

**МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
БУКОВИНСЬКИЙ ДЕРЖАВНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ»**



МАТЕРІАЛИ

**104-ї підсумкової науково-практичної конференції
з міжнародною участю
професорсько-викладацького персоналу
БУКОВИНСