ABSTRACT&REFERENCES

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RESEARCH ON THE CONSUMPTION OF TWO-COMPONENT FIXED COMBINATIONS OF MEDICINES FOR THE TREATMENT OF ARTERIAL HYPERTENSION IN UKRAINE IN THE PERIOD FROM 2020-2023 AND THE USE OF THE RESULTS IN THE CONTEXT OF OPTIMIZATION OF PHARMACEUTICAL ASSISTANCE AND THE PROSPECTS OF THEIR INCLUSION IN STATE REIMBURSEMENT PROGRAMS

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The aim *to conduct a retrospective study of the consumption of 4 groups of two-component combined drugs for the treatment of arterial hypertension and to determine the structure of their consumption by the number of tablets, , taking into account active substances and their doses, to further formulate proposals to improve the provision of medicines to consumers, in particular through the state reimbursement program "Affordable Medicines".*

Materials and methods: *The objects of the study were retail sales data for the period 2020–2024 on the pharmaceutical market of Ukraine for four groups of combined antihypertensive drugs. The data was provided by the Ukrainian pharmaceutical market research system «Pharmstandard» of the Morion company. The study used statistical and mathematical methods, as well as content analysis, comparative, logical, and systemic analysis, and data generalization.*

Results: *showed that combined drugs of ACE inhibitors and diuretics are the most consumed among all two-component combined drugs for the treatment of hypertension in Ukraine in 2020–2023. By median share of consumption, the following fixed-dose combinations of captopril/HCTZ (50 mg/25 mg) median 29.04%; enalapril/HCTZ (10 mg/25 mg) median 11.74%; lisinopril/HCTZ (10 mg/12.5 mg) median 11.64% and perindopril tertbutylamine with indapamide (8 mg/2.5 mg) –11.42% among ACE inhibitors and diuretics combinations; valsartan/HCTZ (160 mg/12.5 mg (median 40.02%); and 80 mg/12.5 mg (median 29.07%); losartan/HCTZ (50 mg/12.5 mg) median 11.30% among ARB and diuretic combinations; lisinopril/amlodipine (5mg/5mg) median 15.25%; and (10 mg/5 mg) median 11.98% perindopril arginine and amlodipine (5 mg/5 mg) median 13.77%; and perindopril tertbutylamine and amlodipine (4 mg/5 mg) median 11.08%; of all combinations of ACE inhibitors and CCBs; and valsartan/amlodipine, in all three available doses (160 mg/5 mg, 8 0mg/5 mg and 160 mg/10 mg) median 43.71%; 31.36% and 20.32% respectively, among the combinations of ARBs and CCBs had the highest median consumption share in each respective group of combination drugs and were used by patients for the treatment of hypertension in Ukraine in 2020–2024.*

Conclusion: *Retail sales results showed that combined drugs of ACE inhibitors and diuretics, as well as combined drugs of ARBs and diuretics, are the most consumed among all two-component combined drugs for the treatment of hypertension in Ukraine in 2020–2023. Further analysis of the structure of consumption of fixed-dose combinations, considering active substances and their doses, made it possible to determine within each study group those fixed doses that have the highest median consumption share values over four years.*

It is regarding them that we propose conducting further clinical and economic studies on their use in the context of discussing the issue of expanding the list of combined drugs for the treatment of hypertension that are subject to reimbursement in Ukraine

Keywords: *arterial hypertension, marketing and pharmacoeconomic research, optimization of pharmaceutical care, rational use of medicines, socio-economic accessibility, adherence to treatment*

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STRUCTURAL-FRAGMENT ANALYSIS OF ACTIVE PHARMACEUTICAL INGREDIENTS OF ANTIEPILEPTIC DRUGS IN GROUP N03A OF THE UKRAINIAN PHARMACEUTICAL MARKET AND THEIR PHARMACOPHORIC FEATURES

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Epilepsy affects approximately 50 million people globally, with one-third of patients remaining resistant to available therapies, emphasizing the need for new and safer anticonvulsants. Although fragment-based and in silico approaches are effective for drug discovery, a unified structural analysis of antiepileptic APIs on the Ukrainian market remains unexplored.

The aim of the study. *To analyze 16 antiepileptic APIs registered in Ukraine using fragment-based methods to identify shared pharmacophoric features, structural similarities, and correlations between structural fragments and ADME properties (including drug-likeness patterns for structure-property insights) as a basis for rational anticonvulsant design.*

Materials and methods. *Data were collected from the State Register of Medicinal Products of Ukraine and Compendium (June 2025) using ATC code N03A. Literature review used PubMed, PubChem, DrugBank, Scopus, Elicit, and ResearchRabbit. Structural analysis was performed using Python libraries.*

Results. *The study classified 16 active pharmaceutical ingredients (APIs) into structural clusters (e.g., barbiturates, dibenzazepines, amino acid derivatives) based on Tanimoto similarity coefficients and ECFP4 molecular fingerprints. Commonly identified fragments included carbonyl, amino, amide, carboxyl groups, and aromatic rings. ADME profiling revealed consistent relationships between structural features and physicochemical properties: high lipophilicity in benzodiazepines and good absorption characteristics in gabapentinoids. This analysis was performed to identify structure-dependent ADME patterns, providing a basis for fragment-based design of novel anticonvulsants.*

Conclusions. *Despite chemical diversity, the analyzed APIs exhibit shared spatial pharmacophore arrangements with recurring groups supporting activity at NaV, CaV, GABA-A, SV2A, and GABA-T. ADME profiling and structure–property correlations provide a basis for pharmacophore fragment modelling and CNS-oriented fragment-library design to enable rational discovery. Future design should leverage the identified pharmacophoric fragments to build multitarget molecules within a CNS ADME window*

Keywords: *antiepileptic drugs, APIs, FBDD, pharmacophore, structural clustering, ADME, Tanimoto similarity, NaV, GABA-A, SV2A, carbonic anhydrase, Ukrainian pharmaceutical market*

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DOSE-DEPENDENT EFFECTS OF MITOMYCIN C IN NON-HEALING WOUND MODELING

p. 35–42

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Non-healing or chronic wounds are widely distributed complications of several pathologic states. A study of healing mechanisms requires an adequate animal model of such wounds. Use of rodents, one of the most available laboratory animals, is linked with

some problems: wound edge contraction that precedes re-epithelialization. Mitomycin C (MMC), as a pharmacological inhibitor of cell proliferation, can be used in chronic wound modelling.

