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## COMPARISON OF THE EFFECT OF ANTISEPTICS BASED ON DECAMETHOXINE, CHLORHEXIDINE BIGLUCONATE AND IODOFORM ON THE ADHESIVE POTENTIAL OF BACTERIA OF THE GENUS *KOCURIA SPP*

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Antiseptics can block the adhesion of bacteria, thus facilitating the course of the purulent-inflammatory process. Therefore, we investigated the adhesive properties of clinical isolates of the genus *Kocuria* isolated from the oral cavity of patients with infectious-inflammatory post-extraction complications. Remedies based on decamethoxine, chlorhexidine bigluconate and iodoform were used as test antiseptics. The adhesive properties of clinical isolates under the action of remedies based on decamethoxine, chlorhexidine bigluconate and iodoform were determined by V.I. Brillis. The adhesion index values of microorganisms of clinical isolates of the genus *Kocuria* under the action of subbacteriostatic concentration of remedy based on decamethoxine were 1.6 times ( $p < 0.05$ ) and 2.1 times ( $p < 0.05$ ) lower compared to those of the adhesion index of microorganisms after the action of remedies based on chlorhexidine bigluconate subbacteriostatic concentrations and iodoform respectively. In the presence of remedy based on chlorhexidine bigluconate SBsC, relative to the clinical isolates *Kocuria kristinae* 1 and *Kocuria kristinae* 2, IAM indices increased 1.3 times, and IAM indices of *Kocuria rosea* increased 1.1 times compared to the IAM indices of the controls of these isolates. Considering the results of action remedy based on iodoform SBsC on clinical isolates *Kocuria kristinae* 1 and *Kocuria kristinae* 2, IAM increased in 2.1 times and in 1.5 times, IAM of clinical isolate *Kocuria rosea* also increased, but in 1.4 times, considering the control cultures.

**Key words:** adhesion of microorganisms, pathogenic factors, antiseptics, clinical isolates, purulent-inflammatory process.

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## ПОРІВНЯННЯ ДІЇ АНТИСЕПТИКІВ НА ОСНОВІ ДЕКАМЕТОКСИНУ, ХЛОРГЕКСИДИНУ БІГЛУКОНАТУ ТА ЙОДОФОРМУ НА АДГЕЗИВНИЙ ПОТЕНЦІАЛ БАКТЕРІЙ РОДУ *KOCURIA SPP*

Досліджували адгезивні властивості клінічних ізолятів роду *Kocuria*, виділених з порожнини рота пацієнтів з інфекційно-запальним постекстракційним ускладненням. В якості досліджуваних препаратів використовували засоби на основі декаметоксину, хлоргексидину біглюконату і йодоформу. Адгезивні властивості клінічних ізолятів під дією антисептичних засобів на основі декаметоксину, хлоргексидину біглюконату і йодоформу визначали за методикою В.І. Бриліс. Показники індексу адгезії мікроорганізмів клінічних ізолятів роду *Kocuria* під дією суббakteriостатичної концентрації антисептичного засобу на основі декаметоксину були в 1,6 рази ( $p < 0,05$ ) та 2,1 рази ( $p < 0,05$ ) меншими в порівнянні з показниками індексу адгезії мікроорганізмів після дії суббakteriостатичних концентрацій антисептичних препаратів на основі хлоргексидину біглюконату і йодоформу відповідно. У присутності СБсК Хлоргексидину, щодо клінічних ізолятів *Kocuria kristinae* 1 та *Kocuria kristinae* 2 показники IAM збільшувались у 1,3 рази, а показники IAM *Kocuria rosea* – у 1,1 рази порівняно з показниками IAM контролю цих ізолятів. Враховуючи результати дії СБсК Йодоформу щодо клінічних ізолятів *Kocuria kristinae* 1 та *Kocuria kristinae* 2, IAM збільшувалися у 2,1 рази та у 1,5 рази, IAM клінічного ізоляту *Kocuria rosea* також збільшувався, але у 1,4 рази, враховуючи контроль культур.

**Ключові слова:** адгезія мікроорганізмів, фактори патогенності, антисептики, клінічні ізоляти, гнійно-запальний процес.

The study is a fragment of the research project "Investigating the role of conditionally pathogenic and pathogenic infectious agents with different sensitivity to antimicrobial antiviral drugs in human pathology", state registration No. 0118U004456.

