ABSTRACT&REFERENCES

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CHARACTERISTICS OF THE STRUCTURE AND COMPOSITION OF THE OROPHARYNGEAL MICROBIOTA IN PATIENTS WITH ACUTE TONSILLITIS DEPENDING ON SMOKING STATUS

p. 4-9

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The aim *of the study was to compare alpha and beta diversity indices, assess the overall structure and identify taxa of the oropharyngeal microbiota in patients with acute tonsillitis under the influence of smoking.*
Materials and methods. *54 samples of oropharyngeal swabs from patients with acute tonsillitis were analyzed, which were divided into groups, namely Group 1 (26 people), who smoked, and Group 2 (28 people), who did not smoke. To assess alpha diversity, the Shannon, Simpson, Pielu, Fisher and Chao-1 indices were used, for beta diversity, the Whittaker, Harrison, Wilson-Schmidt and Bray-Curtis indices. The PAST v.4.03 program was used with PERMANOVA, ANOSIM (9999 permutations) and SIMPER statistical analysis.*
Results. *Analysis of the results of alpha-diversity indices did not reveal statistically significant differences between groups ($p > 0.05$). The results of beta-diversity indices demonstrated a greater diversity of microbial communities in group 1 (smokers) (Whittaker indices 3.59 vs. 3.05; Harrison indices 0.33 vs. 0.28). The results of multivariate analyses (PERMANOVA, ANOSIM) did not reveal statistically significant differences in the structure of the microbiome of patients with tonsillitis ($p > 0.05$). SIMPER analysis demonstrated that α-hemolytic streptococci (20.28%), Neisseria spp. (19.59%) belong to taxa responsible for 74.58% of the total intergroup differentiation of the oropharynx, however, they show different colonization densities (5.15 in smokers vs. 4.96 in non-smokers for α-hemolytic Streptococcus spp. and 1.50 in smokers vs. 2.21 in non-smokers for Neisseria spp.)*
Conclusion. *Regardless of smoking status, the oropharyngeal microbiota of patients with acute tonsillitis is characterized by taxa similarity. However, in patients who smoke, increased variability of microbial communities is observed, in particular, a decrease in commensal bacteria of the genus Corynebacterium spp., a tendency to increase β-hemolytic streptococci and the appearance of fungi of the genus Candida spp., which may affect the course of the inflammatory process*
Keywords: *tonsillitis; oropharyngeal microbiota; smoking; alpha diversity; beta diversity; dysbiosis; PERMANOVA; SIMPER analysis*

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EVOLUTION OF INSULIN PRODUCTION TECHNOLOGIES: FROM HISTORICAL DISCOVERIES OF THE MOLECULE STRUCTURE TO MODERN INNOVATIONS

p. 10–31

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The aim *of the study is to assess the current state of the pharmaceutical market for insulins, including historical stages of studying the structure of the insulin molecule and its properties, which formed the basis for the development of commercial preparations and analogs, as well as analysis of promising biotechnological approaches to improve the treatment of diabetes mellitus (DM).*

Materials and methods. *The materials used were scientific publications, official websites of manufacturing companies, FDA and EMA databases, clinical trial registries. Methods of content analysis, comparative, analytical, and generalization of information were applied.*

Results and discussion. *The results indicate that recombinant insulin preparations (from rapid-acting analogs to long-acting ones) provide better glycemic control but are limited by high development and production costs. Innovations include combined preparations with GLP-1 agonists, glucose-sensitive insulins, and oral forms, which face bioavailability challenges.*

Conclusions. *The analysis points to the evolution of insulin production technologies from determining the molecule structure and implementing recombinant DNA technologies, which enabled the transition to human recombinant preparations and analogs. The market offers preparations with various profiles (from ultra-rapid to ultra-long), including biphasic mixtures, improving glycemic control. Combinations of insulin with GLP-1 agonists, amylin analogs (pramlintide), and the development of glucose-sensitive insulins have potential for personalized therapy but are limited by technical challenges (stability, biocompatibility). Oral forms face low bioavailability, but the use of nanotechnology and effective excipients opens prospects for improving accessibility and effectiveness of DM treatment*

Keywords: *Insulin, recombinant DNA technologies, biosimilars, insulin analogs, oral delivery systems*

