically significant illness, although excess intake of water-soluble vitamins is less likely to do so. The aim of the study was a detailed review and description of the classification, nomenclature, physiological and physicochemical properties, methods of their extraction and synthesis, physical and chemical properties, characteristics of qualitative and quantitative analysis, application in medicine of vitamins with heterocyclic structure and their analogues.

Results. Based on literature data the nomenclature, classification and physiological properties, features of qualitative and quantitative analysis and medical usage of heterocyclic vitamins including chromane (benzodihydropyran), flavan, oxymethylpyridine, pyridine-3-carboxylic acid, pyrimidine-thiazole, isoalloxazine, pteridine and corrine derivatives were analyzed.

Alpha-tocopherol is the primary form of vitamin E that is preferentially used by the human body to meet appropriate dietary requirements. Nevertheless, vitamin E is known to be a fat-soluble antioxidant that has the capability to neutralize endogenous free radicals. This biologic action of vitamin E consequently continues to generate ongoing interest and study in whether or not its antioxidant abilities may be used to help assist in preventing or treating a number of different conditions like cardiovascular disease, ocular conditions, diabetes, cancer and more.

Rutin is a rutinoside that is quercetin with the hydroxy group at position C-3 substituted with glucose and rhamnose sugar groups. It has a role as a metabolite and an antioxidant. It is a disaccharide derivative, a quercetin O-glucoside, a tetrahydroxyflavone and a rutinoside. A flavonol glycoside found in many plants, including buckwheat; tobacco; forsythia; hydrangea; viola, etc. It has been used therapeutically to decrease capillary fragility.

Pyridoxine is the 4-methanol form of vitamin B_6, an important water-soluble vitamin that is naturally present in many foods. Vitamin B_6 is the collective term for a group of three related compounds, pyridoxine, pyridoxal, and pyridoxamine, and their phosphorylated derivatives. Vitamin B_6, principally in its biologically active coenzyme form pyridoxal 5'-phosphate, is involved in a wide range of biochemical reactions, including the metabolism of amino acids and glycogen, the synthesis of nucleic acids, hemogloblin, sphingomyelin and other sphingolipids, synthesis of the neurotransmitters serotonin, dopamine, norepinephrine and gamma-aminobutyric acid (GABA).

Niacin, also known as nicotinic acid and vitamin B_3, is a water soluble, essential B vitamin that, when given in high doses, is effective in lowering low density lipoprotein (LDL) cholesterol and raising high density lipoprotein (HDL) cholesterol, which makes this agent of unique value in the therapy of dyslipidemia. It has a role as an antidote, an antilipemic drug, a vasodilator agent, a metabolite, a B vitamin, an nicotinamidase inhibitor, an Escherichia coli metabolite and a mouse metabolite. It is a pyridinemonocarboxylic acid and a pyridine alkaloid.

Thiamine is a heat-labile and water-soluble essential vitamin, belonging to the vitamin B family, with antioxidant, erythropoietic, mood modulating, and glucose-regulating activities. Thiamine reacts with adenosine triphosphate (ATP) to form an active coenzyme, thiamine pyrophosphate. Thiamine pyrophosphate is necessary for the actions of pyruvate dehydrogenase and alpha-ketoglutarate in carbohydrate metabolism and for the actions of transketolase, an enzyme that plays an important role in the pentose phosphate pathway.

Riboflavin is an essential human nutrient that is a heat-stable and water-soluble flavin belonging to the vitamin B family. Riboflavin is a precursor of the coenzymes flavin mononucleotide (FMN) and flavin adenine dinucleotide

(FAD). These coenzymes are of vital importance in normal tissue respiration, pyridoxine activation, tryptophan to niacin conversion, fat, carbohydrate, and protein metabolism, and glutathione reductase mediated detoxification. Riboflavin may also be involved in maintaining erythrocyte integrity. This vitamin is essential for healthy skin, nails, and hair.

Folic acid is a collective term for pteroylglutamic acids and their oligoglutamic acid conjugates. As a natural water-soluble substance, folic acid is involved in carbon transfer reactions of amino acid metabolism, in addition to purine and pyrimidine synthesis, and is essential for hematopoiesis and red blood cell production. Folic acid is found in many foods and particularly in leafy green vegetables that is essential for the critical biosynthetic pathways involving transfer of methyl groups to organic compounds.

Cyanocobalamin is a cobalt-containing coordination compound generated by intestinal microbes, and a natural water-soluble vitamin of the B-complex family that must combine with Intrinsic Factor for absorption by the intestine. Cyanocobalamin is necessary for hematopoiesis, neural metabolism, DNA and RNA production, and carbohydrate, fat, and protein metabolism. Vitamin B_{12} improves iron functions in the metabolic cycle and assists folic acid in choline synthesis. Vitamin B_{12} deficiency causes pernicious anemia, megaloblastic anemia, and neurologic lesions.

Conclusions. A comparative description of heterocyclic vitamins which belong to chromane (*tocopheryl acetate*), flavan (*rutin, quercetin*), oxymethylpyridine (*pyridoxine hydrochloride, pyridoxal phosphate*), pyridine-3-carboxylic acid (*nicotinic acid, nicotinamide*), pyrimidine-thiazole (*thiamine chloride, cocarboxylase, phosphothiamine, benfotiamine*), isoalloxazine (*riboflavin, riboflavin mononucleotide, flavinatum*), pteridine (*folic acid, calcii folinas, methotrexate*) and corrine (*cyanocobalamin, hydroxocobalamin, cobamamide*) derivatives was considered. As a result, the methods of their extraction and synthesis, qualitative and quantitative analysis, the features of the pharmacological actions were systematized.

BIOLOGICALLY ACTIVE MOLECULES WITH ANTIPYRILE FRAGMENTS

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Keywords: heterocycles, antipyrine, 4-thiazolidone, biological activity.

Introduction. The antipyrine fragment is one of the oldest structural pharmacophore elements used in medical chemistry, and at the same time it does not lose its relevance and attractiveness to researchers. Today, antipyryl-containing molecules occupy an important place in the arsenal of potential

biologically active compounds and the basic heterocycle of their structure - pyrazolin-5-one belongs to the privileged heterocycles. The pharmacological profile of these compounds is very broad and the therapeutic vector is aimed at the treatment and improvement of many serious pathologies and diseases. Scientific teams have developed, synthesized and successfully investigated new molecules with pharmacophore pyrazolin-5-one/antipyryl fragment as selective inhibitors to a number of potential anticancer targets, such as vascular endothelial growth factor receptor (VEGFR-2), c-mesenchyme transit factor (c-Met), sirtuins (SIRT), etc., and demonstrated high and selective cytotoxic activity in *in vitro* models. In addition, it should be noted that a number of antipyryl-containing compounds have promising hypolipidemic, antihyperglycemic, antioxidant and anti-inflammatory activities. Thus, the synthesis and study of pharmacological properties of new antipyryl-substituted heterocycles is an interesting and promising topic for research.

Materials and methods. The objects of this work was to systematize data on the current of the problem of medical chemistry of small molecules that contain in their structure an antipyrine fragment with an emphasis on their use in the design of non-steroidal anti-inflammatory agents; synthesis using a hybrid-pharmacophore approach of 5-aryl/heterylidene derivatives of 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino)thiazole-4(5H)-one, the study of their physicochemical, spectral and biological properties. Methods: literature monitoring, chemical, pharmacological, physical-chemical, and mathematical.

Results. The systematic review devoted to synthetic methods for construction of some types of antipyrine-bearing molecules has been presented. The main trend such as non-steroidal anti-inflammatory drug discovery in pharmacological application of these molecules has been described. The focused synthesis of 5-aryl/heterylidene derivatives of 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino)thiazole-4(5H)-one in multicomponent preaction, study of their physicochemical and spectral properties have been performed.

Conclusions. The novel 5-aryl/heterylidene derivatives of 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino)thiazole-4(5H)-one were synthesized in multicomponent reaction, and evaluated *in vivo* as non-steroidal anti-inflammatory drug as well as their ulcerogenic and hepatotoxic properties have been evaluated. Also, tautomerism of synthesized compounds has been studied.