According to the literature, a large number of bacteria can form biofilms. Bacterial cells composing biofilms differ in their properties from free-floating bacteria in the plankton state. Microorganisms within biofilms are protected from unfavorable conditions by a matrix of extracellular polymeric substances. As a result, they are significantly more resistant to antimicrobial agents and host defence mechanisms than their planktonic counterparts [9]. The biofilm formation process begins with the interaction of bacteria with macroorganism cells through adhesion due to the ability of the infectious agent to attach to the host cells with subsequent colonization. The close interaction of pathogens with the body's cells can lead to the appearance of a purulent-inflammatory process of certain organs or even entire systems of the human body [7].

Adhesion refers to the pathogenicity of microorganisms, which is characterised by bacteria's potential ability to cause an infectious process. This ability of microorganisms can be more or less pronounced depending on the species of bacteria. Adhesion of the infectious agent occurs in the presence of adhesins, which surface proteins can represent, capsular polysaccharides, teichoic acids, and others [6, 7].

It has been proved that alveolitis of the jaw, which occurs as a post-extraction complication during outpatient dental surgery, has an infectious-inflammatory genesis, one of the etiological factors of which is bacteria [1, 2, 15].

Recently, more and more information is appearing about purulent-inflammatory processes associated with microorganisms of the genus *Kocuria spp.*, which are part of the resident microflora of human skin and mucous membranes. Foreign literature sources indicate infections such as cholecystitis, endocarditis, peritonitis, and meningitis, among the etiological factors of which *Kocuria spp.* was identified. This fact indicates that this bacterial genus is involved in infectious and inflammatory processes [12, 14]. In addition, scientific studies show the presence of this genus of bacteria in the oral cavity, particularly in carious tooth cavities [8].

Microbial resistance to antimicrobial agents is increasing rapidly worldwide, so antiseptic drugs are increasingly used to treat and prevent purulent inflammatory processes. At the same time, there are reports of scientists about the appearance of new strains of microorganisms that can cause infectious processes, so the use of antiseptics is an alternative to the use of antibiotics during the treatment and prevention of purulent-inflammatory processes. Considering the literature, it is known that resistance to antiseptics appears less frequently than to antibiotics. Still, most importantly, antiseptics can block bacterial adhesion, which facilitates the course of the purulent-inflammatory process [3, 11].

**The purpose** of the study was to establish the action of remedies based on decamethoxine, chlorhexidine bigluconate and iodoform on the adhesive properties of clinical isolates of *Kocuria spp.*, isolated from the mouth of patients with infectious-inflammatory postextraction complications.

**Materials and methods.** Clinical isolates of *Kocuria kristinae* and *Kocuria rosea* isolated from patients treated for infectious and inflammatory post-extraction complications in the medical and surgical department of the "Poltava Regional Dental Center-Dental Clinical Polyclinic" municipal institution were studied. The isolated cultures were identified using an automatic bacteriological analyzer Vitec-2 compact bioMarieux (France).

Decasan manufactured by Yuriya-Pharm LLC in Kyiv (decamethoxine solution 0.2 mg/ml) was used as the studied antiseptics; Chlorhexidine produced by LLC "DKP Pharmaceutical Factory" Vishpha Zhytomyr region. (0.05 % solution of chlorhexidine bigluconate); Iodoform produced by PE "Latus" Kharkiv (fine crystalline powder). As a carrier of iodoform used 5 % iodoform bandage, prepared independently. The study used the average values of subbacteriostatic concentrations (SBsC) of the above antiseptics against *Kocuria spp.* SBsC of Decasan- $0.65 \pm 0.2 \mu\text{g/ml}$ , SBsC of Chlorhexidine- $0.3 \pm 0.1 \mu\text{g/ml}$ , SBsC of Iodoform- $1.16 \pm 0.76 \text{mg/ml}$ .

The adhesive properties of clinical isolates under the action of remedies based on decamethoxine, chlorhexidine bigluconate and iodoform were determined by the method of V.I. Brillis using erythrocytes of blood group 1 (O) Rh+ (1986). The effect of SBsC remedies based on decamethoxine, chlorhexidine bigluconate and iodoform on the adhesive properties of the studied clinical isolates was evaluated taking into account the index adhesiveness of microorganism (IAM). According to the method of V.I. Brillis all microorganisms according to the value of IAM were divided into microorganisms that do not show adhesion (with  $\text{IAM} \leq 1.75$ ); microorganisms that are low-adhesive (with  $\text{IAM} = 1.75 - 2.49$ ); microorganisms that are moderately adhesive (with  $\text{IAM} = 2.50 - 4.0$ ); and microorganisms that are highly adhesive (at  $\text{IAM} > 4.0$ ).

The study with antiseptics was repeated three times using the IAM index of the studied isolates without antiseptics as a control. Variation and statistical processing of the study results was performed using Microsoft Excel with a determination of the main variation indices: mean values (M), mean errors (m), p-value (p). The reliability of the results was determined using Student's t-test.