The aim. *The objective of the research was to create a model of non-healing (chronic) wound by surgically limiting its contraction and inhibiting recovery rate with the pharmaceutical agent mitomycin C (MMC).*

Materials and methods. *Male Balb/c mice were used. Two layers of skin were pierced through, resulting in the simultaneous formation of two wounds (~0.6 cm^3), whose edges were sutured surgically to hinder their contraction. Wounds were additionally treated with 0.5, 1, 2, and 3 mg/ml MMC. The delay of healing was assessed by measuring wound area and by morphological and histological examination.*

Results. *The application of 2 and 3 mg/ml MMC for surgically fortified excision wounds resulted in a significantly increased area by day 21 and 28 compared with groups treated with lower doses. Also, wounds had loci of necrosis and infiltration. Delayed re-epithelialization and irregular collagen fibres were observed histologically after treatment with 2 and 3 mg/ml. Considering the absence of differences between wounds treated with 2 and 3 mg/ml MMC and its potential toxic effects, 2 mg/ml was recommended for non-healing wound modelling.*

Conclusions. *An optimal model of non-healing (chronic) wound was created. The main aspects of the murine model can be outlined as follows: the use of surgical fixation of wound edges to a dense polymer base and treatment with 2 mg/ml MMC*

Keywords: *non-healing wound, chronic wound, mitomycin C, re-epithelialization, scar, fibrous tissue, keratinocytes, endothelial cells, fibroblasts*

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BIOISOSTERIC REPLACEMENT IN THE SEARCH FOR ANTIMICROBIAL AGENTS: DESIGN, SYNTHESIS AND ACTIVITY OF NOVEL 6-(1*H*-BENZIMIDAZOL-2-YL)-1-ALKYL-3,5-DIMETHYLTHIENO[2,3-*d*]PYRIMIDINE-2,4(1*H*,3*H*)-DIONE DERIVATIVES

p. 43–55

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The aim. *To apply the concept of bioisosterism for the structural optimization of benzimidazole–thieno[2,3-d]pyrimidine hybrids aimed at developing effective antibacterial agents as potential inhibitors of the bacterial enzyme TrmD.*

Materials and Methods*. Organic synthesis methods; structure confirmation by ^{1}H, ^{13}C, and HMBC NMR spectroscopy, LC-MS, and elemental analysis. Molecular docking was performed using AutoDock Vina, AutoDockTools 1.5.6, and Discovery Studio Client. Antimicrobial activity was evaluated using the agar diffusion method, and the impact on biofilm formation/disruption was assessed using the crystal violet assay.*

Results and Discussion. *The bioisosteric modification involved oxidation of the thione group in 3,5-dimethyl-4-oxo-2-thioxothieno[2,3-d]pyrimidine-6-carboxylate. The resulting 2,4-dioxothieno[2,3-d]pyrimidine-6-carboxylic acid was activated with 1,1'-carbonyldiimidazole to form a benzimidazole fragment in*

a one-pot procedure. Alkylation of the obtained hybrid with chloroacetamides led to regioselective products confirmed by HMBC. All synthesized compounds demonstrated significant antimicrobial activity against both Gram-positive and Gram-negative test strains. Compound 5c with a 4-ethoxyphenyl substituent processed the highest activity, including effectiveness against clinical strains of S. aureus and P. aeruginosa. Compound 5c also demonstrated notable biofilm disruption capacity against S. aureus, E. coli, P. aeruginosa, and C. albicans. Molecular docking to the TrmD bacterial enzyme confirmed the formation of a hydrogen bond between the 2-oxo group and Glu121.

Conclusions. *An efficient method was developed for the synthesis of a novel series of 2-[6-(1H-benzimidazol-2-yl)-3,5-dimethyl-2,4-dioxo-3,4-dihydrothieno[2,3-d]pyrimidin-1(2H)-yl]-N-arylacetamides. Bioisosteric hybrids showed enhanced antimicrobial properties and improved binding affinity to bacterial TrmD. Compound 5c demonstrated high activity against both Gram-positive and Gram-negative strains, including clinical isolates, as well as the ability to disrupt biofilms, highlighting its potential as a promising lead for further development*

Keywords*: thienpyrimidine, benzimidazole, alkylation, antimicrobial activity, docking*

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DRUG-RELATED PROBLEMS IN COMORBID PATIENTS WITH ANXIETY-DEPRESSIVE DISORDERS

p. 56–64

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Drug-related problems (DRPs) pose a significant threat to patient safety, especially in conditions of comorbidity and polypharmacy. DRPs can manifest as adverse reactions, drug interactions, etc., potentially negatively affecting the effectiveness and safety of treatment. Since most DRPs are potentially predictable if timely detection and correction of pharmacotherapy are provided, the role of the clinical pharmacist is increasing, who can be included in the interdisciplinary team of specialists and, within the framework of pharmaceutical counselling, contribute to their minimization.

The aim: *The aim of our study was to assess the frequency and nature of DRPs in comorbid patients with anxiety and depressive disorders to develop a model of pharmaceutical counselling.*

Materials and methods: *A retrospective analysis of 55 medical histories of comorbid patients who were inpatients in the therapeutic department of a multidisciplinary hospital in Kyiv and were treated for the main disease and anxiety-depressive disorders was conducted. Most patients (67%) had 3–4 concomitant diseases, including anxiety-depressive disorder, in addition to the main one. The analysis of potential drug-drug interactions was carried out using the DrugBank database and official instructions for medical use of medicines.*

Statistical analysis included correlation analysis to assess the relationships between variables and comparison of qualitative indicators using the Pearson χ^2 test. The level of statistical significance was taken as $p < 0.05$. Data processing was carried out using the Microsoft Excel package.

Results: *The total frequency of DRPs per patient was 3.73 ± 2.58, polypharmacy was detected in 84% of patients.*

A significant correlation ($p < 0.05$) was found between the patient's age and the number of comorbid conditions ($r=0.48$), as well as between the patient's age and the number of medications he received ($r = 0.45$).

Patients were significantly more likely to receive benzodiazepines than antidepressants (89.1% vs. 38.2%; Pearson's $\chi^2 = 30.80$, $p < 0.001$).

Conclusions: *Among comorbid patients with anxiety and depressive disorders who were treated in a somatic hospital, a significant prevalence of drug-related problems was found. The number of drugs per course of treatment correlated with the age of the patients. Almost all patients received benzodiazepines, including the majority of elderly patients, which is dangerous due to the risk of increasing cognitive impairment. In addition, clinically significant drug-drug interactions were found in 42% of patients, and in 29% – the prescription of drugs in the presence of restrictions or contraindications. The results of the study emphasize the importance of individualizing pharmacotherapy considering age, comorbidity and potential interactions and justify the need to involve a clinical pharmacist in a multidisciplinary team to minimize the risk of drug-related problems*

Keywords: *drug-related problems, comorbid patients, antidepressants, sedative drugs, polypharmacy*

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PHARMACOLOGICAL EVALUATION AND POTENTIAL EPIGENETIC MODULATION OF A ZINC-CYSTEINE COMPLEX FOR TYPE 2 DIABETES THERAPY

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Type 2 Diabetes (T2D) is a complex metabolic disorder that involves more than just glucose imbalance. Protein glycation, and epigenetic dysregulation – particularly aberrant DNA methylation – play critical roles in the onset and progression of the disease. However, current therapies remain limited in directly targeting these underlying molecular mechanisms.

***The aim**. This study investigated a zinc-monocysteine complex (ZMC) as a potential multi-target therapeutic candidate for T2D, exploring its novel application in modulating protein glycation and DNA methylation events.*

***Materials and methods**. The structural integrity of ZMC was confirmed through NMR, FT-IR, UV-visible, CHN analysis, and powder XRD techniques. In vitro assays compared ZMC and unbound L-cysteine (CYS) for their abilities to inhibit advanced glycation end-products (AGEs) and preserved protein secondary structure under glycation stress, using BSA-glucose and methylglyoxal (MGO) model systems. To support potential epigenetic modulation, molecular docking studies were conducted to evaluate the interaction of ZMC with DNA methyltransferase, DNMT1. Live-cell imaging was performed on C2C12 and HEK293T cells*

to assess changes in methylation-associated signals following ZMC treatment.

***Results**. ZMC was defined structurally as a 1:1 amorphous cyclic salt. It outperformed CYS in inhibiting AGE formation at 5 mM (BSA-glucose) and 1 mM (BSA-MGO). It also better preserved protein secondary structure at 5 mM (BSA-glucose) and 10 mM (BSA-MGO). Although docking suggested limited affinity for DNA methyltransferase (DNMT1: –5.1 kcal/mol) , live-cell imaging indicated reduced methylation-associated signals in especially in C2C12 cells following treatment.*

***Conclusion**. Together, ZMC demonstrates multi-target potential in addressing key metabolic and epigenetic factors involved in T2D. Its protective effects are primarily attributed to metabolic regulation. These findings support the continued development of ZMC as a promising scaffold for future T2D therapeutics*

***Keywords**: type 2 Diabetes, zinc-cysteine complex, AGEs, DNA methylation, molecular docking*

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ANALYSIS OF WORKFORCE STABILITY FACTORS IN PHARMACY ORGANIZATIONS

p. 78-87

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The aim *of this study is to determine the level of need for pharmacists to ensure optimal functioning of pharmacy organizations, as well as to analyze the current state of workforce planning and its impact on the effectiveness of pharmaceutical structures.*

Materials and methods*. A survey of 121 employees of the pharmacy organization in Almaty city (Kazakhstan) using Likert scale was conducted. Pearson's χ^2 criterion was used to analyze the data. The methodology was based on adaptation of Job Satisfaction Survey (JSS), "WISN" method, "360° degree" assessment and Australian Bureau of Statistics (ABS) data. The study was approved by the local ethical committee of Al-Farabi Kazakh National University (Protocol No. IRB-A871).*

Results*. The analysis revealed that staff turnover, workforce replenishment and seasonal shortage of staff are the key problems of retail pharmacy organizations. Significant factors affecting the stability of the workforce composition were identified, and their association with the workplace environment was statistically confirmed.*