TROPANE ALKALOIDS AS DRUGS

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Keywords: tropane, atropine, anticholinergic drugs, hyoscyamine, scopolamine, cocaine.

Introduction. Tropane is a nitrogenous bicyclic organic compound. Its chemical IUPAC name – *N*-methyl-8-azabicyclo[3.2.1]octane. Its mainly known for a group of alkaloids derived from it (called tropane alkaloids), which include, among others, atropine and cocaine. Tropane alkaloids occur in plants of the families Erythroxylaceae (including coca) and Solanaceae (including mandrake, henbane, deadly nightshade, datura, potato, tomato). The nitrogen bridge is between C-1 and C-5; these two are asymmetric carbons, but tropane is optically inactive due to mirror symmetry. The aim of the study was the detailed review and description of the classification, physiological and physicochemical properties, methods of their extraction and synthesis, physical and chemical properties, characteristics of qualitative and quantitative analysis, application in medicine of tropane alkaloids and their synthetic analogues as drugs.

Results. Based on literature data the nomenclature, classification and physiological properties, features of qualitative and quantitative analysis and medical usage of tropane derivatives as anticholinergic, antiparkinsonian anti-adrenergic, and local anesthetic drugs were analyzed.

Tropane alkaloids (TAs) are valuable secondary plant metabolites which are mostly found in high concentrations in the Solanaceae and Erythroxylaceae families. The TAs, which are characterized by their unique bicyclic tropane ring system, can be divided into three major groups: hyoscyamine and scopolamine, cocaine and calystegines. Although all TAs have the same basic structure, they differ immensely in their biological, chemical and pharmacological properties. Scopolamine, also known as hyoscine, has the largest legitimate market as a pharmacological agent due to its treatment of nausea, vomiting, motion sickness, as well as smooth muscle spasms while cocaine is the 2nd most frequently consumed illicit drug globally.

Atropine is an enantiomeric mixture of d-hyoscyamine and l-hyoscyamine, with most of its physiological effects due to l-hyoscyamine. Its pharmacological effects are due to binding to muscarinic acetylcholine receptors. It is an antimuscarinic agent. Atropine is a medication used to treat certain types of nerve agent and pesticide poisonings as well as some types of slow heart rate and to decrease saliva production during surgery. Hyoscyamine and scopolamine are widely used as anticholinergic drugs. They affect the central and peripheral nervous system as competitive, non-selective muscarinic

acetylcholine receptor (mAChR) antagonists, that prevent binding of the physiological neurotransmitter acetylcholine.

Scopolamine causes mydriatic, spasmolytic and local anaesthetic effects yet exhibit side effects which can be hallucinogenic and even lethal. Hyoscyamine and atropine have similar modes of action and effects as scopolamine. The pharmacological action of TAs is stereoselective, due to the difference of the stereoisomers concerning affinity and binding to muscarinic receptors. Homatropine, the mandelic acid ester of tropine, is used in ophthalmology to evoke a more rapid and less paralytically effect than atropine. Cocaine is now predominantly used for nasal and lacrimal duct surgery. The major disadvantages of this use are cocaine's potential for cardiovascular toxicity, glaucoma, and pupil dilation.

Conclusions. A comparative description of tropane alkaloids (*atropine sulfate, hyoscyamine camphorate, scopolamine camphorate and hydrochloride*) and their semisynthetic analogues (*homatropine hydrobromide, atrovent, troventol*) as anticholinergic drugs, tropane derivatives as antiparkinsonian (*tropacin*), anti-adrenergic (*tropaphen*) and local anesthetic (*cocaine hydrochloride*) drugs was considered. As a result, the methods of their extraction and synthesis, qualitative and quantitative analysis, the features of the pharmacological actions were systematized.

SYNTHESIS AND BIOLOGICAL ACTIVITY EVALUATION OF 5-METHYL-7-PHENYL-3H-THIAZOLO[4,5-B]PYRIDINE-2-ONES

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Keywords: thiazolo[4,5-*b*]pyridines, anticancer activity, drug-likeness parameters, acute toxicity

Introduction. Among biologically relevant molecules there is interest in the pyridine heterocyclic framework, which represents a main structural fragment found in a number of natural compounds many of which displaying activities against a diverse set of biological targets. For instance, polycyclic pyridine architectures including five and six-membered sulfur and nitrogen heterocycles are important structural components of bioactive molecules, and as a result, they serve as attractive targets in the modern drug discovery process. Bicyclic heterocycles, with condensed thiazole and pyridine moieties, the thiazolopyridines have received considerable attention recently due to their diverse biological activity and clinical applications. Many literature reports of these compounds indicate antioxidant, anticancer, anti-inflammatory, antimicrobial, antifungal and herbicidal activities. Earlier it was reported the [3+3]-cyclization of 4-amino-5*H*-thiazol-2-one and α,β-unsaturated ketones or

α-ketoacids providing series of thiazolo[4,5-b]pyridin-2(3*H*)-one derivatives and further their evaluation of biological activities. As a result the purpose of this work was to explore our continuous research effort in the synthesis of a series of novel thiazolo[4,5-*b*]pyridine derivatives based on [3+3]-cyclization of 4-amino-5*H*-thiazol-2-one and benzylideneacetones and biological activity evaluation of these compounds.

Materials and methods. Synthesized thiazolopyridine derivatives were evaluated by the National Cancer Institute, Bethesda for their anticancer activity at 10-μm concentration toward full NCI 60 cell lines panel representing nine different types: leukemia, melanoma, lung, colon, CNS, ovarian, renal, prostate and breast cancers. Druglikeness properties was determined based on Lipinski and Veber rules using the SwisAdme platform of Swiss Institute of Bioinformatics.

Results and Discussion. The starting arylidene benzylideneacetones were synthesized using known methods from appropriate aromatic aldehydes and acetone in methanol medium. The obtained benzylideneacetones were utilized in the [3+3]-cyclocondensation reaction with 4-amino-5*H*-thiazol-2-one in glacial acetic acid, providing 5-methyl-7-phenyl-3*H*-thiazolo[4,5-*b*]pyridin-2-ones. The structure of synthesized compounds was confirmed by NMR spectra. The anticancer screening assay (performed according NCI protocol within Developmental Therapeutic Program) allowed detecting some aspects of structure – anticancer activity relationships, most sensitive cell lines and identify the most active compounds for further investigation. Study of the drug-likeness parameters of synthesized compounds showed that mentioned compounds possess satisfactory ADME parameters, pharmacokinetic properties and medicinal chemistry friendliness according modern requirements for potential drug-like molecules. The synthesized compounds showed low acute toxicity in mice with the LD_{50} values within the range of 900–1050 mg/kg.

Conclusion. Considering all the above, the construction of novel chemical entities as possible chemotherapeutic agents among 5-methyl-7-phenyl-3*H*-thiazolo[4,5-*b*]pyridin-2-ones is justified and promising direction in the modern medicinal chemistry.

THE STUDY OF THE ANTIMICROBIAL ACTIVITY OF SOME NOVEL 4-THIAZOLIDINONE DERIVATIVES

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Keywords: heterocyclic compounds, thiazolidinones, thiazolo[4,5-*b*]pyridines, antimicrobial activity, antiproliferative activity.

Introduction. A wide range of infectious diseases caused by different pathogens is main focus of the searching for new highly active and low-toxic antimicrobials in modern drug discovery. A special issue in this contest is occupied by heterocyclic compounds, due to the unique ability to mimic the structure of prokaryotic cell metabolites and to bind reversibly to diverse biotargets. As part of our research in the field of biologically active fused thiazoles, herein we report the antimicrobial and antiproliferative properties of some thiazolo[4,5-*b*]pyridine derivatives. Moreover, the pharmacological potential of thiazolopyridines have been associated with their affinity to various biotargets, especially EGFR/ErbB family of protein-tyrosine kinases, histamine H_3-receptors, G-protein coupled receptors (mGluR 5), fibrillar amyloid-β peptide (Aβ), liver-selective glucokinase (GK), 3',5'-cyclic adenosine monophosphate phosphodiesterase (PDE) III etc. Noteworthy, it was established a significant antitumor activity of this class of compounds. To take into account the above facts, it is promising to evaluate biological activity of the mentioned compounds as a realization of the polypharmacological strategy in the design of prospective drug-like molecules among condensed 4-thiazolidinone derivatives.

