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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.
GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.
ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

Содержание:

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COMPREHENSIVE ASSESSMENT OF BIOFILM FORMATION AND ANTIMICROBIAL RESISTANCE OF STAPHYLOCOCCUS IN PURULENT-INFLAMMATORY DISEASES

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Abstract.

Introduction: Treatment of biofilms is a priority in purulent surgery. A biofilm consists of 75–85% extracellular polymeric matrix and 15–20% microbial cells. Polysaccharides, proteins, and extracellular DNA within the matrix protect bacteria from adverse environmental factors (pH, antibiotics, phagocytosis). Communication between bacteria occurs through the “quorum sensing” system. Bacteria within biofilms are 100–1000 times more resistant to antibiotics compared to planktonic forms. This is explained by the limited penetration of antibiotics into the matrix and the reduced metabolic activity of the cells. Bacteria of the genus *Staphylococcus*, particularly *Staphylococcus aureus*, are currently recognized as the main causative agents of purulent-inflammatory diseases.

Objective of the study: to comprehensively assess the biofilm-forming activity of staphylococcal strains isolated from patients with purulent-inflammatory diseases of soft tissues (PIDs), as well as to determine the characteristics of their sensitivity to the main antimicrobial agents.

Materials and Methods: To achieve the objectives of the study, we conducted a research project and examined 80 strains of the genus Staphylococcus isolated from purulent-inflammatory diseases. Of these, 50 belonged to the main group (MG) and 30 to the control group (CG). The identification of species characteristics of the 80 strains from the main and control groups was carried out based on their morphological, cultural, and biochemical properties. In addition, these strains were identified using MALDI-TOF mass spectrometry.

Results: Analysis of the obtained results showed that *S. aureus* was predominant in both groups. During the study, 50 staphylococcal strains and two species—*S. aureus* and *S. epidermidis*—were identified among samples collected from patients with purulent-inflammatory diseases. In the control group, out of 30 strains, only one species—*S. aureus*—was identified. Biofilm-forming activity was also assessed based on microcolony size, and the morphological and tinctorial properties of isolated biofilm samples were studied. The field of view, number of objects, and their proportion within the field of view were calculated using digital images of the samples. The following microcolony sizes were taken into account: up to 10 µm², from 10 to 100 µm², from 100 to 1000 µm², from 1000 to 10,000 µm², and over 10,000 µm².

Key words. Biofilm, purulent-inflammatory diseases, *Staphylococcus aureus*, *Staphylococcus epidermidis*.

Introduction.

Purulent-inflammatory diseases of soft tissues remain one of the most pressing problems of modern surgery and clinical microbiology, characterized by high prevalence, a tendency to chronicity and a risk of complications [1]. In the structure of the causative agents of these infections, the leading role belongs to staphylococci, primarily *Staphylococcus aureus*, as well as coagulase-negative staphylococci, which have significant adaptive potential and a pronounced ability to persist in tissues [2,3].

One of the key factors in the pathogenicity of staphylococci is their ability to form biofilms, structured microbial communities encapsulated in a matrix of extracellular polymers. Biofilms provide microorganisms with protection from the effects of innate and adaptive immunity factors, and also significantly reduce the effectiveness of antimicrobial therapy [3,4]. It has been shown that bacteria in biofilms can exhibit antibiotic resistance exceeding that of planktonic forms by tens and hundreds of times [5].

In recent years, a significant amount of data has accumulated indicating that the ability to biofilm in clinical strains of staphylococcus varies widely and may correlate with the level of their antibiotic resistance [6]. Thus, it was found that strong biofilm producers are more likely to demonstrate multidrug resistance, including resistance to beta-lactams, macrolides, and fluoroquinolones. At the same time, a number of studies indicate the ambiguity of this relationship, which may be due to differences in biofilm assessment methods, sources of clinical material, and regional characteristics of circulating strains [7].

Objective of the study.

To comprehensively assess the biofilm-forming activity of staphylococcal strains isolated from patients with purulent-inflammatory diseases of soft tissues (PIDs), as well as to determine the characteristics of their sensitivity to the main antimicrobial agents.

Materials and Methods.

To achieve the objectives of the study, we conducted a research project and examined 80 strains of the genus Staphylococcus isolated from purulent-inflammatory diseases. Of these, 50 belonged to the main group (MG) and 30 to the control group (CG). The identification of species characteristics of the 80 strains from the main and control groups was carried out based on their morphological, cultural, and biochemical properties. In

I. Bacteriological research methods

Taking materials

Microscopic examination of native tissue for confirmation.

II. Bacteriological examination: isolation of pure culture and its identification

Culture identification. Cultivation on yellow salt agar.

Morphological identification.

Biochemical identification by carbohydrate fermentation method.