Conclusions. *The article examines the factors contributing to staff turnover in retail pharmacy organizations. A structured employee survey was conducted, identifying the primary reasons for resignation, including low wages (18.43%), limited opportunities for career advancement (19.22%), and unfavourable working conditions (31.37%). The findings also indicate that the work environment and management practices significantly influence employee satisfaction. Dynamics highlighted the impact of turnover, workplace conditions, and career prospects on organisational stability. Statistical analysis ($\chi^2 = 13.96$; $p = 0.00019$) confirmed a significant association between the work atmosphere and human resource policies.policies. Optimizing HR strategies is essential to enhanceemployee satisfaction and reduce turnover*

Keywords*: workforce policy, pharmacy organizations, staff turnover, employee satisfaction, survey*

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MORPHOLOGICAL AND SIZE CHARACTERIZATION OF ZINC OXIDE NANOPARTICLES AND EVALUATION OF THEIR CYTOTOXICITY ON THE MCF-7 CELL LINE

p. 88–96

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The aim. *This study aimed to synthesize zinc oxide nanoparticles (ZnO NPs) using a green method based on Scutellaria Iscanderi L. extract and to evaluate their physicochemical properties and in vitro cytotoxic effects on MCF-7 human breast cancer cells.*

Methods. *ZnO nanoparticles were obtained via green synthesis using the aqueous extract of Scutellaria Iscanderi L. as a reducing and stabilizing agent. The morphology, size, and distribution of the nanoparticles were analyzed by atomic force microscopy (AFM), scanning electron microscopy (SEM), and dynamic light scattering (DLS). Elemental composition was determined by SEM-EDX. Cytotoxic activity was assessed using the CCK-8 assay on MCF-7 breast adenocarcinoma cells.*

Results. *The synthesized ZnO NPs exhibited predominantly spherical morphology with a size range of 40–120 nm. DLS measurements showed a mean particle diameter of ~40 nm and a polydispersity index of 0.3, indicating good colloidal stability. EDX confirmed the presence of zinc with a content of 6.87% by mass. Cytotoxicity analysis revealed a dose-dependent reduction in cell viability, with an IC_{50} value of 126.4 μg/mL.*

Conclusion. *Green-synthesized ZnO nanoparticles demonstrated favorable structural characteristics and moderate cytotoxic effects against MCF-7 cells. These findings suggest their potential application as a basis for further development of anticancer nanotherapeutics*

Keywords: *zinc oxide nanoparticles, green synthesis, Scutellaria Iscanderi, breast cancer, MCF-7, cytotoxicity, atomic force microscopy (AFM), scanning electron microscopy (SEM), dynamic light scattering (DLS)*

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АНОТАЦІЇ

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ДОСЛІДЖЕНЬ СПОЖИВАННЯ ДВОКОМПОНЕНТНИХ ФІКСОВАНИХ КОМБІНАЦІЙ ЛІКАРСЬКИХ ЗАСОБІВ ДЛЯ ЛІКУВАННЯ АРТЕРІАЛЬНОЇ ГІПЕРТЕНЗІЇ У ПЕРІОД З 2020-2023 РОКИ В УКРАЇНІ ТА ВИКОРИСТАННЯ РЕЗУЛЬТАТІВ В КОНТЕКСТІ ОПТИМІЗАЦІЇ ФАРМАЦЕВТИЧНОЇ ДОПОМОГИ ТА ПЕРСПЕКТИВИ ЇХ ВКЛЮЧЕННЯ В ДЕРЖАВНІ ПРОГРАМИ РЕІМБУРСАЦІЇ (с. 4–19)

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Мета: *провести ретроспективне дослідження споживання 4 груп двокомпонентних комбінованих лікарських засобів лікарських засобів для лікування артеріальної гіпертензії та визначити структуру їх споживання за кількістю таблеток, з урахуванням діючих речовин та їх доз, задля подальшого формування пропозицій щодо удосконалення забезпечення споживачів лікарськими засобами, зокрема через державну програму реімбурсації «Доступні ліки».*

Матеріали та методи: *об'єктами дослідження були дані роздрібних продажів за період 2020–2024 років на фармацевтичному ринку України чотирьох груп комбінованих антигіпертензивних лікарських засобів. Дані були надані системою вивчення фармацевтичного ринку України «Фармстандарт» компанії «Моріон». У дослідженні використовувались статистично-математичні методи, а також контент-аналізу, порівняльного, логічного та системного аналізу та узагальнення даних.*

Результати *показали, що комбіновані ЛЗ іАПФ та діуретиків є найбільш споживаними серед всіх двокомпонентних комбінованих ЛЗ для лікування АГ в Україні в 2020–2023 роках. За медіаною частки споживання, наступні фіксовані дози комбінацій каптоприл/ГХТЗ (50 mg/25 mg) медіана 29,04%; еналаприл/ГХТЗ (10 mg/25 mg) медіана 11,74%; лізиноприл/ГХТЗ (10 mg/12,5 mg) медіана 11,64% та периндоприл тертбутиламін з індапамідом (8 mg/2,5 mg) – 11,42% поміж комбінацій іАПФ та діуретиків; валсартан/ГХТЗ (160 mg/12,5 mg (медіана 40,02%); та 80 mg/12,5 mg (медіана 29,07%;); лозартан/ГХТЗ (50 mg/12,5 mg) медіана 11,30% серед комбінацій БРА та діуретиків; лізиноприл/амлодипін (5 mg/5 mg) медіана 15,25%; та (10 mg/5 mg) – медіана 11,98% периндоприл аргінін та амлодипін (5 mg/5 mg) медіана 13,77%; та периндоприл тертбутиламін та амлодипін (4 mg/5 mg) медіана 11,08%; зі всіх комбінацій іАПФ та БКК; а також валсартан/амлодипін, в усіх трьох наявних дозах (160 mg/5 mg, 80 mg/5 mg and 160 mg/10 mg) медіана 43,71%; 31,36% та 20,32% відповідно, серед комбінацій БРА та БКК мали найвищі показники медіани частки споживання в кожній відповідній групі комбінованих ЛЗ та використовувались пацієнтами для лікування АГ в Україні в 2020–2024 роках.*