Materials and methods. The antibacterial and antifungal activities of synthesized thiazolopyridines were evaluated *in vitro* with the agar diffusion and broth microdilution methods towards clinical and reference strains of Gram-positive, Gram-negative bacteria and yeasts. The structure-antibacterial/antifungal activity relationships of screened compounds were established. Target compounds were screened for their cytotoxicity effects on HaCaT and HEK293 cells using MTT assay.

Results and Discussion. The best antimicrobial activity was observed for compound V 2-oxo-7-thiophen-2-yl-2,3-dihydrothiazolo[4,5-*b*]pyridine-5-carboxylic acid with minimal inhibitory concentration (MIC) 12.5 μg/mL against *Candida albicans*. At the same time, the synthesized compounds were explored in the interaction with amoxicillin against multidrug resistant clinical isolates of ESβL+ *Klebsiella pneumonie* and *Staphylococcus haemolyticus* (MRSH). The best activity synergistic activity with amoxicillin was exhibited by compound VI. HaCaT human keratinocytes and HEK293 human embryonic kidney cells demonstrated resistance to the thiazolopyridine derivatives treatment and didn't reached the IC_{50} value up to 100 μM.

Conclusion. The tested thiazolopyridines constitute an interesting background for further development of new chemotherapeutic agents.

DEPARTMENT OF FARMACOGNOSY AND BOTANY

(Head of the department – assoc. prof. **Natiliya Shapovalova**)

THE CURRENT STATE OF USE OF MEDICINAL PLANTS CONTAINING VITAMINES

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Keywords: vitamins, medicinal plants, vitamin collection

Introduction. Unfavorable environmental and social factors of modern society have caused a significant and often pandemic prevalence of hypovitaminosis and deficiency due to mindless consumption of vitamins and minerals. The global problem is changing in nutrition structure due to the transition from natural food to refined products, the deterioration of lifestyle, and a significant reduction in human energy consumption. As a result, the number of cardiovascular pathologies, obesity, diabetes, tumors is growing in modern society, which requires rational preventive and curative use of vitamins. It is necessary to search for and introduce new medicines, including herbal ones and more advanced treatment methods.

Materials and research methods. The work aimed to search for modern information sources on medicinal plant raw materials containing vitamins and phytomedicines based on them to study the composition of the new vitamin collection and its analysis.

Results. The literature data on vitamin medicines are summarized; information analysis of the domestic market of vitamin collections and herbal teas carried out; the composition of a new vitamin collection developed; a phytochemical study of a new herbal medicine conducted, and methods of its standardization worked out.

Conclusions. The new herbal medicine developed by the US-based on plant raw materials can use in preventive therapy as a vitamin remedy.

PHARMACOGNOSTIC RESEARCH OF AESCULUS CARNEA HAYNE

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Keywords: phytochemical, microbiological research, leaves, flowers, bark Aesculus carnea

Introduction. Plants of the genus Aesculus have a wide range of pharmacological action, as it contains biologically active substances that conduct venotonizing, anticoagulant, anti-inflammatory, analgesic, cytotoxic, otic, antioxidant and antigenotoxic activity, which is due to the presence of tannins, triterpene saponins, coumarins, flavonoids, anthocyanins, carotenoids

and chlorophyll. Study of the chemical composition, pharmacological properties of Aesculus carnea are presented in fragments. The purpose of the work - pharmacognostic study of leaves, flowers and bark to standardize its raw materials, including phytochemical study of plant materials, in particular, qualitative and quantitative determination of tannins, anthocyanins, flavonoids, saponins, carotenoids and chlorophylls that cause bactericidal, anti-inflammatory, analgesic effect, as well as a study of the antimicrobial activity of the infusion of leaves and decoction of the bark of the Aesculus carnea.

Materials and methods. The objects of the study were medicinal plant raw materials - fresh and dried leaves, flowers, bark of Aesculus carnea, collected in May-June 2020 in the arboretum of the National University "Lviv Polytechnic".

Biologically active substances investigated specific qualitative reactions to investigate medicinal plant material for the content of polyphenolic compounds, in particular, the amount of oxidized phenols, the amount of flavonoids and anthocyanins, as well as saponins, carotenoids and chlorophylls. The study of antimicrobial activity was performed by diffusion into agar.

Results. Medicinal plant raw materials are standardized - leaves, flowers, bark of Aesculus carnea according to physical and chemical quality indicators. Studies of morphological features of the structure of the of Aesculus carnea revealed their characteristic diagnostic features. Phytochemical study of water, water-alcohol and alcohol extracts of leaves flowers, bark of Aesculus carnea identified biologically active substances: tannins, saponins, anthocyanins, flavonoids, coumarins, carotenoids and chlorophylls. The quantitative content of the sum of oxidized phenols in the bark of Aesculus carnea is 1,2 times higher than their content in the leaves and 2,4 times higher than their content in flowers. A study of the quantitative content of the amount of flavonoids found that their number in the leaves of *Aesculus carnea* leaves is 1,8 times higher than their content in flowers. The quantitative content of the amount of anthocyanins in the leaves of Aesculus carnea is 2,75 times higher than their number in flowers. Studies of antimicrobial activity against Gram-positive bacteria - Starculossus aureus and Gram-negative bacteria - Pseudomonas aeruginosa have shown that these bacterial species are sensitive to both the infusion of leaves and, especially, to the decoction of bark of Aesculus carnea, which is evidence of their antimicrobial action.

Conclusions. The leaves, flowers and bark of *Aesculus carnea* contain a biologically active complex of polyphenolic compounds - tannins, flavonoids, coumarins, anthocyanins, as well as saponins, carotenoids and chlorophylls, which cause antimicrobial, anti-inflammatory, analgesic, antioxidant effect of the plant, so it is a promising medicinal plant raw material for use in medicine.

PHARMACOGNOSTIC INVESTIGATION OF MEDICINAL PLANTS WITH ANTIBACTERIAL PROPERTIES

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Scientific advisor: prof. N.M. Vorobets, PhD, ScD

Keywords: antibacterial activity, pharmacognostic investigation, *Salix fragilis, Pyrola rotundifolia*

Introduction. Microbial resistance has been described WHO as a global crisis - a more balanced use of antibacterial agents and the discovery or creation of new ones - is part of the solution. Side effects of antibiotics on the host is generally accepted. So that, it is important to search and study plants with antibacterial properties that would be non- or low-toxic to humans. Extracts derived from medicinal plants are a source of biologically active compounds, many of which could become the basis for the creation of pharmaceuticals and the development of new treatments for bacterial infections. The object of the study was a comprehensive pharmacognostic study of two species common in Western Ukraine: *Salix fragilis* L. and *Pyrola rotundifolia* L. The subject of the study was the qualitative and quantitative analysis of BAS leaves of *Salix fragilis* L. and *Pyrola rotundifolia* L.

Material and methods. Materials of investigation were leaves of *S.fragilis* L. and *P. rotundifolia* L. harvested in Western Ukraine. Research methods: theoretical - elaboration of scientific articles and monographs, reference and information materials, Internet search database; experimental: morphological (morphological characteristics of the object), biochemical - spectrophotometric, titrimetric; microbiological – antibacterial properties investigation; statistical.