Refinement by MALDI-TOF MS

Evaluation of biofilm formation activity

Main group (50 people):
Skin abscess, carbuncle, furuncle (N=32)
Skin phlegmon (N=18)

Control group (30 people): healthy

III. Formation of isolated biofilm samples in a closed system in vitro using the methods of G. O'Toole and R. Kolter

IV. Formation of isolated biofilm samples in an open in vitro system

IV. Statistical research methods

Figure 1. *Study design.*

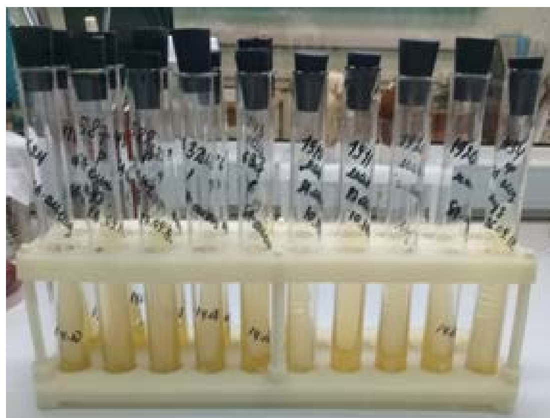

Figure 2. *S. aureus cultivation on slant agar.*

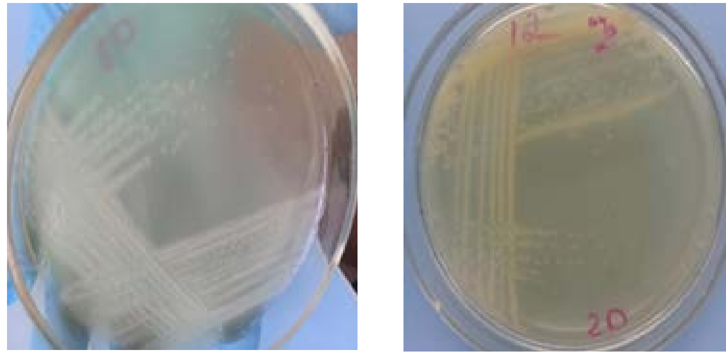

Figure 3. *S. aureus growth in SSA medium inoculated using Gould's method.*

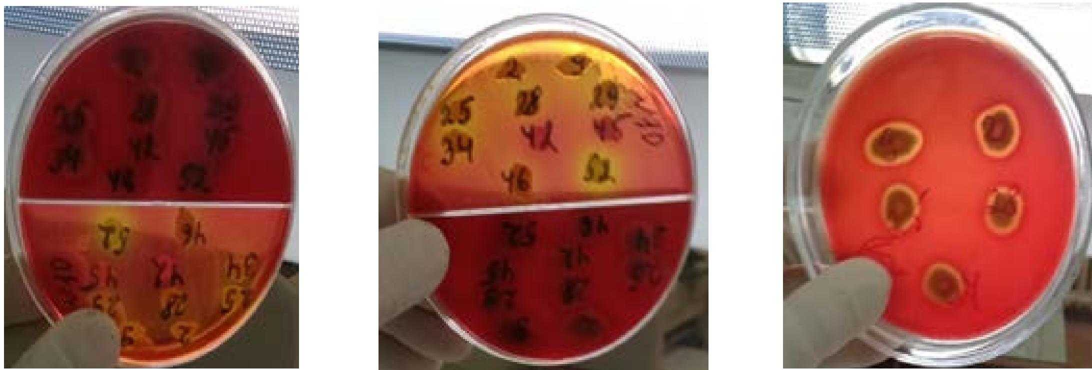

Figure 4. *Growth characteristics of S. aureus on mannitol salt agar.*

Figure 5. *Set of carbohydrates for biochemical identification.*

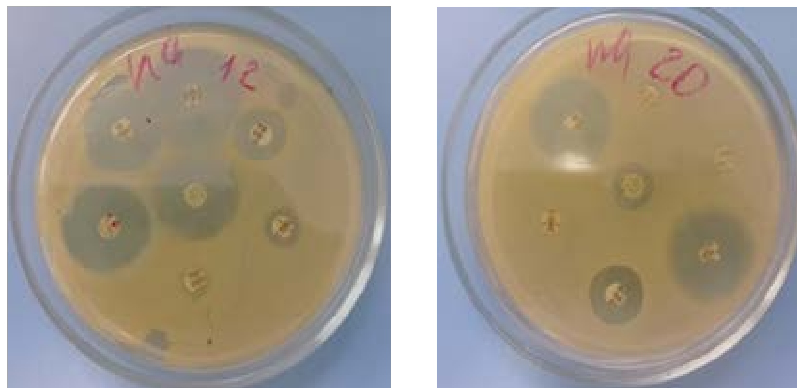

Figure 6. *Determination of susceptibility to antibiotics by the disc diffusion method.*

addition, these strains were identified using MALDI-TOF mass spectrometry.

Collection of Clinical Material:

The study was conducted at the Regional Clinical Hospital of Karaganda and at a shared-use laboratory facility. For the main group, the following materials were used: purulent discharge, scrapings, and swabs collected before the initiation of antimicrobial therapy. In the control group, swabs from the nasal and oropharyngeal mucosa of healthy individuals were examined. Samples were collected using sterile swabs and inoculated onto slanted agar. Incubation was carried out at 37°C for 24–48 hours.

Gould's method was used for quantitative analysis and culture isolation. The material was inoculated into Petri dishes filled with yellow salt agar (SSA) in four sections using a bacteriological loop (sterilizing the loop after each section). Incubation: at 37°C for 24-48 hours.

Assessment: The number of colonies was counted and the number of colony-forming units (CFU/ml) was determined.

Clinical significance: 10^5–10^6 CFU/ml — highly pathogenic; 10^2–10^3 CFU/ml — normal microflora.

Smears were prepared from isolated colonies and then stained using the Gram method. The smears were identified using an immersion microscope. At this stage, the tinctorial properties (Gram-positive) and morphological similarity of the microorganisms were assessed.

Mannitol salt agar: *S. aureus* ferments mannitol on mannitol salt agar, forming yellow colonies around the medium. Other strains form red or small red colonies around the medium (Figure 4).

Biochemical identification by sugar fermentation:

For biochemical identification, we used a carbohydrate medium based on its breakdown into acid and gas. *S. aureus* breaks down lactose, glucose, and sucrose into acid without gas formation, ferments mannitol without gas formation, and produces the aggressive enzyme plasmacoagulase. The specificity of plasmacoagulase production in *S. aureus* distinguishes it from other bacterial species of the genus Staphylococcus, as only *S. aureus* is capable of producing plasmacoagulase. *S. epidermidis* breaks down glucose and sucrose into acid, and lactose into acid and gas. It does not produce plasmacoagulase; mannitol is shown in Table 1 "Carbohydrate Fermentation".

We inoculate Hugh-Leifson medium with bromothymol blue indicator by injection. Activity is assessed by the color change of the carbohydrates (Figure 5).

To refine the isolated pure cultures, MALDI-TOF MS was used, based on comparing the "molecular fingerprints" of bacterial proteins with a database of reference spectra. During the study, a portion of a pure colony grown on CTA medium was spotted on a 96-well steel plate (Bruker Daltonics, Germany) in duplicate and air-dried. Then, 2 μl of matrix (α-cyano-4-hydroxycinnamic acid in 50% acetonitrile and 2.5% trifluoroacetic acid) were added to the samples, and the samples were dried again at room temperature. The identification results were assessed on a scale from 0 to 3 (score): values above 1.7 were considered the lower threshold of species identification, values above 2.0 indicated reliable identification, and values approaching 3.0 indicated a high degree of identification reliability at the species level.

Determination of the sensitivity of Staphylococcus species to antibiotics:

To determine the sensitivity of microorganisms to antibiotics, we used the disk diffusion method in accordance with EUCAST guidelines. The museum's *Staphylococcus aureus* (ATCC 6538) was used for quality control. During the study, individual colonies were collected from a 24-hour agar culture using a sterile inoculation loop, and a microbial suspension was prepared in a glass test tube containing 1 ml of saline. The resulting microbial suspension was applied to a solid nutrient medium (AGV, Givental-Vedmin agar), spread evenly with a spatula, and left at room temperature for 30 minutes.

Studying the ability to form biofilms:

Quantitative Assessment of the Capacity of a Biofilm Sample Obtained in a Closed In vitro Environment. Staphylococcus strains *S. aureus* and *S. epidermidis* were used to obtain a biofilm sample. Quantitative assessment of biofilm formation capacity was performed in a 96-well flat-bottomed polystyrene plate using enzyme-linked immunosorbent assay (ELISA) according

Table 1. *Carbohydrate Fermentation.*

Types of pathogens	Lactose	Glucose	Sucrose	Plasma coagulase	Mannitol
S.aureus	+	+	+	+	+
S.epidermidis	+	+	+	-	-

Table 2. *Distribution of Etiologic Agents by Clinical Types of IBD.*

Clinical manifestations of inflammatory bowel disease of soft tissues	Etiological agents			
	S.aureus		*S.epidermidis*	
	abs	%	abs	%
Skin abscess, furuncle, carbuncle. N=32 (85%)	22	68,75	10	31,25
Skin phlegmon N=18 (15%)	16	88,8	2	11,1

Table 3. *Biofilm Formation Activity MG.*

	Main group				
Pathogen	Min	Max	M	SD	All
S.aureus	0,57	1,38	0,875	0,158	38
S.epidermidis	0,43	0,62	0,538	0,096	12

Table 4. *Biofilm-forming activity of CG.*

	Main group				
Pathogen	Min	Max	M	SD	Bce
S.aureus	0,324	0,720	0,441	0,112	30
S.epidermidis	-	-	-	-	-

Table 5. *Descriptive statistics of the OT index in the three study groups.*

Group	N	Middle	Lower limit 95% confidence interval	Upper limit 95% confidence interval	Median	Minimum	Maximum	Lower quartile	Upper quartile	Standard Deviation
1	32	0,800	0,708	0,853	0,788	0,501	1,175	0,604	0,895	0,189
2	18	0,786	0,725	0,846	0,769	0,426	1,360	0,615	0,887	0,197
0	30	0,435	0,387	0,484	0,400	0,321	0,717	0,376	0,431	0,10

Table 6. *Bioavailability in the Study and Control Groups.*

Types of pathogens	**Biofilm density MG**			**Other**	**Microbial load density CG**			**Other**
	tight	weak	average		tight	weak	average	
S.aureus	34	-	16	50	-	27	3	30

Table 7. *Frequency analysis of pathogen types and microbial load density found in the MG and CG groups.*

Biomass density	**MG**	**CG**
	S.aureus	***S.aureus***
tight	34(68%)(CI: 53,30%-80,48%)	-
average	16(32%)(CI:19,52%-46,70%)	3(10%)(CI: 2,11%-26,53%)
weak	-	27(33,75%)(CI: 73,47%-97,89%)
$\chi 2$ Pearson=45,23; p=1,501; α=0,05.		

Note: *Confidence intervals for relative values were calculated using the Clopper Pearson method.*

Table 8. *Results of assessment of biofilm formation capacity depending on microcolony size in MG and CG.*

Trigger type	**MG microcolony size**				**Other**	**CG microcolony size**				**Other**
	up to 10 μm^2	from 10 to 100 μm^2	from 100 to 1000 μm^2	from 1000 to 10000 μm^2		up to 10 μm^2	from 10 to 100 μm^2	from 100 to 1000 μm^2	from 1000 to 10000 μm^2	
S.aureus	-	11	37	2	50	25	5	-	-	30

Table 9. *Results of assessing the ability of S. aureus to form biofilms depending on the size of MG and CG microcolonies.*

Microcolony size	**MG**	**CG**
Up to 10 μm^2	0	25
%	0	83,3% (CI: 65,28%-94,36%)
From 10 to 100 μm^2	11	5
%	22% (CI: 11,53%-35,96%)	16,6% (CI: 5,64%-34,72%)
From 100 to 1,000 μm^2	37	0
%	74% (CI: 59,6%-85,3%)	0,000% (CI: 0,000%-16,11%)
From 1,000 to 10,000 μm^2	2	0
%	5,2% (CI: 0,49%-13,7%)	0
$\chi 2$ Pearson=126,3; p=3,58; α=0,05.		

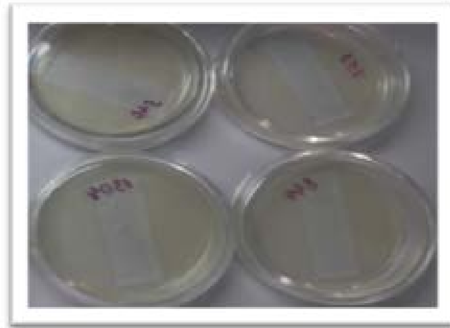

Figure 7. *Creation of an isolated biofilm model under open conditions in vitro.*

