



The prevalence of penicillin-resistant *S. aureus* strains was 7.6 % in 1946-49, 76.4- 91.9 % in 1958, 68.0-94.0 % in 1968 (Volyansky Yu.L., 1971). Nowadays more than 90 % of staphylococcal isolates are resistant to this antibiotic.

In the Chernivtsi region, according to Voljansky Yu.L., in 1970, 60 % of *S. aureus* strains isolated from nasal noses were resistant to penicillin. In 1997-2004 - 83.2 % of *S. aureus* strains were resistant to penicillin, and the proportion of MRSA was 52.2 % (Blinder O. O, 2005). According to the research results in 2015-2016 years, resistance to penicillin is established in 72.2 % strains of *Staphylococcus aureus*.

Determining the sensitivity of antibiotics to clinical isolates and monitoring the prevalence of antibiotic-resistant bacteria in healthcare facilities and regions is important and essential for epidemiological analysis.

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## **FUNGAL DISEASES OF HUMANS AND DETERMINATION OF THE ANTIFUNGAL ACTIVITY OF NEW DERIVATIVES OF THE QUINOLONE-CONTAINING COMPOUNDS**

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Mycosis is one of the widespread groups of infections caused by various types of pathogenic and opportunistic fungi belonging to eukaryotic microorganisms of plant origin. The problem of mycoses today is quite acute: the fungal lesions distort the skin of the patient, the inflammation of the body occurs alongside the disease (with the exception of keratomycosis), many organs and tissues are affected (systemic mycoses develop), also, the granulomas appear to disrupt the function of many organs.

The microorganisms of this group are characterized of a high level of cellular organization, morphological diversity, complex life cycles, sexual and asexual reproductive cycles. Fungi can exist in the form of unicellular microorganisms (yeast, yeast-like mushrooms), or as a micelle. The features of metabolism, chemical composition and morphofunctional organization of fungi determine the peculiarity of infections having been caused by these microorganisms. In addition to the discomfort experienced by the patient (itching, non-aesthetic condition of the skin or nails), mycoses can cause allergic reactions, even bronchial asthma. An urgent problem of the present is the treatment itself and the search of new antimycotic remedies.

For the recent years, there has been a sharp increase in the frequency and severity of fungal infections, including chronic and deep mycosis. Deep mycoses include several groups of different diseases: opportunistic systemic mycosis; subcutaneous deep mycosis (chromoblastomycosis, sporotrichosis). Severe systemic mycoses is observed to have a significant increase nowadays. All mycoses are contagious, but this does not mean that patients should be isolated from each other. They simply need to adhere to some precautionary rules: to avoid handshake, wash your bathroom thoroughly, adhere to the rules of hygiene, but the main thing is not to cause a delay with the treatment. When planning anti-fungal therapy, special attention should be paid to the action of the therapeutic agent on the pathogen (fungistatic or fungicidal) and on the macroorganism (considering both the state of the immune system and the individual sensitivity to this drug). All this suggests to search for new anti-fungal drugs for fighting against candidiasis. A goal of identifying the minimal fungistatic (MFsK) and minimal fungicidal (MFcK) activity of quinolone-containing salts was set. The common method of double serial dilutions in the Saburro broth was applied. As a test object the *C. albicans* ATCC 885-653 was used in the case. 10 derivatives of quinolone-containing salts were selected for the study.

All the compounds are found to show an anti-candidiasis activity in the course of the study. The smallest anti-candidal activity have C1, C5, and C11, with minimal fungistatic concentrations of 125.0 µg/ml. The rest of the compounds having been studied show a higher anti-candidal activity. The most active activity among this group was shown by the compounds C9 and C10, with minimal fungistatic concentrations of 31.25 µg/ml and minimal fungicides of 62.5 µg/ml.

The indicated results allow us to continue the search for anti-candidiasis agents among derivatives of quinolone-containing salts, including the purposeful synthesis of new compounds with the predicted antifungal properties.

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## **THE PROBLEM OF ANTIBIOTIC RESISTANCE IN MEDICINE**

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Today, such a concept as antibiotic resistance is not only a medical problem, it has a huge socioeconomic significance and is seen as a threat to national security. Infections caused by resistant strains of pathogenic microorganisms are characterized by a more severe course, prolong the stay of the patient in a hospital, requiring the use of combined antibiotic therapy with the use of rescue drugs. All this leads to a big expenses of treatment, worsens the health and life prognosis of patients, and increases the risk of the resistant strains spread, which, in turn, leads to the emergence of epidemics.