Results and discussion. Qualitative reactions in the composition of the leaves of *S.fragilis* and *P. rotundifolia* revealed tannins, phenolic compounds, flavonoids, saponins, coumarins, alkaloids, arbutin. The content of chlorophyll a and b in the extracts of *S.fragilis* and *P. rotundifolia* was 0.54 ± 0.35 and μg/g dry weight and 2.30 0.30 μg/g dry weight, respectively. The content of carotenoids in the studied plants is: 1.25 ± 0.05 and 0.66 ± 0.05 mg/g dry weight in the leaves of *S. fragilis* and *P. rotundifolia*, respectively. The content of ascorbic acid in *S.fragilis* and *P. rotundifolia* leaves is 557.6 ± 0.05 mg% by dry weight and 680.6 ± 0.05 mg%, respectively. The content of tannins is 4.55 ± 0.10 and 15.53 ± 3.3% in the leaves of *S.fragilis* and *P. rotundifolia*, respectively. The flavonoid content is 5.46 ± 0.25% in the leaves of *P. rotundifolia* and 3.26 ± 0.04% in the leaves of *S. fragilis*. High activity of ethanol extracts was detected: leaves of *P. rotundifolia* when using 70% ethanol as an extractant against *Staphylococcus aureus* and *Bacillus subtilis*; of *S. fragilis* leaves - against *Staphylococcus albus* and *Proteus vulgaris*, which is obviously due to the combined action of BAS in their composition. Extracts of

S. fragilis and *P. rotundifolia* leaves made using 20% ethanol as an extractant showed medium or low antimicrobial activity against the studied strains. Scientific novelty of the obtained results. A comprehensive comparative pharmacognostic study of two species of Salix fragilis L. and Pyrola rotundifolia L., showed to contain them a wide range of BASs that are effective against several bacteria.

Conclusions. Since *Salix fragilis* and *Pyrola rotundifolia* leaves accumulate a significant amount of biologically active substances and posses high antibacterial properties against several bacteria, both of them can obviously be offered for a more biochemical and pharmacological study and used, in particular as bacteriostatic agents.

PHARMACOGNOSTIC INVESTIGATION OF POKEWEED (*PHYTOLACCA AMERICANA L.*)

Victoriia Lakhmanych
Scientific supervisor: assoc. prof. N**.V. Shapovalova**, PhD

Keywords: Phytolacca americana, biologically active substances (BAS), macroscopic and microscopic features, triterpenoid saponins, polysaccharides

Introduction. American pokeweed (Phytolacca americana L.) is a promising plant for development of medicines. In our country the plant is still unofficial. Pokeweed roots are used in domestic medicine only in homeopathy for treatment of inflammatory diseases of the pharynx (sore throat, tonsillitis, *etc*.), as well as for mastopathy and inflammatory diseases of the mammary glands. However, due to the rich chemical composition of biologically active substances, Phytolacca americana is used worldwide for the prevention and treatment of many diseases.

Therefore, it is important to conduct a comprehensive pharmacognostic study of American pokeweed, and the development of modern methods for standardization of medicinal plant materials for their further implementation in medical practice.

Materials and methods. The objects of the research comprised fresh and dried roots of Phytolacca americana, harvested in the Botanical garden of the Department of Pharmacognosy and botany at Danylo Halytsky Lviv National Medical University. Methods: information search, comparison and systematic analysis, macro- and microscopic, phytochemical analysis.

Results. Modern literature data on the chemical composition, pharmacological properties and uses in medicine of American pokeweed have been collected and summarized in the project. Diagnostic macro- and microscopic features of the analyzed plant material have been determined. Detection of BAS in the roots Phytolacca americana has been carried out by

means of identification reactions; the quantitative content of the main groups of BAS has been determined, including the totality of polysaccharides and triterpenoid saponins.

Conclusions. The results of macro- and microscopic analysis of the roots of American pokeweed, as well as quantitative determination of the content of BAS can be used to develop criteria for standardization of the studied kinds of the plant material. Phytolacca americana, due to the high content of the main groups of biologically active compounds (polysaccharides and triterpenoid saponins), is a valuable source of plant materials and a promising plant for further investigation with an objective of its introduction into medical practice.

PHARMACOGNOSTIC STUDY OF PLANTS OF THE GENUS *HIBISCUS* L., CULTIVATED IN UKRAINE

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Keywords: *Hibiscus*, Syrian hibiscus, anatomical structure, anthocyanins.

Introduction. Representatives of the genus Hibiscus are of scientific and practical interest. Several species of the genus Hibiscus are cultivated in Ukraine. Considering the availability of the plant materials, experience of growing and using them in folk medicine of other countries, we consider relevant and promising task to perform pharmacognostic study of various types of the plant materials from Syrian hibiscus (Hibiscus syriacus), which is most common in Ukraine, as well as obtaining active phytosubstances and developing new original drugs on its basis.

The aim of our work was to conduct a pharmacognostic study of plants of the genus Hibiscus L.

Materials and methods. The objects of the research were plants of the genus Hibiscus L. cultivated in Ukraine. Methods: information search, comparison and systematic analysis, chemical, microscopic, phytochemical analysis.

Results. Modern literature data on the chemical composition, pharmacological properties and applications of species of the genus Hibiscus have been collected and summarized; the anatomical structure of Syrian hibiscus leaves and flowers has been studied, as a result of which microscopic diagnostic signs of these types of the raw materials have been established. The content of anthocyanins has been detected and quantified: 0.76 ± 1.16% in Syrian hibiscus leaves and 2.1 ± 0.17% in its flowers.

Conclusions. Therefore, representative of the genus Hibiscus, namely the most common in culture Syrian hibiscus is a promising plant for further

pharmacognostic study in order to introduce it as a new type of medicinal plant raw materials.

SUBSTANTIATION OF THE COMPOSITION AND ANALYSIS OF HERBAL COLLECTION FOR TREATMENT OF MENOPAUSAL SYMPTOMS

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Keywords: herbal drugs, menopausal symptoms, herbal collection, analysis, development.

Introduction. 1,2 billion postmenopausal women by the year 2030 will occur worldwide; in developed countries 30% of life expectancy will be carried out in the postmenopausal stage, that is characterized by decreased production of estrogen and progesterone. Hormone replacement therapy is often used for treatment of premenstrual syndrome (PMS), menopausal symptoms and related complications, but it frequently causes side effects and raises the risk of breast cancer, endometrial carcinoma and some chronic disorders. Therefore, natural drugs, mostly known as phytoestrogens, due to their estrogen-like effects, are considered as a safe and effective alternative to synthetic compounds for the prevention and/or treatment of PMS, menopausal symptoms, osteoporosis and breast cancer.

Materials and methods. Information search in scientific periodicals, search databases and analytical platforms (Pubmed, Researchgate, ScienceDirect, Springer Link, Google Scholar, Funding Institutional, JStore, Wiley, Cortellis, Expert Lookup) have been performed. The generally accepted research methods have been used: collection, systematization, analysis and generalization of information data. With an application of the PASSOnline program, *in silico* research on 57 individual compounds from 5 medicinal plant materials has been performed. Other applied methods compise macroscopical, microscopical, phytochemical techniques.

Results. The search for promising official and accessible herbal substances, considering their medical application for facilitation of menopausal complaints, as well as the content of active compounds with high Pa values of effects, related to female health, on the basis of *in silico* PASS analysis has been performed. The composition of the herbal collection that has potential to be used for the prevention and treatment of *women's hormonal* status items, recommendations and indications for its use have been corroborated and developed. Experimental macroscopic and anatomical studies on ingredients of the developed herbal collection (*Lupuli flos, Melissae folium, Glycyrrhizae*

radices, Origani herba, Salviae officinalis folium) for enhancement of female health state, related to estrogen deficiency, have been carried out. The performed histochemical and phytochemical analysis of the herbal mixture for the prevention and treatment of menopausal and related symptoms revealed occurrence in the analyzed samples of volatile oils and triterpenoid saponins.

Conclusions. The developed and further analyzed herbal collection of potential specific activity for enhancement of menopausal symptoms comprises official medicinal plants with sufficient resources. Several of the described medicinal plants are increasingly of interest as promising agents, therefore, deserve particular attention and wider application as effective remedies for amelioration of menopausal symptoms.

SELECTION OF PLANTS FOR THE TREATMENT OF HUMAN RESPIRATORY TRACT AND THEIR PHARMACOGNOSTIC INVESTIGATION

Zahorodnia Kateryna
Scientific advisor: Prof. N.M. Vorobets

Keywords: *Monarda fistulosa* L. - var. Premiera and var. Fortuna, pharmacognostic investigation, essential oil antimicrobial activity

Introduction. Diseases of the upper respiratory tract and bronchopulmonary system are one of the main causes of morbidity and mortality. To date, most of the fundamental issues in the fight against respiratory infections in scientific, methodological and practical terms don't solve due to the polyetiology and diversity of clinical forms of diseases. Drug treatment of respiratory diseases has become more complicated due to the increased incidence of drug allergies and other complications. As a result, non-drug treatments, including herbal medicine, are becoming more popular. Further study of the species that can be used to treat the respiratory tract remains relevant. As the resources of medicinal plants have been declining recently and the demand for raw materials is growing, there is a need to study more completely the selected varieties, in particular the *Monarda* spp. for the presence of BAS, and their pharmacological significance. **The aim of our study** was to analyze scientific resources on the species used to treat respiratory diseases, *Monarda* spp., which are in nature, as well as created selectively; to conduct a pharmacognostic study of two varieties of *Monarda fistulosa* L. - var. Premiera and var. Fortuna, which were created by Ukrainian breeders, but insufficiently studied and therefore practically not used for treatment.