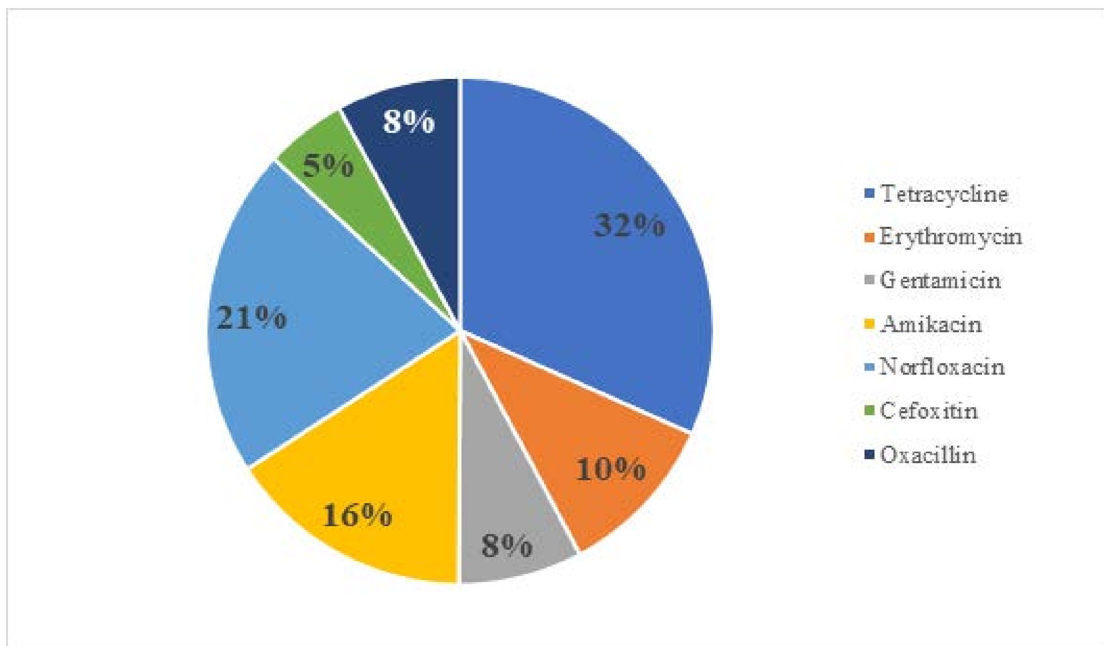

Figure 8. *Antibiotic susceptibility of MG S. aureus.*

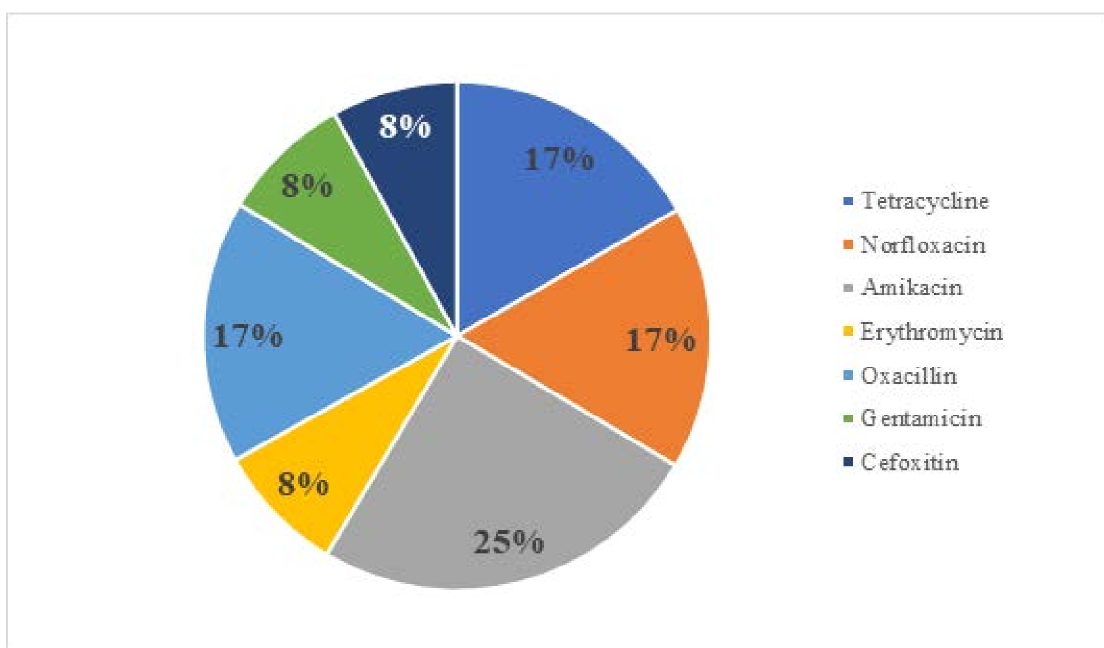

Figure 9. *Antibiotic susceptibility of MG S. Epidermidis.*

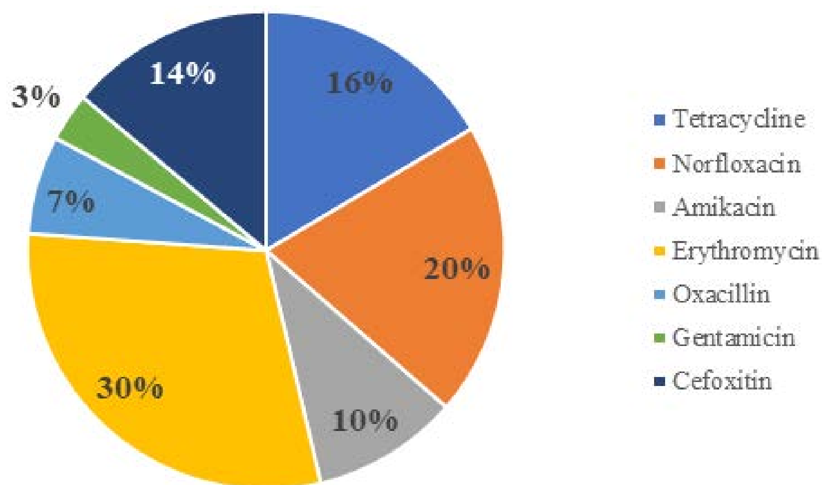

Figure 10. *Sensitivity of S. aureus CG to antibiotics.*

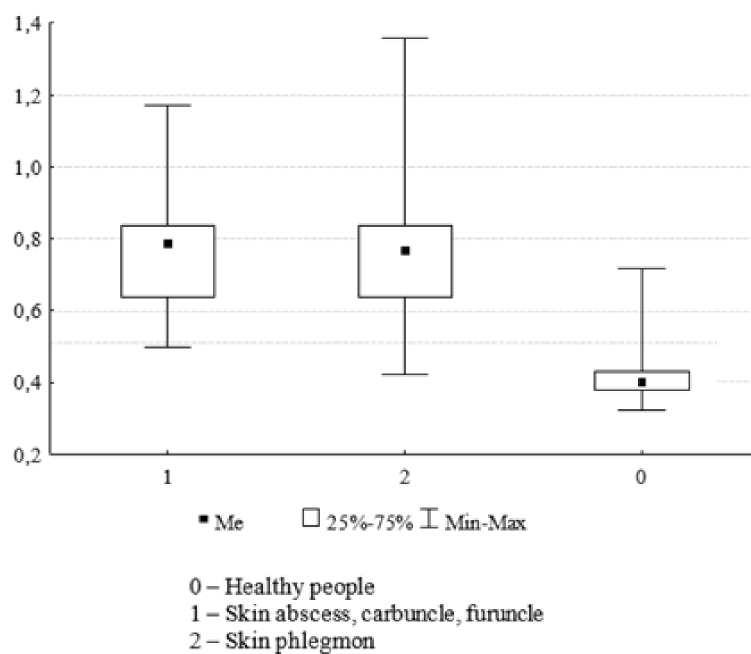

Figure 11. *Values of the OT indicator in the three study groups.*

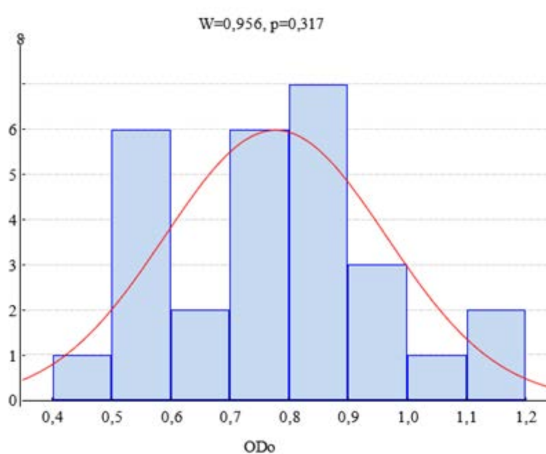

Figure 12. *Histogram of the distribution of average optical density values in the group of skin abscesses, carbuncles and furuncles.*