Висновки: *Результати роздрібних продажів показали, що комбіновані ЛЗ іАПФ та діуретиків, а також комбіновані ЛЗ БРА та діуретики є найбільш споживаними серед всіх двокомпонентних комбінованих ЛЗ для лікування АГ в Україні в 2020–2023 роках. Подальший аналіз структури споживання фіксованих доз комбінацій, з урахуванням діючих речовин та їх доз, дозволило визначити в всередині кожній досліджуваній групі ті фіксовані дози, які мають найбільші значення медіани частки споживання за чотири роки. Саме щодо них ми пропонуємо проведення подальших клініко-економічних досліджень щодо їх використання в контексті обговорення питання щодо розширення ними переліку комбінованих ЛЗ для лікування АГ, які підлягають реімбурсації в Україні*

Ключові слова: *артеріальна гіпертензія, маркетингові та фармакоекономічні дослідження, оптимізація фармацевтичної допомоги, раціональне використання ліків, соціально-економічна доступність, прихильність до лікування*

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СТРУКТУРНО-ФРАГМЕНТНИЙ АНАЛІЗ ДІЮЧИХ РЕЧОВИН ПРОТИЕПІЛЕПТИЧНИХ ПРЕПАРАТІВ ГРУПИ N03A НА ФАРМАЦЕВТИЧНОМУ РИНКУ УКРАЇНИ ТА ЇХ ФАРМАКОФОРНІ ОСОБЛИВОСТІ (с. 20–34)

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Епілепсією страждають близько 50 мільйонів людей у світі, при цьому приблизно третина пацієнтів залишається резистентною до наявної терапії, що підкреслює потребу в розробці нових і безпечніших протисудомних засобів. Попри ефективність фрагментно-орієнтованих і in silico підходів у створенні ліків, уніфікований структурний аналіз АФІ протиепілептичних засобів, зареєстрованих на фармацевтичному ринку України, досі не проводився.

Мета дослідження. *Провести фрагментно-орієнтований аналіз 16 протиепілептичних АФІ, зареєстрованих в Україні, з метою виявлення спільних фармакофорних ознак, структурної подібності та кореляцій між структурними фрагментами та ADME-параметрами (включаючи «drug-likeness» для розуміння структури та властивостей) з метою подальшого раціонального дизайну нових протисудомних препаратів.*

Матеріали і методи. *Дані отримано з Державного реєстру лікарських засобів України та ресурсу «Compendium» (станом на червень 2025 р.) за кодом ATC N03A. Огляд літератури здійснено через PubMed, PubChem, DrugBank, Scopus, Elicit та ResearchRabbit. Структурний аналіз проведено з використанням бібліотек Python.*

Результати. *У дослідженні 16 АФІ були класифіковані за структурною подібністю (наприклад, барбітурати, дибензазепіни, похідні амінокислот) на основі коефіцієнтів схожості Танімото та молекулярних відбитків ECFP4. Найбільш поширеними фрагментами виявлено карбонільні, аміно-, амідні, карбоксильні групи та ароматичні кільця. ADME-аналіз показав чіткі зв'язки між структурними ознаками й фізико-хімічними властивостями: високу ліпофільність бензодіазепінів, добру абсорбцію у габапентиноїдів. Цей аналіз був проведений для виявлення структурно-залежних патернів ADME-властивостей як основа для фрагментно-орієнтованого дизайну нових протисудомних засобів.*

Висновки. *Незважаючи на структурну різноманітність, досліджені АФІ демонструють конвергентне просторове розташування ключових фармакофорів, що забезпечують взаємодію з NaV, CaV, GABA-A, SV2A та GABA-T. ADME профілювання та кореляції між структурою і властивостями забезпечують міцну основу для моделювання фармакофору та проектування бібліотеки фрагментів, орієнтованої на ЦНС, що дозволить раціонально відкривати нові протисудомні засоби. Майбутнє проектування повинно використовувати ідентифіковані фармакофорні фрагменти для створення молекул з множинною мішенню в межах вікна ADME ЦНС*
Ключові слова: *протиепілептичні препарати, активні фармацевтичні інгредієнти, фрагментно-орієнтований дизайн ліків (FBDD), фармакофор, структурна кластеризація, ADME, коефіцієнт Танімото, натрієві канали (NaV), рецептор GABA-A, білок SV2A, карбонгідраза, фармацевтичний ринок України*

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ДОЗОЗАЛЕЖНІ ЕФЕКТИ МІТОМІЦИНУ С У МОДЕЛЮВАННІ РАНИ, ЩО НЕЗАГОЮЄТЬСЯ (с. 35–42)

О. В. Пахомов, О. Б. Ревенко, Д. В. Черкашина, Г. А. Божок, Н. А. Труфанова, С. П. Мазур, О. Ю. Петренко