Object of research: complex pharmacognostic investigation of two varieties of *Monarda fistulosa* L. - Premiera and Fortuna. **Subject of research**:

identification and quantification of the main groups of BAS in flowering shoots of two varieties of *Monarda fistulosa* L. - Premiera and Fortuna; detection of antimicrobial properties of the essential oils of studied varieties.

Material and methods. Materials of investigation were herbs of two varieties of *Monarda fistulosa* L. - Premiera and Fortuna harvested in Kherson region of Ukraine. Research methods: theoretical - elaboration of scientific articles and monographs, reference and information materials, Internet search database; experimental: morphological (morphological characteristics of the object), biochemical - spectrophotometric, titrimetric; microbiological – antimicrobial properties investigation; statistical.

Results and discussion. Qualitative reactions in the composition of the herbs of two varieties of *Monarda fistulosa* L. - Premiera and Fortuna revealed tannins, phenolic compounds, flavonoids, saponins, alkaloids. The content of chlorophyll a and b is: 0,960 and 0,840; and 0.250 and 0.310 mg/g dry weight in Premiere and Fortuna, respectively. The carotenoid content is: 0.600 and 0.560 mg/g dry weight in the varieties Premier and Fortuna, respectively. The content of ascorbic acid in the material of Premiere and Fortuna is 400.6 and 420.5 mg%, respectively; the content of hydroxycinnamic acids is 3.46 ± 0.45 and 2.40 ± 0.22%, respectively. The content of flavonoids in the material of Premier and Fortuna varieties is 2.55 and 2.60% in terms of dry weight and quercetin, respectively; the content of tannins is 12.5 and 10.5% in terms of dry weight, respectively. The content of saponins in the studied varieties Premier and Fortuna is 5.20 ± 0.2 and 6.86 ± 0.8% of dry weight, respectively. High antibacterial activity of essential oils isolated from flowering shoots of Premiere and Fortuna varieties was revealed: at the level of 20-40 mm growth retardation against *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus albus*, *Proteus vulgaris*. Anticandidal activity of essential oils from flowering shoots of Premier and Fortuna varieties at the level of 30-40 mm growth retardation was detected against *Candida pseudotropicalis, C. curvata, C. kefyr, C. parapsilosis, C. tenuis.*

Conclusions. A wide range of BAS and the ability to obtain in sufficient quantities and in accordance with Good Practice of cultivation and collection of medicinal plants (GACP) raw materials, as well as antibacterial and anticandidal properties of their essential oils allows to recommend varieties *Monarda fistulosa* L. - Premiere and Fortuna for more detailed investigation and use.

DEPARTMENT OF TOXICOLOGICAL AND ANALYTICAL CHEMISTRY

(Head of the department – assoc. prof. **Iryna Halkevych**)

RAPID DIAGNOSIS ACUTE OF CYHALOTHRIN INTOXICATION

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Keywords: cyhalothrin, synthetic pyrethroids.

Introduction. A relatively new class of compounds used as pesticides are synthetic pyrethroids - analogues of natural pyrethrin. Synthetic pyrethroids are the fourth generation of pesticides that replaced the organochlorine compounds, carbamates and organophosphate pesticides. For research we chose cyhalothrin - synthetic pyrethroids, which is widely used in practice, but little studied in chemical-toxicological terms.

Materials and methods. Research object is cyhalothrin. Methods: color reactions, thin-layer chromatography, gas-liquid chromatography, extraction. Materials: internal organs, blood, urine, soil, groundwater.

Results. We worked out and proposed methods of identification and quantification of cyhalothrin.

Conclusions. Worked out methods of cyhalothrin isolation from objects of chemical-toxicological studies are suitable for use in laboratory diagnosis of pesticides poisoning. They can also be used for sanitation analysis.

FORENSIC TOXICOLOGICAL INVESTIGATION OF DIPHENHYDRAMINE INTOXICATIONS

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Keywords: diphenhydramine, acute intoxication, forensic-toxicological investigation.

Introduction. The methods of diphenhydramine isolation from blood, urine, stomach and washing water and methods of its detection and determination were proposed. The influence of pH nature of organic solvent on extraction of diphenhydramine was studied.

Thin layer chromatography, UV spectrophotometry and gas-liquid chromatography have been proposed to identify diphenhydramine. Photocolorimetric and spectrophotometric methods were proposed for quantification of diphendramine. Methods of isolation of diphendramine are developed from the researched objects such as blood, urine and gastric lavage. The developed methods of diphendramine analysis can be used for in the practice of chemical-toxicological laboratories.

Materials and methods. Research object: diphenhydramine. Methods: color reactions, thin-layer chromatography, gas-liquid chromatography, extraction, spectrophotometry, photocolorymetry. Materials: water after gastric

lavage, blood, urine.

Results. We have developed methods of identification and quantification of diphenhydramine.

Conclusions. Were proposed methods of diphenhydramine isolation from objects of chemical-toxicological studies are suitable for use in laboratory diagnosis of diphenhydramines poisoning. They can also be used for sanitation analysis.

CHEMICAL-TOXICOLOGICAL RESEARCH OF TEMAZEPAM

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Keywords: temazepam, acute intoxication, chemico-toxicological investigation.

Introduction. The methods of temazepam isolation from blood, urine, stomach and washing water and methods of its detection and determination were proposed. The influence of pH nature of organic solvent on extraction of temazepam was studied. For temazepam identification were used thin layer chromatography and by UV spectrophotometry. For temazepam quantification proposed photocolorimetric and spectrophotometric methods. Two methods temazepam isolation from objects of research: as native form and as benzophenone (product of acid hydrolysis) were developed. Worked out methods of analysis temazepam can be used in the practice of chemical-toxicological laboratories.

Materials and methods. Research object: temazepam. Methods: color reactions, thin-layer chromatography, gas-liquid chromatography, extraction. Materials: internal organs, blood, urine.

Results. We have developed methods of identification and quantification of temazepam.

Conclusions. Were proposed methods of temazepam isolation from objects of chemical-toxicological studies are suitable for use in laboratory diagnosis of pesticides poisoning. They can also be used for sanitation analysis.

CHEMISTRY CHEMICO-TOXICOLOGICAL ANALYSIS OF RAMIPRIL

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Keywords: Ramipril, medication used to treat high blood pressure, chemical analysis, intoxycations, isolation, extraction, thin layer chromatography, photocolorimetry.

Introduction. Ramipril is used to treat hypertension, symptomatic heart failure, and asymptomatic left ventricular dysfunction. It has been proven to protect the function of the kidneys in hypertension, heart failure, and diabetes, and may be used in the absence of hypertension for its kidney protective effects. It is widely used in chronic kidney failure. Furthermore, ramipril is an emerging treatment for psychogenic polydipsia. A double-blind, placebo-controlled trial showed that when used for this purpose, ramipril led to decreased water consumption (determined by urine output and osmality) in 60% of patients. A few of reports can be found in the literature about intoxications with combined intoxications. Takin this into consideration, chemico-toxicological investigation of ramipril is actual problem.

Materials and methods. Research object is ramipril and biological samples poisoned this drug. Research subject:element of chemical development of ramipril for identification, quatification and isolation of this substance. Methods: literature monitoring, physical, physical-chemical, and mathematical.