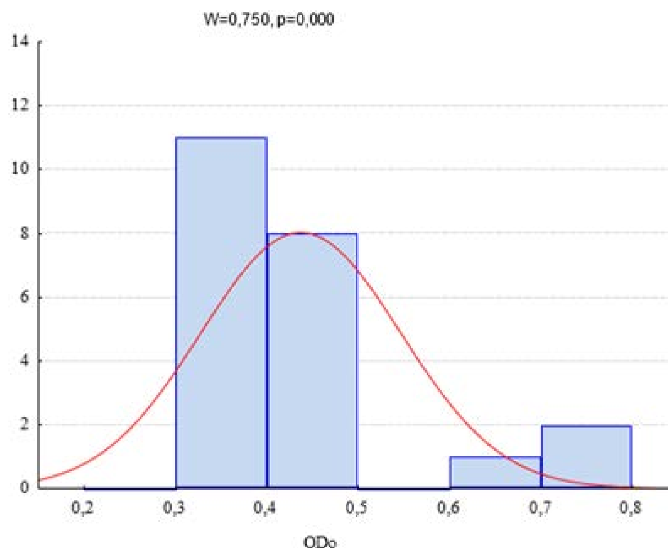

Figure 13. *Histogram of the distribution of mean optical density values in a group of healthy individuals.*

to the method of G. O'Toole and R. Coulter. This method is based on the binding of crystal violet (CV) dye to cells and the biofilm matrix. Biofilm formation activity is determined by the adsorption level of ethanol solutions of the dye at a wavelength of 540 nm using an EVOLIS BIO RAD (OD540) automated enzyme-linked immunosorbent assay analyzer.

In this study, 24-hour pure cultures of staphylococcal species were used to form biofilms. To prepare the inoculum, material was collected from isolated colonies on a solid nutrient medium and placed in sterile saline. The optical density of the inoculum was adjusted to a standard of 0.5 McFarland (approximately 1.5×10^8 CFU/mL) using a densitometer II (ERBA Lachema). Biofilm formation was carried out in a 96-well flat-bottomed polystyrene plate:

- **Experimental group:** Wells 1–7 were filled with the appropriate medium and inoculum.
- **Control group:** Wells 8–9 were filled with 200 µl of Lowry medium (without microorganisms).

All wells were filled with 150 µl of Lowry medium and 50 µl of inoculum and incubated at 37°C for 24 hours.

After incubation, the biofilm was washed three times (2-3 minutes each time) with sterile buffer. After completely removing the buffer, the plate was dried in an incubator at 60°C for 60 minutes. To stain the prepared samples, 200 µl of 0.1% Crystal violet solution was added to each well.

The biofilm and dye are left at room temperature for 10-15 minutes. After 15 minutes, the dye is removed from the well using a suction device, followed by three washes with buffer solution.

To extract the biofilm, add 150 µl of 95% ethanol to the well and leave for 30 minutes at room temperature. To determine biofilm density, the wavelength is measured and determined using the EVOLIS BIO RAD ELISA instrument at 540 nm.

Qualitative assessment of biofilm formation capacity by creating an isolated biofilm model under open conditions in vitro:

To qualitatively determine the ability of staphylococcal species to form biofilms on coated glass surfaces, sterile Petri dishes with a diameter of 100 mm were used. Sterile 24 x 24 mm coverslips were placed in each dish.

A 3-ml sample of a 24-hour strain culture (suspension in Lowry medium) at a cell concentration of 10^6 was applied to a coverslip. The samples were incubated for 24 hours at 37°C. After 24 hours, another 2 ml of Lowry medium was added to the wells, and incubation was continued for another 24 hours. After two days, the culture medium was discarded, and the glass surface was washed with phosphate buffer. 96% alcohol was used to fix the biofilm, after which the samples were completely dried. The prepared samples were stained with Crystal violet for 2 minutes at room temperature. After staining was complete, the slides were again washed with phosphate buffer and prepared for microscopic analysis.

The resulting specimens were examined under a microscope, and digital images of the visual field were obtained using a UCMOS 14000KPA+AMA037 digital eyepiece camera.

Statistical Data Processing.

Statistical data processing was performed using STATISTICA 8.0 and Microsoft Excel software packages. Descriptive statistics, such as mean, maximum, minimum, and standard deviation, were used. When stratifying by age, selection is based on the Shapiro-Wilk (SW-W) test. All data were tested for normal distribution using the Shapiro-Wilk test (if $p \leq 0.05$, then the distribution of the random variable under study differs from the normal value, and conversely, if $p > 0.05$, then the distribution is normal). The nonparametric Kruskal-Wallis H-test was used to compare groups of the random variable under study. Statistical significance was set at $p=0.05$. The Mann-Whitney U-test was used to determine differences between independent samples for quantitative indicators. A correlation table with Pearson's χ^2 test was used to study nominal characteristics. Confidence intervals for relative values were calculated using the Clopper-Pearson method. Cramer's V test, which is applicable to different strains of the genus Staphylococcus, was used to compare the microbial load density.

Results.

A distinctive feature of the MALDI-TOF MS method is the ability to quickly analyze daily test material down to subspecies. In the study, 50 strains and two species of staphylococcal bacteria, *S. aureus* and *S. epidermidis*, were identified in patients with IBD. In the control group, one species of *S. aureus* was identified out of 30 strains.

In the study group, two species of Staphylococcus were identified. Thirty-eight strains of *S. aureus* (76%) and 12 strains of *S. epidermidis* (24%) were the leading etiologic causes of IBD of the skin and subcutaneous sebaceous glands.

In the control group, *S. aureus* was detected in 100% of cases. It is worth noting that only one species of staphylococcus was detected in healthy individuals, as their bodies were relatively healthy. We see that in patients, the presence of not one, but two species of bacteria plays a significant role in the development and course of IBD.