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STRATEGIES FOR COMBATING ANTIBIOTIC RESISTANCE: SEEKING NEW SOLUTIONS

p. 32–39

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The aim: *study of innovative world strategies of fight with antibiotic resistance.*
Materials and methods. *The study was conducted by analyzing available scientific literature, open sources in the databases Google Scholar, PubMed, Clarivate, Web of Science, Scopus, etc., as well as the results of our own research.*
The results. *The Global Action Plan on Antimicrobial Resistance, developed by WHO, was approved in 2015, and in 2023, it was found that 134 out of 194 countries, including Ukraine, which is 69% of the world's countries, had officially adopted national action plans. However, today there are difficulties in effective communication between all countries and the full implementation of the Global Plan, national action plans due to the fact that developing countries have limited resources for the necessary measures. Antibiotic-resistant bacteria and antibiotic resistance genes are extremely dangerous for human health, which can be compared to a time bomb. Therefore, the fight against antimicrobial resistance requires the consolidation of the work of various industries and should be based on the following areas: the development of partnership programs to optimize the use of antibiotics; the introduction of effective intelligent control and prevention systems; financing programs for the development of new antimicrobial drugs and alternative treatment methods; increased control and intensification of monitoring of the development and spread of resistant microorganisms.*
Conclusions. *The main reservoirs of antibiotic-resistant bacteria and resistance genes are livestock farms, hospitals, sewage treatment plants and agricultural lands, so the strategy to combat antibiotic resistance should be based primarily on One Health approaches. The solutions proposed by scientists to combat antimicrobial resistance – new antibiotics; pro-, pre-, symbiotic drugs; enzymes for the destruction of biofilms, adhesion inhibitors and associated therapy with adjuvants or phages – have a positive effect, but currently still require regulatory intervention for large-scale use. Effective control of antimicrobial resistance requires investment, training of specialists, raising public awareness, comprehensive policies and regulatory systems that ensure a balance between public health protection and the appropriate use of antibiotics*
Keywords: *antimicrobial drugs, antibiotic resistance, «One Health», resistant bacteria, biofilms, adjuvants, CRISPR-Cas system*

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АНОТАЦІЇ

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ХАРАКТЕРИСТИКА СТРУКТУРИ ТА СКЛАДУ МІКРОБІОТИ РОТОГЛОТКИ У ПАЦІЄНТІВ ІЗ ГОСТРИМ ТОНЗИЛІТОМ ЗАЛЕЖНО ВІД СТАТУСУ КУРІННЯ (С. 4–9)

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Мета *дослідження – порівняння індексів альфа- та бета-різноманіття, оцінка загальної структури та ідентифікація таксонів мікробіоти ротоглотки у пацієнтів з гострим тонзилітом під впливом куріння.*

Матеріали і методи. *Проведено аналіз 54 зразків мазків з ротоглотки пацієнтів з гострим тонзилітом, які були розділені на групи, а саме Група 1 (26 осіб), які курили, та Група 2 (28 осіб), які не курили. Для оцінки альфа-різноманіття використовували індекси Шеннона, Сімпсона, Пієлу, Фішера та Чао-1, для бета-різноманіття, індекси Віттекера, Гаррісона, Вілсона-Шміди та Брея-Кертіса. Використовували програму PAST v.4.03 з використанням аналізів PERMANOVA, ANOSIM (9999 пермутацій) та статистичний аналіз SIMPER.*

Результати. *Аналіз результатів індексів альфа-різноманіття не виявив статистично значущих відмінностей між групами (p > 0,05).Результати індексів бета-різноманіття продемонстрували більшу різноманітність мікробних спільнот у групі 1 (курці) (індекси Віттекера 3,59 проти 3,05; індекси Гаррісона 0,33 проти 0,28). Результати проведеного мультиваріантних аналізів (PERMANOVA, ANOSIM) не виявили статистично значущих відмінностей у структурі мікробіому пацієнтів хворих на тонзиліт (p > 0,05). SIMPER-аналізом продемонстрував, що α-гемолітичні стрептококи (20,28%), Neisseria spp. (19,59%) належать до таксонів, що відповідають за 74,58% загальної міжгрупової диференціації ротоглотки , однак, демонструють різну щільність колонізації (5,15 у курців проти 4,96 у некурців для α-гемолітичного Streptococcus spp. та 1,50 у курців проти 2,21 у некурців для Neisseria spp.).*

Висновки. *Незалежно від статусу куріння, мікробіота ротоглотки пацієнтів з гострим тонзилітом характеризується схожістю таксонів. Проте, у пацієнтів ,що курять спостерігається підвищена варіабельність мікробних спільнот, зокрема зменшення коменсальних бактерій роду Corynebacterium spp., тенденція до збільшення β-гемолітичних стрептококів та поява грибів роду Candida spp., які можуть вплинути на хід запального процесу*

Ключові слова: *тонзиліт, мікробіота ротоглотки, куріння, альфа-різноманіття, бета-різноманіття, дисбіоз, PERMANOVA, SIMPER-аналіз*

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ЕВОЛЮЦІЯ ТЕХНОЛОГІЙ ВИРОБНИЦТВА ІНСУЛІНУ: ВІД ІСТОРИЧНИХ ВІДКРИТТІВ СТРУКТУРИ МОЛЕКУЛИ ДО СУЧАСНИХ ІННОВАЦІЙ (с. 10–31)

О. С. Калюжная, Н. В. Хохленкова

Метою *дослідження є оцінка сучасного стану фармацевтичного ринку інсулінів, включаючи історичні етапи вивчення структури молекули інсуліну та її властивостей, які лягли в основу розробки комерційних препаратів та аналогів, а також аналіз перспективних біотехнологічних підходів для покращення лікування цукрового діабету (ЦД).*

Матеріали та методи. *Матеріалами слугували наукові публікації офіційні сайти компаній-виробників, бази FDA та EMA, реєстри клінічних досліджень. Застосовувалися методи контент-аналізу, порівняльного, аналітичного та узагальнення інформації.*

Результати і обговорення. *Результати свідчать, що рекомбінантні препарати інсуліну (від швидкодіючих аналогів до тривалих) забезпечують кращий контроль глікемії, але обмежені високою вартістю розробки та виробництва. Інновації включають комбіновані препарати з агоністами GLP-1, глюкозо-чутливі інсуліни та пероральні форми, які стикаються з викликами біодоступності.*

Висновки*. Аналіз вказує на еволюцію технологій виробництва інсуліну від визначення структури молекули та впровадження технологій рекомбінантної ДНК, що забезпечило перехід до людських рекомбінантних препаратів та аналогів. Ринок пропонує препарати з різними профілями (від ультрашвидких до ультратривалих), включаючи біфазні суміші, що покращують контроль глікемії. Комбінації інсуліну з агоністами GLP-1, аналогами аміліну (прамлінтид) та розробка глюкозо-чутливих інсулінів, мають потенціал для персоналізованої терапії, але обмежені технічними викликами (стабільність, біосумісність). Пероральні форми стикаються з низькою біодоступністю, але використання нанотехнологій та ефективних допоміжних речовин відкривають перспективи до покращення доступності та ефективності лікування ЦД*

Ключові слова. *Інсулін, технології рекомбінантних ДНК, біосиміляри, аналоги інсуліну, пероральні системи доставки*

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СТРАТЕГІЇ БОРОТЬБИ З РЕЗИСТЕНТНІСТЮ ДО АНТИБІОТИКІВ: ПОШУК НОВИХ РІШЕНЬ (с. 32–39)

Є. В. Ващик, О. О. Цимерман, О. В. Ладогубець, К. А. Дученко, А. В. Захар'єв, О. В. Шаповалова

Мета: *вивчення інноваційних світових стратегій боротьби з антибіотикорезистентністю*

Матеріали та методи. Дослідження проведено методом аналізу доступної наукової літератури, відкритих джерел в базах даних Google Scholar, PubMed, Clarivate, Web of Science, Scopus та ін., а також результатів власних досліджень.

Результати. Глобальний план дій щодо стійкості до антимікробних препаратів, розроблений ВООЗ, був схвалений в 2015 році, а у 2023 році встановлено, що 134 зі 194 країн, в тому числі й Україна, що становить 69% країн світу, офіційно прийняли національні плани дій. Але на сьогодні є складнощі у ефективній комунікації між всіма країнами та повноцінному виконанні Глобального плану, національних планів дій через те, що у країнах, що розвиваються, обмежені ресурси для необхідних заходів. Стійкі до антибіотиків бактерії та гени антибіотикорезистентності є надзвичайно небезпечними для здоров'я людства, що можна порівняти з бомбою уповільненої дії. Тому боротьба з антимікробною резистентністю потребує консолідації роботи різних галузей та повинна ґрунтуватися на таких напрямах: розвиток партнерських програм з оптимізації застосування антибіотиків; введення ефективних систем інтелектуального контролю та профілактики; фінансування програм розробки нових протимікробних препаратів та альтернативних методів лікування; підвищення контролю та інтенсифікація моніторингу розвитку та поширення резистентних мікроорганізмів.

Висновки. *Переважно резервуарами стійких до антибіотиків бактерій та генів резистентності є тваринницькі підприємства, лікарні, очисні споруди та сільськогосподарські угіддя, тому стратегія боротьби з антибіоткорезистентністю повинна ґрунтуватися в першу чергу згідно підходів «Єдине Здоров'я». Запропоновані вченими способи рішення для боротьби з антимікробною стійкістю – нові антибіотики; про-, пре-, симбіотичні препарати; ферменти для руйнування біоплівок, інгібітори адгезії та асоційована терапія з ад'ювантами або фагами, мають позитивний ефект, але на даний час ще потребують регуляторного втручання для широкомасштабного застосування. Ефективна боротьба з антимікробною резистентністю вимагає інвестування, навчання фахівців, підвищення обізнаності населення, комплексної політики та регуляторних систем, які забезпечать баланс між захистом громадського здоров'я та доцільним застосуванням антибіотиків*

Ключові слова: *антимікробні засоби, антибіотикорезистентність, «Єдине Здоров'я», стійкі бактерії, біоплівки, ад'юванти, система CRISPR-Cas*