Results. The UV-spectrophometry and thin layer chromatography methods were developed for identification of ramipril in pharmaceutical formulations and samples from biological liquids. The spectrum of ramipril in acid solution isn`t had characteristic maximum of absorbtion. Four eluent system, which recommended for systematic analysis in forensic toxicology, for determination of ramipril in biological samples: ethyl acetate-chloroform (2:3), acetone-chloroform (2:5), acetone-chloroform-25% ammonia solution (6:3:1), dichloroethane-ethanol (4:1) were used. Determination was developing on “Sorbfil” plates. Ramipril identification can be achieved with such reagents: Dragendorf, Wagner, Bushard, Marquis, Frede, ningidrine solution, potassium permanganate in 0.1 M sulfate acid, solution iron trichloride.

The spectrophotometric method was used for ramipril quantification. This method based on reaction between ramipril and ningidrine solution. Limit of ramipril detection is 10 μg/ml. Linearity of calibration curve is in concentration range 10-70 μg/ml. The proposed method was successfully applied to biological samples for ramipril analysis. Relation between pH and ramipril extraction amount was investigated. This substance was extracted in

high quantities from solution with pH 9-10. The WHO recommended techniques were used for enalapril isolation from blood and urea samples.

Conclusions. The techniques for identification, quatification and isolation of ramipril were developed and demonstrated good results for enalapril determination in biological samples.

TOXICOLOGICAL ASSESSMENT OF METAL ACCUMULATION IN MEDICINAL PLANTS OF THE CARPATHIAN REGION

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Keywords: heavy metals, accumulation in plants, plant material, adaptation.

Introduction. Formation of the chemical composition of plants under natural conditions occurs at the same time as a large number of environmental factors, including the geochemical conditions of the ecotype and the exogenous entry of elements into the soil. However, it cannot be excluded that the translocation of heavy metals from the layer of soil into plants depends not only on edaphic factors, but also on the physiological and biochemical characteristics of plants.

Results. This study presents the results of heavy metals content in medicinal plants in the territory of Carpathian region. The content of Lead, and Cadmium in medicinal plants was analyzed by atomic absorption spectroscopy (AAS) method. As a result of the researches it was established that the accumulation of heavy metals (Cd and Pb) in the studied plants differs depending on the location of the samples. It was found the higher level of Lead ions accumulation in the next species: Taraxacum officinale L and Plantago major L., and the concentrators of Cadmium ions ware Plantago major L. and Capsella bursa-pastoris (L.) Medik. Also, it was evaluated the spatio-temporal variability of the accumulation of Lead and Cadmium ions in the studied plants. Analysis of the obtained data on the Lead content in various species of medicinal plants in May did not reveal an excess of MPC, except for Taraxacum officinale L. (F_{risk} = 1.32) and Plantago major L. (F_{risk} = 1.43). Excessive accumulation of Cadmium was founded in Plantago major L. (F_{risk} = 1.75). Instead, analysis of the accumulation of heavy metal ions in different species of medicinal plants collected in September revealed the exceed of the MPC for Lead ions for all tested samples (in particular, in Capsella bursa-pastoris (L.) (F_{risk} = 1.83), Polygonum aviculare (L.) (F_{risk} = 1.96), Taraxacum officinale L. (F_{risk} = 2.79), Plantago major L. (F_{risk} = 3.39), Leonurus guinguelobatus Gilib. (F_{risk} = 2.43)). Excessive accumulation of Cadmium ions in plants collected in September was shown for Capsella bursa-pastoris (L.)

Medik., (F_{risk} = 2.89), Polygonum aviculare (L.) (F_{risk} = 2.18), and Plantago major L. (F_{risk}) = 2.53).

Conclusions. As a result of the researches it was established that the accumulation of heavy metal ions (Cd and Pb) in the studied plants differs depending on the location of the samples. Wild medicinal plants in the area of Morshyn, Stryi district and the village of Volytsia of Mosty district, in comparison with plants in the area of Novyi Rozdil, Mykolayiv district, and Chervonohrad, Sokal district, are characterized by a higher content of most heavy metals. This, obviously, can be related both to the geomorphology of the studied areas and to the anthropogenic load.

TOXICOLOGICAL CHARACTERISTICS AND CHEMICO-TOXICOLOGICAL ANALYSIS OF PHENIBUT

Khrystyna Kozyniak
Scientific supervisor: sen. lec. **Serhiy Kramarenko**, PhD

Keywords: Phenibut, inhibitory neurotransmitter GABA, chemical analysis, intoxycations, isolation, extraction, thin layer chromatography, spectrophotometry.

Introduction. Phenibut is a central nervous system depressant with anxiolytic effects, and is used to treat anxiety, insomnia, and for a variety of other indications. It is usually taken by mouth as a tablet, but may be given intravenously. A lot of reports can be found in the literature about lethal intoxications with Phenibut, with combined intoxications, Phenibut recreation and suicide poisoning. Takin this into consideration, chemico-toxicological investigation of Phenibut is actual problem.

Materials and methods. Research object is Phenibut and biological samples poisoned this drug. Research subject: element of chemical development of Phenibut for identification, quatification and isolation of this substance. Methods: literature monitoring, physical, physical-chemical, and mathematical.

Results. The UV-spectrophometry and thin layer chromatography methods were developed for identification of Phenibut in pharmaceutical formulations and samples from biological liquids. The spectrum of Phenibut in acid solution is characterised by one maximum absorption at 255 nm. Four eluent system, which recommended for systematic analysis in forensic toxicology, for determination of Phenibut in biological samples: chloroform-acetone (4:1), ethyl acetate, chloroform-methanol (9:1) and ethyl acetate-methanol-25% solution of ammonia (17:2:1) were used. Determination was developing on “Sorbfil” plates. Phenibut n identification can be achieved with such reagents: 5% ningidrine solution in 10% acetate acid, Dragendorf and

Bushard reagents. The spectrophotometric method was used for Phenibut quantification. It based on reaction between Phenibut and 3% vanilinesolution in alkaline environment. Limit of Phenibut detection is 5 μg/ml. Linearity of calibration curve is in concentration range 5-40 μg/ml. The proposed method was successfully applied to biological samples for Phenibut analysis. Relation between pH and Phenibut extraction amount was investigated. This substance was extracted in high quantities from light base solutions with pH 8.0-8.5. The WHO recommended techniques were used for Phenibut isolation from blood and urea samples.

STUDY OF THE INFLUENCE OF ANTI-NUTRITIONAL FACTORS ON THE HUMAN BODY

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Scientific supervisor: assist. prof. **N.M. Darmohrai**

Keywords: food, safety, toxic component, anti-nutritional factor, poisoning, overdose, contamination.

Introduction. Food safety is the absence of the threat of harmful effects of food, food raw materials and related materials on the human body, as well as the absence of their toxic, carcinogenic, mutagenic and teratogenic effects**.** Intensive industrial development, widespread urbanization, and chemicalization of agriculture lead to the entry of foreign substances into food raw materials and food products, which negatively affect the health of the population. The use of various additives in new food production technologies may pose a certain danger.. In addition to the necessary nutrients, food may contain anti-nutrient compounds of different chemical nature, which have no nutritional value, and, moreover, are harmful and potentially dangerous to human health. The aim of the work was to study the general principles of food safety, to study the main anti-nutritional food components and their toxic effects on the human body.

Materials and methods. Analysis of scientific literature and its interpretation were used.

Results. The main ways of food contamination with foreign substances were studied: by heavy metals, products used in plant growing and animal husbandry. It has been established that foreign chemicals can get into food accidentally from the environment or in the process of technological processing during contact with the equipment or in the form of food additives. It is established that the main groups of anti-nutritional food factors are digestive enzymes inhibitors, antivitamins, substances that reduce the absorption of minerals, cyanogenic glycosides, lectins, alkaloids and biogenic amines. It is established that the glycoalkaloid solanine can have a negative effect on the

human body. Toxic effects of solanine are mostly presented in the form of gastrointestinal and nervous disorders. It has been established that some fruits contain the glycoside amygdalin, which in the stomach under the influence of the enzyme amygdalase is broken down to form hydrocyanic acid, which causes severe poisoning by blocking respiratory enzymes and disrupting oxidative processes in cells. Products with a high content of oxalic acid can lead to serious disorders of salt metabolism and irreversibly bind calcium ions.