**Results of the study and their discussion.** According to the study results of adhesive properties of clinical isolates of *Kocuria spp.* according to IAM criteria, a remedy based on decamethoxine SBsC reduced the adhesive properties of clinical isolates compared to IAM parameters in 1.3 times ( $p < 0.05$ ), after the action of remedy based on chlorhexidine bigluconate SBsC the tendency to increase IAM parameters of clinical isolates in 1.3 times also compared to IAM of control was followed. In turn, remedy based on iodoform SBsC increased IAM values of clinical isolates of *Kocuria spp.* 1.7-fold ( $p < 0.05$ ) compared to IAM values of the control (Table 1).

IAM indices of clinical isolates of *Kocuria spp.* under the action of remedy based on decamethoxine SBsC were 1.6 times ( $p < 0.05$ ) and 2.1 times ( $p < 0.05$ ) lower compared to IAM indices after the action of remedy based on chlorhexidine bigluconate SBsC and of remedy based on iodoform, respectively. Such data are important to consider when treating and preventing infectious and inflammatory processes, the etiological factor of which is bacteria of the genus *Kocuria*.

Table 1

**IAM indices of clinical isolates of *Kocuria* spp. under the action of SBsC of remedies based on decamethoxine, chlorhexidine bigluconate, iodoform (M±m)**

Antiseptics Culture	Control	Remedy based on decamethoxine	Remedy based on chlorhexidine bigluconate	Remedy based on iodoform
<i>Kocuria</i> spp	17.73±2.08	13.73±1.01 <sup>#€£</sup>	21.46±2.98	29.33±2.08 <sup>#</sup>

Note: # – the significance of the difference in IAM cultures in the presence of antiseptics with IAM control ( $p < 0.05$ ); € – the significance of the difference between IAM cultures in the presence of remedy based on decamethoxine and IAM cultures in the presence of remedy based on chlorhexidine bigluconate ( $p < 0.05$ ); £ – the significance of the difference between IAM cultures in the presence of remedy based on decamethoxine with IAM cultures in the accessibility of remedy based on iodoform ( $p < 0.05$ ).

In the course of the study, we studied the anti-adhesive properties of each clinical isolate separately. According to the criteria of V. I. Brillis, the clinical isolate *Kocuria kristinae* 1, the clinical isolate *Kocuria kristinae* 2 and the clinical isolate *Kocuria rosea* belong to highly adhesive microorganisms (Table 2).

Table 2

**IAM indices of clinical isolates of *Kocuria kristinae* 1, *Kocuria kristinae* 2, and *Kocuria rosea* under the action of SBsC of remedies based on decamethoxine, chlorhexidine bigluconate, iodoform**

Clinical isolates	Control	remedy based on decamethoxine	remedy based on chlorhexidine bigluconate	remedy based on iodoform
<i>Kocuria kristinae</i> 1	15.2	12.7	20.0	32.5
<i>Kocuria kristinae</i> 2	20.0	13.5	25.4	29.5
<i>Kocuria rosea</i>	18.0	15.0	19.0	26.0

The IAM of clinical isolates *Kocuria kristinae* 1 and *Kocuria kristinae* 2 decreased by a factor of 1.2 and 1.5, respectively, under the action of remedy based on decamethoxine SBsC. The IAM values of the clinical isolate *Kocuria rosea* decreased 1.2-fold. Analyzing the results of the study, we observed a tendency of decrease in IAM parameters of clinical isolates under the action of remedy based on decamethoxine, taking into account IAM parameters of control of these organisms.

In the presence of remedy based on chlorhexidine bigluconate SBsC, relative to the clinical isolates *Kocuria kristinae* 1 and *Kocuria kristinae* 2, IAM indices increased by 1.3 times, and IAM indices of *Kocuria rosea* increased 1.1 times compared to the IAM indices of the controls of these isolates. Evaluating the study results, there was a tendency for the IAM indices to increase under the action of the antiseptic agent remedy based on chlorhexidine bigluconate, which is important when choosing a drug for the treatment and prevention of an infectious and inflammatory process.

Considering the results of action remedy based on iodoform SBsC on clinical isolates *Kocuria kristinae* 1 and *Kocuria kristinae* 2, IAM increased in 2.1 times and in 1.5 times, IAM of clinical isolate *Kocuria rosea* also increased, but in 1.4 times, considering the control cultures. That is, remedy based on iodoform did not reduce the adhesive properties of clinical isolates of *Kocuria kristinae* and *Kocuria rosea*, and this in turn is important when choosing antiseptic drugs for adequate treatment and prevention of the pathological process.