Формування ран, що не загоюються, або хронічних ран є поширеним ускладненням ряду патологічних станів. Для вивчення механізмів загоєння необхідна адекватна тваринна модель таких ран. Використання гризунів – одних із найпоширеніших лабораторних тварин – пов'язане з певними труднощами, зокрема скороченням країв рани, що передує реепітелізації. Мітоміцин С (ММС) як фармакологічний інгібітор проліферації клітин може бути використаний у моделюванні хронічних ран.
Мета. *Створити модель рани, що не загоюється (або хронічної рани) шляхом хірургічного обмеження її скорочення та уповільнення процесу відновлення за допомогою фармацевтичного агента мітоміцину С (ММС).*
Матеріали та методи. *Було використано самців мишей лінії Balb/c. Було створено дві ексцизійні рани, за рахунок проколу шарів шкіри (~0,6 см^3), краї яких хірургічно фіксували з метою попередження їх скорочення. Рани додатково обробляли розчинами ММС у концентраціях 0,5, 1, 2 та 3 мг/мл. Затримку загоєння оцінювали шляхом вимірювання площі рани, а також за допомогою морфологічного та гістологічного дослідження.*
Результати. *Застосування 2 та 3 мг/мл ММС до хірургічно укріплених ексцизійних ран призводило до значного збільшення площі рани на 21-й та 28-й день порівняно з групами, які отримували менші дози препарату. Також у цих ранах спостерігалися осередки некрозу та інфільтрації. Гістологічно після обробки 2 та 3 мг/мл відзначалася затримка реепітелізації та наявність нерівномірно розташованих волокон колагену. З огляду на відсутність істотних відмінностей між групами, що отримували 2 та 3 мг/мл ММС, а також потенційну токсичність вищої дози, для моделювання незагойної рани рекомендовано використовувати концентрацію 2 мг/мл.*
Висновки. *Було створено оптимальну модель рани, що не загоюється (хронічної рани). Основні характеристики моделі з використанням мишей включають хірургічну фіксацію країв рани до щільної полімерної основи та обробку 2 мг/мл ММС*
Ключові слова: *рана, що не загоюється, хронічна рана, мітоміцин С, реепітелізація, рубець, фіброзна тканина, кератиноцити, ендотеліальні клітини, фібробласти*

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БІОІЗОСТЕРНА ЗАМІНА В ПОШУКУ АНТИМІКРОБНИХ АГЕНТІВ: ДИЗАЙН, СИНТЕЗ ТА АКТИВНІСТЬ НОВИХ ПОХІДНИХ 6-(1H-БЕНЗІМІДАЗОЛ-2-ІЛ)-1-АЛКІЛ-3,5-ДИМЕТИЛТІЄНО[2,3-D]ПІРИМІДИН-2,4(1H,3H)-ДІОНУ (с. 43–55)

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Мета. *Застосувати концепцію біоізостеризму для структурної оптимізації гібридів бензімідазол-тієно[2,3-d]піримідину з метою створення ефективних антибактеріальних агентів як потенційних інгібіторів бактеріального ферменту TrmD.*
Матеріали та методи. *Методи органічного синтезу, доведення будови –^{1}H, ^{13}C, HMBC ЯМР спектроскопія, LC-MS, елементний аналіз. Молекулярний докінг – AutoDock Vina та AutoDockTools 1.5.6, DiscoveryStudioClient. Визначення антимікробної активності (метод дифузії в агар, дослідження впливу на формування/руйнування біоплівок – кристал-фіолетовий метод). Результати і обговорення. Біоізостерну заміну проведено окисненням тіонної групи 3,5-диметл-4-оксо-2-тіоксо-тієно[2,3-d]піримідин-6-карбоксилату. Одержану 2,4-діоксотієно[2,3-d]піримідин-6-карбонову кислоту активували за допомогою 1,1'-карбоніл-діімідазолу у якості пептидного каплінгового реагенту, в умовах одностадійної процедури сформовано фрагмент бензімідазолу. Алкілування одержаного гібриду хлороацетамідами дало регіоселективні продукти, що підтверджено методом HMBC. Усі синтезовані сполуки продемонстрували значну антимікробну активність проти грампозитивних і грамнегативних тест-штамів. Найвищу активність виявлено для похідної 5c із 4-етоксифенільним замісником, зокрема і проти клінічних штамів S. aureus та P. aeruginosa. Встановлено здатність 5c до руйнування біоплівок на рівні S. aureus, E. coli, P. aeruginosa, C. albicans. Докінгове дослідження до бактеріального ферменту TrmD підтвердило формування водневого зв'язку між 2-оксогрупою та Glu121.*
Висновки. *Розроблено ефективний метод синтезу нової серії 2-[6-(1H-бензімідазол-2-іл)-3,5-диметил-2,4-діоксо-3,4-дигідротієно[2,3-d]піримідин-1(2H)-іл]-N-арилацетамідів. Доведено підвищення протимікробних властивостей та афінності до бактеріальної TrmD біоізостеричних гібридів. Виявлено ефективність сполуки 5c щодо грампозитивних і грамнегативних*

штамів, включаючи клінічні ізоляти, а також здатність руйнувати біоплівки, що підкреслює її потенціал як кандидата для подальшої розробки

Ключові слова: *тієнопіримідин, бензімідазол, алкілування, протимікробна активність, докінг*

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ЛІКОПОВ'ЯЗАНІ ПРОБЛЕМИ У КОМОРБІДНИХ ПАЦІЄНТІВ З ТРИВОЖНО-ДЕПРЕСИВНИМИ РОЗЛАДАМИ (с. 56–64)

К. С. Гоштинар, М. В. Хайтович, О. В. Криванич, В. С. Потаскалова

Лікопов'язані проблеми (ЛПП) становлять суттєву загрозу безпеці пацієнтів, особливо в умовах коморбідності та поліпрагмазії. ЛПП можуть виявлятись небажаними реакціями, взаємодією лікарських засобів тощо, потенційно негативно впливаючи на ефективність та безпеку лікування. Оскільки більшість ЛПП є потенційно передбачуваними за умови своєчасного виявлення та корекції фармакотерапії, зростає роль клінічного фармацевта, який може бути включений в міждисциплінарну команду спеціалістів і в рамках фармацевтичного консультування сприяти їх мінімізації.