Dividing the number of cases by disease type, *S. aureus*, which causes skin abscesses, carbuncles, and furuncles, accounts for 68.75%, while *S. epidermidis* accounts for 31.25%. In cutaneous phlegmon, *S. aureus* accounts for 88.8%, while *S. epidermidis* accounts for 11.1%. Based on these results, we can conclude that *S. aureus* is more prevalent in both types of diseases. It is clear that *S. aureus* more often causes idiopathic pulmonary fibrosis (IPF).

Based on the presented data, as shown in Table 2, the species composition of Staphylococcus bacteria in the clinical forms of skin abscess, furuncle, carbuncle, and cutaneous phlegmon is not particularly diverse and includes two species of this type of bacteria. In skin abscess, carbuncle, and furuncle, the proportion of *S. aureus* species was 22 strains (68.75%), while *S. epidermidis* represented 10 strains (31.25%). In cutaneous phlegmon, 16 *S. aureus* strains (88.8%) and two *S. epidermidis* strains (11.1%) were detected.

In addition, the sensitivity of the isolated pure cultures to antimicrobial drugs was determined: tetracycline, oxacillin, erythromycin, gentamicin, norfloxacin, cefoxitin and amikacin.

S. aureus is known to be one of the main pathogens in patients with IBD. This pathogen is unique in that it is present in the human body under normal conditions and can cause opportunistic infections due to a weakened immune system.

Regarding antibacterial drug sensitivity, drugs with high sensitivity include tetracycline, norfloxacin and amikacin, while drugs with low sensitivity include cefoxitin.

Our study identified 12 strains of *S. epidermidis* causing invasive aspergillosis (IA). The antibiotic susceptibility of the identified strains was tested using disk diffusion. Based on the study results, the following antibiotics are effective: amikacin, tetracycline, norfloxacin, and oxacillin. Antibiotics with low susceptibility include gentamicin and cefoxitin.

When determining the susceptibility of CG bacteria to antibiotics, the following parameters can be observed. Antibacterial drugs with high susceptibility include erythromycin, norfloxacin, and tetracycline, while the drug with the lowest susceptibility is gentamicin.

Quantitative Activity of the Biomolecule:

The signal-to-noise ratio (SNR) value for biofilm formation activity of the main group of Staphylococcus bacteria in the wells of polystyrene plates ranged from M = 0.538 (SD = 0.096) to M = 0.875 (SD = 0.158).

The highest SNR value was 1.38 for *S. aureus*. The lowest SNR value was 0.43 for *S. epidermidis*.

In the control group, the highest biofilm-forming activity of *S. aureus* in healthy individuals was 0.720. *S. epidermidis* was not detected in the control group.

When dividing the main IA group into types and comparing the statistical results, no significant differences were found in the OT indices for biofilm formation activity in skin abscesses and skin phlegmons across the three study groups. When comparing these two groups with CG, it is clear that the OT index for biofilm formation activity is higher in MG (Table 5).

The results of the test for the normal distribution of the random variable under study showed that the mean value of the VO2 (single variance of bioactivity) in the two groups with soft tissue IA was normally distributed, while in the group of healthy individuals, the distribution of this indicator deviated from the normal distribution (Figure 11).

According to the results of the random variable's distribution validity test, the study group had a normal distribution, while the control group deviated from this distribution. This allows us to select the nonparametric Kruskal-Wallis test (Kruskal-Wallis H-test) for further comparison of the study groups.

When comparing skin abscesses and skin phlegmon, the mean ODO values were not different (p=1.000). When comparing the values of these two groups with the healthy group, a difference was found (p=0.000).

According to the presented data, the species composition of Staphylococcus bacteria, and the biofilm formation efficiency in the main group, which formed biofilms of varying densities, included three species: weak – 27 (33.75%), moderate – 19 (23.75%), and dense – 34 (42.5%).

In the study group, *S. aureus* formed high- and medium-density biofilms. The proportion of *S. aureus* strains forming high-density biofilms (68%) was 34 (32%), while the proportion of *S. aureus* strains forming medium-density biofilms was 16 (32%). In the control group, the proportion of low-density *S. aureus* strains forming biofilms was 27 (33.75%), while the proportion of medium-density *S. aureus* strains forming biofilms was 3 (10%).

Regarding the results of the studies conducted on these two groups, the biofilm density in the MG group was high, the average density was significantly higher than in the CG group, and no weak biofilm density was detected in the MG group. Based on this, it can be concluded that the biofilm density in the MG group was significantly higher than in the CG group, indicating that the treatment course will be longer and more complex.

When comparing *S. aureus* biofilm density in the treatment and control groups using the χ^2 statistical test, it was found that the *S. aureus* biofilm density obtained using MG did not differ statistically significantly (p=1.501) from the biofilm density of the CG pathogen.

After creating an individual in vitro biofilm model under open conditions, we assessed the activity of biofilm formation on a glass surface, taking into account the microcolony size according to the MG results: up to 10 μm² - 25 (31.25%), from

10 to 100 μm² - 16 (20%), from 100 to 1000 μm² - 37 (46.25%), from 1000 to 10,000 μm² - 2 (2.5%).

MG *S. aureus* formed 3 different microcolony sizes: from 10 to 100 μm² - 11 (22%), from 100 to 1000 μm² - 37 (74%), from 1000 to 10,000 μm² - 2 (5.2%)/

The size of microcolonies formed by *S. aureus*, examined by the CG method, does not exceed 25 (83.3%) for sizes up to 10 μm2 and 5 (16.6%) for sizes from 100 to 1000 μm2.