It should be noted that the reservations of foreign scientists about the bacteria of the genus *Kocuria* are quite reasonable. Considering the pathogenic potential, namely the high adhesive properties of microorganisms of this genus, the high possibility of developing a pathological process caused by *Kocuria* spp. Venkataramana Kandi noted in his scientific papers that the genus *Kocuria* was not previously considered as microorganisms that could cause human disease. Recently, however, there have been more and more reports on infections caused by this genus of bacteria. The author notes that when identifying these microorganisms, additional studies should be performed to determine factors affecting bacterial pathogenicity [10]. Brian Nudelman in his research emphasizes that during microbiological diagnosis, as an etiological factor *Kocuria* spp. often remains undetected. This is due to the incorrect interpretation of the results during identification. Because laboratories use a standard set of test systems, which, based on biochemical properties, indicate primarily *Staphylococcus* spp. as the main pathogen of the pathological process, and not *Kocuria* spp. Only with the help of additional studies, it is possible to clarify the difference in the phenotypic similarity of these two genera. Perhaps a false conclusion is also established due to the habit of attributing the genus *Kocuria* to the resident microbiota of the human body and believing that representatives of this genus cannot cause the development of a pathological process [13]. But scientific research refutes such incorrect statements. Because *Kocuria* spp. increasingly began to be identified among the etiological factors of infectious and inflammatory processes [12, 14]. It is necessary to take into account scientific studies, which indicate possible changes in the properties of microorganisms, which in turn can lead to the acquisition of various factors of pathogenicity. Yes, we proved that *Kocuria* spp. have high adhesive properties, not losing them even after the action of antibacterial remedies, and in some cases, on the contrary, increasing them. Moreover, there are currently no publications on the pathogenicity factors of *Kocuria* spp., including their adhesiveness. Therefore, the results of research on the effect of modern

antiseptics on the ability of microorganisms to adhere will help practicing doctors in the correct choice of remedies for the treatment and prevention of pathological processes caused by *Kocuria* spp.

Along with this, a number of authors who studied the effect of agents based on decamethoxine and chlorhexidine bigluconate indicated in their works their ability to reduce the adhesive properties of clinical isolates of microorganisms obtained from different sites of the human body [4, 5]. Thus, it has been established that decamethoxine and remedies based on it have a powerful antimicrobial effect on planktonic and film forms of both Gram-positive and Gram-negative bacteria. In addition, the presence of this antiseptic reliably reduces the adhesive properties of clinical strains of the genus *Staphylococcus*, which correlates with the results presented in the article. Previous studies proved that the adhesion of staphylococci to human erythrocytes in the presence of different concentrations of decamethoxine has been changed from high to low [4]. In turn, studies of the effect of chlorhexidine bigluconate on the adhesive properties of Gram-positive cocci indicate its ineffectiveness. It was proved that the adhesive properties of clinical isolates of *Staphylococcus* spp. were weakly reduced in the presence of chlorhexidine bigluconate [5]. The presented results regarding the influence of chlorhexidine bigluconate on the ability of *Kocuria* spp. to adhere to the surfaces of human erythrocytes have a similar trend. That is, the IAM of *Kocuria* spp. in the presence of this antiseptic was somewhat reduced, however, the result was significantly inferior to the action of the remedy based on decamethoxine.

In turn, there are no modern experimental data on the influence of iodoform on the adhesive properties of clinically significant microorganisms. However, taking into account the frequency of use of this remedy in dental practice for the treatment of post-extraction complications, the presented results may contribute to the revision of the indications for its use. After all, we found a potentiation of the adhesiveness of microorganisms in the presence of iodoform.

Undoubtedly, the obtained results are related to the chemical structure and mechanism of action of the studied antiseptics. Chlorhexidine bigluconate and decamethoxine belong to cationic surface-active compounds. Thanks to this, their mechanism of action is associated with a change in the surface tension of a bacterial cell, which entails its osmotic lysis and death. It is possible that the surface proteins of Gram-positive microorganisms responsible for adhesion are blocked, reducing it. However, this mechanism of reducing adhesive properties requires further research. In turn, iodoform, as an iodine based, upon contact with a bacterial cell forms iodamines, coagulating the cell wall. This leads to the death of the microorganism. However, there is currently no data on the blocking of surface adhesins by remedy containing iodine. Moreover, iodine remedies are weak oxidizers and its widespread use as an antiseptic is due only to economic availability.

Clinical isolates of *Kocuria kristinae* and *Kocuria rosea* were found to be highly adherent microorganisms. The domestic antiseptic Decasan reduces the IAM values of clinical isolates of *Kocuria* spp. In turn, the antiseptic drug Iodoform increases the IAM values of the studied clinical isolates.