Мета: *Метою нашого дослідження було оцінити частоту та характер ЛПП у коморбідних пацієнтів з тривожно-депресивними розладами для формування моделі фармацевтичного консультування.*

Матеріали та методи: *Був проведений ретроспективний аналіз 55 історій хвороб коморбідних пацієнтів, які знаходились на стаціонарному лікуванні у терапевтичному відділенні багатопрофільної лікарні м. Києва і отримували лікування основного захворювання та тривожно-депресивних розладів. Більшість пацієнтів (67%) мали крім основного 3–4 супутні захворювання, в тому числі тривожно-депресивний розлад.*

Аналіз потенційних міжмедикаментозних взаємодій проводився з використанням бази даних DrugBank та офіційних інструкцій для медичного застосування лікарських засобів.

Статистичний аналіз включав кореляційний аналіз для оцінки взаємозв'язків між змінними та порівняння якісних показників за допомогою χ^2-критерію Пірсона. Рівень статистичної значущості приймався за $p<0,05$. Обробку даних здійснювали із використанням пакету Microsoft Excel.

Результати: *Загальна частота ЛПП на 1 пацієнта склала 3.73±2.58, поліпрагмазії виявлено у 84% пацієнтів.*

Виявлено достовірний кореляційний зв'язок ($p<0,05$) між віком пацієнта і кількістю коморбідних станів ($r=0,48$), а також між віком пацієнта і кількістю лікарських засобів, які він отримував ($r=0,45$),

Достовірно частіше пацієнти отримували бензодіазепіни, ніж антидепресанти (89,1% проти 38,2%; χ^2 Пірсона = 30.80, $p < 0,001$).

Висновки: *Серед коморбідних пацієнтів із тривожно-депресивними розладами, які перебували на лікуванні у соматичному стаціонарі, виявлено значну поширеність лікопов'язані проблем. Кількість лікарських засобів на курс лікування корелювала з віком пацієнтів. Практично всі пацієнти отримували бензодіазепіни, в тому числі більшість пацієнтів похилого віку, що є небезпечним через небезпеку наростання когнітивних порушень. Крім того, у 42% пацієнтів виявлено клінічно значущі міжмедикаментозні взаємодії, а у 29% — призначення препаратів при наявності обмежень або протипоказань. Результати дослідження акцентують важливість індивідуалізації фармакотерапії з урахуванням віку, коморбідності й потенційних взаємодій та обґрунтовують необхідність залучення клінічного фармацевта до мультидисциплінарної команди для мінімізації ризику виникнення лікопов'язаних проблем*

Ключові слова: *лікопов'язані проблеми, коморбідність, антидепресанти, заспокійливі препарати, поліпрагмазія*

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ФАРМАКОЛОГІЧНА ОЦІНКА ТА ПОТЕНЦІАЛЬНА ЕПІГЕНЕТИЧНА МОДУЛЯЦІЯ ЦИНК-ЦИСТЕЇНОВОГО КОМПЛЕКСУ ДЛЯ ТЕРАПІЇ ЦУКРОВОГО ДІАБЕТУ 2 ТИПУ(с. 65–77)

Godzelle Ogoc Bulahan, Orlie B. Basalo, Hajime Iwamoto, Aaron L. Degamon, James V. Lavilla Jr., Richemae Grace R. Lebosada, Charlie A. Lavilla Jr.

Діабет 2 типу (ЦД2) – це складне метаболічне захворювання, яке включає не лише дисбаланс глюкози. Глікування білків та епігенетична дисрегуляція, зокрема аберантне метилювання ДНК, відіграють вирішальну роль у виникненні та прогресуванні захворювання. Однак сучасні методи лікування залишаються обмеженими у безпосередньому впливі на ці основні молекулярні механізми.

Мета. *У цьому дослідженні досліджували цинк-моноцистеїновий комплекс (ЦМК) як потенційного багатоцільового терапевтичного кандидата для лікування ЦД2, досліджуючи його нове застосування в модуляції подій глікування білків та метилювання ДНК.*

Матеріали та методи*. Структурну цілісність ЦМК було підтверджено за допомогою методів ЯМР, ІЧ-спектроскопії з перетворенням Фур'є, УФ-видимого випромінювання, аналізу CHN та порошкової рентгенівської дифракції. В аналізах in vitro порівнювали ЦМК та незв›язаний L-цистеїн (CYS) щодо їхньої здатності інгібувати кінцеві продукти глікування (AGE) та зберігати вторинну структуру білка в умовах глікаційного стресу, використовуючи модельні системи BSA-глюкоза та метилгліоксаль (MGO). Для підтвердження потенційної епігенетичної модуляції були проведені дослідження молекулярного докінгу для оцінки взаємодії ЦМК з ДНК-метилтрансферазою, DNMT1. Було проведено візуалізацію живих клітин на клітинах C2C12 та HEK293T для оцінки змін сигналів, пов'язаних з метилюванням, після обробки ЦМК.*