Conclusions. Anti-nutritional food factors can be toxic and have a negative influence on the human body. The influence of anti-nutritional food factors should be taken into account at preparing diets, in the food production, as well as in the process of their culinary processing.

COMPARATIVE ASSESSMENT OF THE ELEMENTAL COMPOSITION OF HAIR UNDER THE INFLUENCE OF VARIOUS FACTORS

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Scientific supervisor: assoc.prof. **Liubov Kostyshyn**, PhD

Keywords: heavy metals; human scalp hair; atomic absorption spectrometry, quantitative analysis; concentration

Introduction: Research has shown that there is personal difference in concentrations of trace elements in the human hair ac- cording to human life or history such as occupation, age, food, habit, social condition. Research have also reported that individual's deviation of elemental concentrations reflects the degree of environ- mental pollutants exposure to the human body, intakes of food and metabolism. Heavy metals, such as zincum, lead, nickel, cadmium, cuprum are extremely toxic even in very small amounts.

Results: Indicator of the elemental status of a person may be the content of metals in its biosubstrates. We used hair as such substrates. The hair follicle is washed with blood and all trace elements in the blood are concentrated in the hair and do not disappear with time. Cutting hair at a different distance from the scalp, and given the approximate speed of hair growth, you can obtain data in dynamics. For the quantitative analysis of hair on the content of trace elements it is necessary to use modern analytical methods. The most convenient for this purpose is the method of atomic absorption spectroscopy (AAS). With this method of analysis, one can determine the concentrations of several elements at once with sufficiently high sensitivity and accuracy. 20 samples of 200-500 mg of hair were selected. The hair samples were further washed in acetone to degrease and weighed on analytical balance to within ± 0,0001 g and subjected to sample preparation. Sample preparation was also used to burn the sample in a muffle furnace at 450° C. Thus, the trace element

status of the surveyed individuals causes some concern regarding the amount of toxic metals.

Conclusions: Analysis carried out by AAS technique for Zn, Cd, Cu, Pb indicates the presence of all the metals in relatively large amounts with Cd and Pb having the highest concentration. The presence of all the heavy metals under investigation is a clear indication of the environmental content as well as the behavioural pattern of the respondents who are randomly selected from the general society. For all the four different heavy metals determined, the coefficients of variation were higher for three elements (Cd and Pb) among the females. This reflects 75% of the total population which indicates that these metals have greater degree of dispersion among the female population.

STUDY OF CORRELATIONS BETWEEN TOXICITY AND BLOOD CONCENTRATION OF CALCIUM CHANNEL BLOCKERS

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Scientific supervisor: assoc, prof. **Iryna Halkevych**, PhD

Keywords: amlodipine, HPLC-UV detection, blood, liquid and solid phase extractions

Introduction. Calcium channel blockers (CCB) are important for clinical implications. Calcium antagonists act at the cellular membrane, inhibiting the influx of extracellular calcium. Calcium antagonists dilate coronary and peripheral arteries indoses that variably inhibit myocardial contractility and have little or no effect on skeletal muscle. Their clinical usefulness in the treatment of hypertension and angina pectoris derives largely from these properties. CCB are the leading cause of cardiovascular drug overdose and are responsible for 48% of deaths related to cardiovascular drug exposure.

Material and methods. Research object are group of CCB, toxicity of amlodipine and determination amlodipine in blood. Research subject: amlodipine. Methods: literature monitoring, HPLC-UV, solid phase extraction (SPE), liquid extraction, TLC and colored tests.

Results. The isolation of amlodipine from blood was performed on a ceolite or liquid extraction after precipitation by acetonitrile. Qualitative and quantitative determination of amlodipine in the studied object was carried out by HPLC. The calibration curves showed good linearity for amlodipine concentration 0,5– 10 μg/mL. SPE allows to isolate 92-99 % of Amlodipine from bloods.

Conclusions. The developed SPE, LE, TLC, color tests and HPLC techniques was applied to the amlodipine identification and quantification in blood samples.

ASSESMENT OF ANTISEPTICS AND DISINFECTANTS TOXICITY

Romaniia Petrash
Scientific supervisor: assist. prof. **N.M. Darmohrai**

Keywords: composition, antiseptics, disinfectants, side effects, toxicity, poisonings.

Introduction. The difficult sanitary-epidemiological and ecological situation in Ukraine and worldwide requires the creation of new universal antiseptics and disinfectants and the introduction of safe technologies for their use. The coronavirus pandemic provoked an increase in demand for antiseptics and disinfectants. Modern universal antiseptics and disinfectants must quickly and reliably neutralize a variety of pathogenic microflora, maintain their antimicrobial activity for a long time, as well as be easy to use: do not have a sharp, unpleasant odor. In addition, antiseptics and disinfectants must be safe for humans, animals and the environment. Most antiseptics and disinfectants, which are traditionally used both in our country and abroad, do not meet all modern criteria for effectiveness, toxicological safety and environmental friendliness. Basic groups of antiseptics that are widely used in all fields of practical medicine are surfactants, alcohols and halogens.

Materials and methods. Analysis of scientific literature and its interpretation were used.

Results. The tendencies of development and application of modern disinfectants, theirs mechanisms of action are worked out. The classification of antiseptics by chemical structure was studied. The composition of antiseptic drugs, which are most often prescribed by doctors and used in medical institutions, was studied: "Dekasan", "Chlorhexidine bigluconate", "AHD 2000", "Iodicycerin". It is established that almost all antiseptics and disinfectants have side effects in the form of hypersensitivity reactions, allergic reactions, dermatitis. It has been established that alcohol-based antiseptic poisoning occurs due to accidental or intentional ingestion of the contents of the antiseptic, which leads to loss of consciousness, dysfunction of all senses, circulatory and respiratory disorders (coma). Poisoning with iodine-containing antiseptics leads to respiratory tract irritation, metabolic acidosis, acute renal failure and coma. It was studied that accidental administration of a large amount of chlorhexidine (300 ml) leads to death with signs of hepato-renal failure.

Conclusions. There are main components of antiseptics and disinfectants that can have a negative effect on the body: ethanol, iodine, chlorhexidine.

FEATURES OF DIAGNOSIS OF DRUG POISONING

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Keywords: analysis of controlled substances, codeine, toxicity, UV-spectrophotometry.

Introduction. One of the common subjects studied by forensic doctors is chronic and acute drug poisoning. Poisoning by them is somehow connected with the use of opiates or their combination with other substances (primarily ethyl alcohol). That is why a number of studies have been devoted to the development of various criteria for diagnosing the cause of death from drug intoxication, especially the opiate group.

Materials and methods. A set of physico chemical methods was used to solve the set tasks, namely, enzyme-linked immunosorbent assays, thin-layer and UV-spectrophotometry. The analysis of the obtained results was performed using statistical analysis.

Results. Immunochromatographic analysis has shown high sensitivity for detection a wide variety of narcotic substances like opiates. The specification of the used narcotic substance takes place at the second confirmative stage of research (chromatography), thus saving time and money for more labor-intensive and expensive research methods. The threshold level of multidisciplinary rapid tests, in particular Sniper-5 for is 50 ng/ml for marijuana, 300 ng/ml for cocaine, 1000 ng/ml for amphetamine and methamphetamine and 2000 ng / ml for morphine. In some cases, the result may be "false" positive. It can be caused by certain medications - antihistamines (antiallergic) drugs, some nasal sprays or cold remedies, antidepressants (tricyclics, quetiapine, bupropion). Experimental studies have shown that UV-spectrometry can be used for preliminary detection of codeine in biological samples. Codeine has absorbance maximum at $\lambda = 278$ nm (molar absorptivity L. $mol.^{-1}$. $Cm^{-1} = 0.367*10^4$). The proposed UV-spectrophotometric method displayed a linear range from 1 to 30 μg/ml for codeine with the correlation coefficients more than 0.9996 (n = 6). The relative standard deviation of quantitative determination of codeine in model solutions is ± 2.99%. LOD and LOQ was 1.08 μg/ml and 1.26 μg/ml, respectively.

Conclusions. A scheme of rapid analysis in the diagnosis of codeine poisoning was offered. A positive result of immunoassay indicates only the presence of the drug or its metabolites and does not indicate or evaluate intoxication. Therefore, it is necessary to conduct additional research, which in the use of sensitive and selective methods of analysis, in particular spectral and chromatographic methods.