The development of microorganism resistance is inevitable, even when prescribing antibiotics in an appropriate therapeutic dose. Many factors contribute to this, including free access to drugs, inappropriate diagnosis, lack of objective information, etc. In most cases, the use of antibacterial drugs is adequate, rational and well-grounded,



and in some other cases it is possible to refuse from their use at all. The frequency of antibacterial drugs usage for viral infections remains rather high.

The prescription of antibiotics in order to prevent bacterial complications often justifies their use in acute respiratory viral infections cases. In order to solve the problem of antibiotic resistance, first and foremost, a well-grounded usage of antimicrobial means are needed, which is difficult to implement in practice. One must also avoid mistakes when choosing an antibiotic dosage regime, especially the use of an insufficient or excessive dose and the wrong choice of interval between the usages.

In Ukraine, the antibiotic resistance has its own peculiarities. First of all, antibiotics are available to the public because they are sold in pharmacies without any prescription. There is also a social problem of inadequate access to these drugs. Poverty of patients or medical institutions, some emergencies lead to the use of low-quality or fake drugs, which predetermines the rapid selection of resistant strains of microorganisms. One of the mistakes during the infections treatment is the unfounded prescription of an antibiotics combination. With the antibacterial drugs of a wide range of effects, indications for combined antibiotic therapy are significantly narrowed and the priority in the treatment of many infections depends on monotherapy. In addition, the recommendations for the length of the treatment course are not always followed. The traditional approach to antibiotic therapy is the beginning of empirical treatment from simple antibiotics, whereas a wide spectrum of antibiotics remains as a reserve for patients whose condition progressively worsens, and also in whom the resistant strains of microorganisms have been identified. The obligatory conditions of antibiotic therapy is that the spectrum of action of the antibiotic, that has been used, should correspond to the likely pathogen or pathogens.

The antibiotic that is being used should overcome the acquired resistance mechanisms of the pathogen. The chosen regime of the dosage should create the appropriate level of concentration of antibacterial preparation in the center of infection, which promotes the rapid death of the pathogen. Antibiotic resistance is a global problem. There is no country that can afford to ignore it, and there is no country that might not respond to it. Only the actions that are carried out simultaneously to control the growth of antibacterial resistance in each individual country can lead to positive results in the whole world.

Thus, the knowledge of pharmacodynamic peculiarities of antibacterial drugs, their dosage and the term of prescription, a well-grounded and rational usage can influence the effectiveness of antimicrobial therapy of infections.

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#### **THE SEARCH OF NEW ANTICANDIDAL PREPARATIONS AMONG THE QUATERNARY BENZOCHINOLINE AND ACREDINE SALTS**

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One of the problematic issues of candida infection is the resistance to antimycotic drugs. Among the already known 150 *Candida species*, 20 of them are pathogenic to humans, 8 of which are most often isolated from patients with candidiasis, and 4 are recognized as major pathogens (*C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. saugrata*).

The main reason that draws attention to the etiological heterogeneity of candidiasis is the resistance of some species to antimycotic drugs. In order to understand the conditions for the emergence of resistance to antimycotics, it is necessary to mention the mechanisms of action of antimycotics. In most cases, this is a fungistatic effect, due to which the antimycotics do not kill, but only stopes the reproduction of fungi, resulting their end afterwards. This fungistatic, and not fungicidal action determines the possibility of resistance. Due to the increased resistance of fungi to traditional antimycotics, the issue of finding new drugs to fight fungal infections, including those caused by candidiasis, is urgently raised.

The aim of the study is to determine the minimal fungistatic (MFsK) and minimal fungicidal (MFcK) activity of new compounds using the common method of double serial dilutions in the Saburro broth. As a test object, *C. albicans* ATCC 885-653 was used.

20 quaternary benzoquinoline and acridine salts were selected to determine anticandidal activity. All of the 20 salts of benzoquinoline and acridine were found to show an anticandidal activity. However, the severity of this activity is significantly different in different salts. Thus, compounds as B3, B5, B6 and B12, with minimal fungicidal concentrations ranging from 125.0 µg/ml to 250.0 µg/ml, show the least anticandidal activity. The rest of the compounds having been studied show the significantly higher antifungal activity - their minimal fungistatic concentrations ranged from 3.9 µg/ml to 31.5 µg/ml, and the minimal fungicides - from 3.9 µg/ml to 125.0 µg/ml.

These results allow us to continue searching the antifungal agents among the quaternary benzoquinoline and acridine salts, including the way of expanding the spectrum of the studied test - cultures and due to the purposeful synthesis of novel compounds with predicted antifungal properties.