Результати. *Структурно ЦМК було визначено як аморфну циклічну сіль 1:1. Вона перевершила CYS в інгібуванні утворення AGE при 5 мМ (BSA-глюкоза) та 1 мМ (BSA-MGO). Вона також краще зберігала вторинну структуру білка при 5 мМ (BSA-глюкоза) та 10 мМ (BSA-MGO). Хоча докінг свідчив про обмежену спорідненість до ДНК-метилтрансферази (DNMT1: –5,1 ккал/моль), візуалізація живих клітин показала зниження сигналів, пов'язаних з метилюванням, особливо в клітинах C2C12 після обробки.*
Висновки. *Разом ЦМК демонструє багатоцільовий потенціал у вирішенні ключових метаболічних та епігенетичних факторів, що беруть участь у розвитку цукрового діабету 2 типу. Його захисні ефекти в першу чергу пояснюються метаболічною регуляцією. Ці результати підтверджують подальший розвиток ЦМК як перспективної основи для майбутньої терапії цукрового діабету 2 типу*
Ключові слова: *діабет 2 типу, цинк-моноцистеїновий комплекс, AGEs, метилювання ДНК, молекулярний докінг*

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АНАЛІЗ ФАКТОРІВ СТАБІЛЬНОСТІ РОБОЧОЇ СИЛИ В АПТЕЧНИХ ОРГАНІЗАЦІЯХ (с. 78–87)

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Метою *цього дослідження є визначення рівня потреби у фармацевтах для забезпечення оптимального функціонування аптечних організацій, а також аналіз поточного стану планування робочої сили та його впливу на ефективність фармацевтичних структур.*
Матеріали та методи. *Було проведено опитування 121 співробітника аптечної організації в місті Алмати (Казахстан) за шкалою Лікерта. Для аналізу даних використовувався критерій χ^2 Пірсона. Методологія базувалася на адаптації Опитування щодо задоволеності роботою (JSS), методу «WISN», оцінки «360° градусів» та даних Австралійського бюро статистики (ABS). Дослідження було схвалено місцевим етичним комітетом Казахського національного університету імені аль-Фарабі (протокол № IRB-A871).*
Результати. *Аналіз показав, що плинність кадрів, поповнення робочої сили та сезонний дефіцит персоналу є ключовими проблемами роздрібних аптечних організацій. Було виявлено суттєві фактори, що впливають на стабільність складу робочої сили, та статистично підтверджено їх зв›язок з умовами робочого місця.*
Висновки. *У статті розглядаються фактори, що сприяють плинності кадрів у роздрібних аптечних організаціях. Було проведено структуроване опитування працівників, в результаті якого були визначені основні причини звільнення, включаючи низьку заробітну плату (18,43%), обмежені можливості кар›єрного зростання (19,22%) та несприятливі умови праці (31,37%). Результати також вказують на те, що робоче середовище та управлінські практики суттєво впливають на задоволеність працівників. Динаміка дослідження висвітлила вплив плинності кадрів, умов на робочому місці та кар›єрних перспектив на стабільність організації. Статистичний аналіз ($\chi^2 = 13,96$; $p = 0,00019$) підтвердив значний зв›язок між робочою атмосферою та політикою управління персоналом. Оптимізація HR-стратегій є важливою для підвищення задоволеності працівників та зменшення плинності кадрів*
Ключові слова: *кадрова політика, аптечні організації, плинність кадрів, задоволеність працівників, опитування*

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МОРФОЛОГІЧНА ТА РОЗМІРНА ХАРАКТЕРИЗАЦІЯ НАНОЧАСТИНОК ОКСИДУ ЦИНКУ ТА ОЦІНКА ЇХ ЦИТОТОКСИЧНОСТІ НА КЛІТИННІЙ ЛІНІЇ MCF-7 (с. 88–96)

Iroda Shermatova Bakhtiyor kizi, Shamansur Sagdullayev Shakhsaidovich, Azizakhon Khusniddinova Ravshan kizi, Gulrano Akhmadova, Nargiza Rajabova Khalimovna, Dilobar Tayirova Bakhtiyarovna

Мета. *Метою цього дослідження було синтезувати наночастинки оксиду цинку (ZnO NP) за допомогою екологічно чистого методу на основі екстракту Scutellaria Iscanderi L. та оцінити їхні фізико-хімічні властивості та цитотоксичну дію in vitro на клітини раку молочної залози людини MCF-7.*
Методи. *Наночастинки ZnO були отримані за допомогою екологічно чистого синтезу з використанням водного екстракту Scutellaria Iscanderi L. як відновлювального та стабілізуючого агента. Морфологію, розмір та розподіл наночастинок аналізували за допомогою атомно-силової мікроскопії (АСМ), скануючої електронної мікроскопії (СЕМ) та динамічного розсіювання світла (ДРС). Елементний склад визначали за допомогою СЕМ-ЕДХ. Цитотоксичну активність оцінювали за допомогою аналізу CCK-8 на клітинах аденокарциноми молочної залози MCF-7.*
Результати. *Синтезовані наночастинки ZnO демонстрували переважно сферичну морфологію з діапазоном розмірів 40–120 нм. Вимірювання ДРС показали середній діаметр частинок ~40 нм та індекс полідисперсності 0,3, що свідчить про добру колоїдну стабільність. EDX підтвердив наявність цинку з вмістом 6,87% за масою. Аналіз цитотоксичності виявив дозозалежне зниження життєздатності клітин зі значенням IC_{50} 126,4 мкг/мл.*
Висновки. *Зелений синтез наночастинок ZnO продемонстрував сприятливі структурні характеристики та помірний цитотоксичний ефект проти клітин MCF-7. Ці результати свідчать про їх потенційне застосування як основи для подальшого розвитку протипухлинної нанотерапії*
Ключові слова: *наночастинки оксиду цинку, зелений синтез, Scutellaria Iscanderi, рак молочної залози, MCF-7, цитотоксичність, атомно-силова мікроскопія (АСМ), скануюча електронна мікроскопія (СЕМ), динамічне розсіювання світла (ДРС)*