TOXICOLOGICAL EVALUATION OF BODY-SHAPING PRODUCTS

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Keywords: cellulite cream, thigh cream, product safety, safety of cellulite creams, body shaping cosmetics.

Introduction: Xanthenes, caffeine, herbal extracts, retinoids and other agents are administered topically to treat cellulite by reducing adipogenesis and inducing thermogenesis, microcirculation and collagen synthesis. This study looked at the ingredients in cellulite creams, how often they were used, and whether they were reported to cause allergies.

Materials and methods: A systematic search of PubMed and Google Scholar databases for publications on ingredients and their safety. Also it has been developed method of caffeine determination in cosmetics. SPE cartridges were conditioned with 3 mL of methanol and 3 mL of deionized water. One milliliter of the prepared sample was loaded on the cartridge at the flow rate of 1 mL/min. Desorption of caffeine was achieved with 4 x 1 mL of methanol.

Results: The most potentially harmful components of cosmetics for modeling the figure include: triclosan (there is a negative effect on thyroid hormones); propylene glycol (oil refining product, has an irritating effect); sodium lauryl sulfate (detergents synthesized from petroleum products, dry the skin); triethanolamine (TEA) (may accumulate in the body and provoke allergies); preservatives (especially DMDM Hydantoin); parabens (may accumulate in the body, provoking hormonal disorders); fragrance (consisting of various ingredients that can cause allergies and inflammation); glycerin (dehydrates the skin in large quantities), mineral oil (oil refining product, comedogenic); cetearyl alcohol (emollients made from coconut oil can provoke allergic reactions). But these ingredients, despite their presence, should not be the main components of the tool, because the first 5 components in a cosmetic product - and are the basis of the cream.

In this study, a solid phase-extraction method followed by UV spectrophotometry to determine caffeine content in anti-cellulite gels has been developed. The method is linear in the concentration range from 0.01 mg / ml to 0.35 mg / ml; the relative uncertainty of the average result is ± 2.29%). The caffeine concentration found in investigated cellulite reduction cosmetics were in agreement with those reported by other authors and with the expected values.

Conclusions: For the first time, a comparative study of the composition of different types of tools for modeling the figure. Based on the obtained results, recommendations for a safe choice of body shaping products are formulated. A purification of the cosmetics and extraction of the active ingredient can be achieved by using SPE technique. The present results show

the applicability of the proposed SPE procedure for the caffeine extraction from anticellulite gels and its UV-determination, which could be used for the routine analysis of these commercial products.

CHEMICAL-TOXICOLOGICAL INVESTIGATION OF METHADONE

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Keywords: methadon, forensic toxicology, analysis.

Introduction. Today in Ukraine, methadone hydrochloride poisoning is the most dangerous type of poisoning, which is confirmed by the highest number of deaths among other poisonings and the early development of fatal complications. On average, the amount of methadone hydrochloride poisoning is 20% of the total number of treated patients with acute poisoning. Forensic examination of methadone-related deaths shows that most of them were caused by a combination of several toxicologically important substances in which methadone played an important role.

Materials and methods. The object of research is urine of poisoned with methadone persons. The subject of research is modern methods of express diagnosis of acute poisoning. Methods: information monitoring, comparison, systematization and classification of information, analysis of the obtained data, toxic compounds isolation from biological samples, chemical reactions, thin-layer chromatography.

Results. To detect methadone in the urine, reagents were used, which allow to detect the investigated drug by the appearance of a specific colour: Liebermann reagent, Marquis reagent, Froehde reagent, a mixture of sulphate and nitrate acids, and Mandelin reagent. All applied reagents gave a positive result with the investigated urine extract. Thin-layer chromatography technique for detecting methadone in extracts from biological material is proposed. The optimal composition of mobile phase (solvent system) is selected. Using the proposed method of thin layer chromatography, methadone and diphenhydramine in the urine at simultaneous presence was detected.

Conclusions. Using chemical tests and thin-layer chromatography, we were able to identify methadone in a biological sample (urine) of poisoned person.

GENERAL CHARACTERISTICS AND METHODS FOR DETERMINATION OF FLUOROQUINOLONE ANTIBIOTICS

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Keywords: fluoroquinolones, chromatography, detection, quantification, spectrophotometry.

Introduction: Fluoroquinolones possess high antimicrobial activity against both gram-positive and gram-negative microorganisms. However, severe side effects identified in clinical studies has even led to the withdrawal from medical use of a number of fluoroquinolones. In this regard, it becomes necessary to develop an express and accurate method for the quantitative determination of fluoroquinolones in substances, dosage forms and biological samples.

Materials and methods: A systematic search of PubMed and Google Scholar databases for publications on therapeutic monitoring of fluoroquinolones in biological fluids. The following words and phrases were used as key words: “ fluoroquinolones ”, “plasma”, “therapeutic drug monitoring”, “detection” and the names of the respective drugs. For the quantitative determination of fluoroquinolones in substances and dosage forms, the pharmacopoeial method is titration in non-aqueous media, which is characterized by high labor intensity and duration, as well as high toxicity of the reagents used. The method of high performance liquid chromatography has become widespread, but the high cost of one analysis, laboriousness and the need for a highly qualified specialist to work with the chromatograph reduce the possible rate of spread of this method. Analysis of the literature shows that spectrophotometric methods for the quantitative determination of fluoroquinolones have not been sufficiently developed.

Results: The possibility of using solid - phase extraction with modified silica gel on Oasis WCX cartridges to extract fluoroquinolones from biological fluids has been investigated. Mixture of 25% ammonia-methanol solution (1:20, v/v) was used for eluation of fluoroquinolones. The efficiency of isolation of levovloxacin, ofloxacin and norfloxacin from biological fluids was 89.72% for ofloxacin, 89.99% for levofloxacin and 85.64% for ciprofloxacin. Methods for the quantitative determination of fluoroquinolones by UV spectrophotometry have been developed (the method is linear in the concentration range from 0.1 μg / ml to 5.0 μg / ml; the relative uncertainty of the average result is ± 2.29%). The influence of medium pH and concentration on optical density absorption indices was studied.

Conclusions: A fast, easily reproducible UV spectrophotometric method for the determination of fluoroquinolones in substances, dosage forms and plasma samples has been developed. The advantages of UV-spectrophotometry

method include high reproducibility and expressibility. The possibility of application of the developed methods for quantitative determination of fluoroquinolones in blood plasma after solid - phase purification is shown.

CHEMICAL-TOXICOLOGICAL INVESTIGATION OF CLOZAPINE

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Keywords: clozapine, forensic toxicology, analysis.

Introduction. In recent years, there has been an increase in the number of cases of poisoning by antipsychotic drugs, both in the treatment of mental illness and due to their non-medical use due to the large number of relatively available cheap drugs on the pharmaceutical market. One such drug is clozapine. Clozapine poisoning in patients with mental and behavioral disorders is often intentional, although it is accidental - due to incorrect intake or violation of dosage. Poisoning with this drug often occurs against the background of alcohol or drug intoxication, when antipsychotics are taken for self-medication or potentiation of the intoxicating effect. Criminal clozapine poisonings are also very common (up to 99.7% of all criminal poisonings) and have virtually supplanted the previously prevalent clonidine poisoning.

Materials and methods. The object of research is urine of poisoned with clozapine persons. The subject of research is modern methods of express diagnosis of acute poisoning. Methods: information monitoring, comparison, systematization and classification of information, analysis of the obtained data, toxic compounds isolation from biological samples, chemical reactions, thin-layer chromatography.

Results. To detect clozapine in urine, reagents were used, which allow to detect the investigated drug by the appearance of a specific colour: Liebermann reagent, Erdmann reagent, and concentrated nitrate acids. All applied reagents gave a positive result with the investigated urine extract. Thin-layer chromatography technique for detecting clozapine in extracts from biological material is proposed. The optimal composition of mobile phase (solvent system) is selected. Using the proposed method of thin layer chromatography, clozapine in urine was detected.

Conclusions. Using chemical tests and thin-layer chromatography, we were able to identify clozapine in a biological sample (urine) of poisoned person.

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