When determining the statistical relationship between biofilm density and microcolony size, the results of the correlation analysis revealed a statistically significant ($p<0.05$) direct relationship between the OT index and microcolony size. Across all studied groups, the higher the number of microcolonies, the higher the OT index of biofilm-forming activity.

In the study group, the size of microcolonies formed by *S. aureus* was statistically significant ($p=3.58$), while in the control group, there was no difference in the size of microcolonies formed by this pathogen.

Discussion.

The findings of the present study further support the central role of biofilm formation in the pathogenesis of purulent-inflammatory diseases of soft tissues. The results demonstrate that *Staphylococcus aureus* exhibits a pronounced ability to form biofilms on both hydrophobic (polystyrene) and hydrophilic (glass) surfaces. This highlights the high adaptive capacity of this pathogen and its ability to colonize both biological tissues and abiotic medical materials. Similar observations have been reported by Jefferson et al. and Otto, who emphasized that the extracellular matrix of *S. aureus* biofilms enhances bacterial adhesion and protects cells from environmental stressors and host immune responses [8-10].

The predominance of *S. aureus* among clinical isolates in this study is consistent with global epidemiological data. According to the World Health Organization, *S. aureus* remains one of the leading etiological agents of skin and soft tissue infections, particularly in healthcare-associated settings [11]. The detection of Staphylococcus epidermidis only in the main group is also noteworthy. Although traditionally considered a commensal organism, *S. epidermidis* is increasingly recognized as an opportunistic pathogen, especially in biofilm-associated infections. This is supported by the work of Costerton et al., who demonstrated that coagulase-negative staphylococci play a significant role in chronic and device-related infections due to their strong biofilm-forming capacity [12].

Quantitative assessment of biofilm formation revealed significantly higher optical density values in the main group compared to the control group, indicating enhanced biofilm-forming ability of clinical isolates. These findings are in agreement with O'Toole et al., who reported that strains isolated from infectious sites exhibit significantly stronger biofilm production than commensal strains [13]. Morphometric analysis further demonstrated the presence of structurally complex biofilms, including large microcolonies exceeding 10,000 μm². Such structural heterogeneity reflects advanced biofilm maturation and is associated with increased resistance to antimicrobial agents, as previously described by Flemming et al. [14].

The antibiotic susceptibility results are of particular clinical relevance. In the present study, tetracycline, norfloxacin, and amikacin demonstrated the highest overall efficacy against the tested staphylococcal strains. However, it is well established that bacterial cells embedded in biofilms exhibit significantly reduced susceptibility to antimicrobial agents due to limited diffusion, altered metabolic activity, and the presence of persister cells. Stewart and Costerton reported that the minimum inhibitory concentrations for biofilm-associated bacteria may be up to 1000-fold higher than those for planktonic cells [15].

Differences in antibiotic susceptibility between *S. aureus* and *S. epidermidis* may be attributed to variations in biofilm architecture and virulence potential. *S. epidermidis* generally exhibits lower virulence but forms highly persistent biofilms, particularly in device-associated infections. This observation is consistent with previous studies reporting species-specific differences in biofilm composition and antimicrobial resistance profiles [2].

Overall, the persistence of susceptibility to tetracycline, norfloxacin, and amikacin across all groups suggests that these antibiotics may retain clinical utility in the treatment of staphylococcal infections. However, their effectiveness in vivo may be limited by biofilm-associated resistance mechanisms. Therefore, treatment strategies should not only focus on antimicrobial therapy but also include approaches targeting biofilm disruption.

In conclusion, the results of this study confirm that clinical isolates of staphylococci, particularly *S. aureus*, possess strong biofilm-forming capacity, which contributes significantly to their persistence and therapeutic resistance. These findings highlight the necessity of integrated treatment strategies combining antimicrobial agents with anti-biofilm approaches [16-18].

Conclusion.

The study provided qualitatively new information about the ability of clinical strains to form biofilms. In particular, a comparative analysis of quantitative data showed that the *S. aureus* strain demonstrates a pronounced ability to form biofilms on both hydrophobic polystyrene surfaces and hydrophilic glass surfaces. During the study, 50 strains of staphylococcus and two species, *S. aureus* and *S. epidermidis*, were identified among samples collected from patients with purulent-inflammatory diseases. Only one species, *S. aureus*, was identified in the control group of 30 strains. The study showed that biofilm-forming activity (optical density) was higher in the study group than in the control group. Biofilm-forming activity was also evaluated based on the size of microcolonies, and morphological and tinctorial properties of isolated biofilm samples were studied. In the main group, tetracycline, norfloxacin and amikacin proved to be the most effective against *S. aureus*. For *S. epidermidis* amikacin, tetracycline, norfloxacin and oxacillin proved to be the most effective. The control group had erythromycin, norfloxacin and tetracycline. In all three groups, the bacteria showed sensitivity to tetracycline, norfloxacin, and amikacin.

Ethics.

The study was approved by the Local Bioethics Committee of NCJSC Karaganda Medical University on December 30, 2025

Conflict of Interest.

The authors declare that they have no conflicts of interest.

Author Contributions.

Conceptualization – MR, ZS; Methodology – ZS, AK, MR; formal analysis – ZS, MR; conducting an experiment – AK, GS, KN; writing – original draft preparation – ZS, AK; writing – review and editing – MR; visualization – GS, KN; statistical analysis and translation – AK, AM. All authors have read and agreed to the published version of the manuscript.

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