### Conclusions

1. According to the results of our research, it was found that the clinical isolates of *Kocuria kristinae* 1, *Kocuria kristinae* 2 and *Kocuria rosea* belong to highly adhesive microorganisms, because their IAM are 15.2, 20.0, 18.0 respectively.
2. An antiseptic remedy based on decamethoxine reduces IAM indices of clinical isolates of *Kocuria* spp. 1.6 times ( $p < 0.05$ ) and 2.1 times ( $p < 0.05$ ) in comparison with the indicators of AMI after the effect of SBsK antiseptic remedies based on chlorhexidine bigluconate and iodoform.
3. An antiseptic remedy based on iodoform increases the IAM indices of *Kocuria kristinae* 1 by 2.1 times, *Kocuria kristinae* 2 by 1.5 times, and *Kocuria rosea* by 1.4 times.
4. It is necessary to take into account presented results, which indicate possible changes in the properties of *Kocuria* spp., which in turn can lead the revision of the indications for use of antiseptics.

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## BIOCHEMICAL CHANGES IN THE EXTRACELLULAR MATRIX OF RAT LIVER DURING CHRONIC ALCOHOL INTOXICATION

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Excessive alcohol consumption is a global health problem worldwide, resulting in more than 3 million deaths each year. The purpose of this work was to study the biochemical markers of intercellular matrix metabolism of rat liver under the conditions of chronic alcohol intoxication modeling. The experiments were performed on 30 male Wistar rats, weighing 180-220 g. The animals were divided into 2 groups: I – control; II – chronic alcohol intoxication. Animals were removed from the experiment on days 10, 14, 21 and 28. We studied concentration of glycosaminoglycans, oxyproline and sialic acids in rat liver. We established that the greatest depolymerization of proteoglycans was on the 21st day, the highest intensity of collagenolysis was on the 14th day. Glycoproteins underwent the greatest catabolism on the 28th day. Chronic alcohol intoxication on the 28th day led to increased breakdown of glycoproteins and proteoglycans of the extracellular matrix of the liver, and increased the intensity of collagenolysis.

**Key words:** alcohol, liver, glycosaminoglycans, sialic acids, oxyproline, extracellular matrix.

## А.О. Микитенко, О.Є. Акімов, Г.А. Єрошенко, О.М. Шевченко, К.С. Непорада БІОХІМІЧНІ ЗМІНИ У ЕКСТРАЦЕЛЮЛЯРНОМУ МАТРИКСІ ПЕЧІНКИ ЩУРІВ ПРИ ХРОНІЧНІЙ АЛКОГОЛЬНІЙ ІНТОКСИКАЦІЇ

Надмірне споживання алкоголю є глобальною проблемою охорони здоров'я у всьому світі, що призводить до понад 3 мільйонів смертей щороку. Метою роботи було вивчити біохімічні маркери метаболізму міжклітинного матриксу печінки щурів за умов моделювання хронічної алкогольної інтоксикації. Експерименти виконані на 30 білих статевозрілих щурах-самцях лінії Вістар, вагою 180-220 г. Тварини були розділені на 2 групи: I – контрольна; II група – група хронічної алкогольної інтоксикації. Виведення тварин з експерименту відбувалося на 10, 14, 21 та 28 добу. В гомогенаті печінки щурів визначали загальну концентрацію глікозаміногліканів та їх фракції, концентрацію вільного оксипроліну та сіалових кислот. Нами встановлено, що найбільшій деполімеризації зазнають протеоглікани позаклітинного матриксу печінки щурів на 21 день хронічної алкогольної інтоксикації. Найвища інтенсивність колагенлізу спостерігається на 14 добу хронічної алкогольної інтоксикації. Глікопротеїни печінки щурів зазнають найбільшого катаболізму на 28 добу хронічної алкогольної інтоксикації. Хронічна алкогольна інтоксикація на 28 день призводить до посилення розпаду глікопротеїнів та протеогліканів позаклітинного матриксу печінки, та посилює інтенсивність колагенлізу.

**Ключові слова:** алкоголь, печінка, глікозаміноглікани, сіалові кислоти, оксипролін, позаклітинний матрикс.

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Excessive alcohol consumption is a global public health problem worldwide with enormous social, economic and medical consequences, resulting in more than 3 million deaths each year [10]. The liver undergoes the earliest and greatest degree of tissue damage from excessive alcohol consumption, as it is the primary site of ethanol catabolism. Alcohol abuse is the world's third risk factor for disease and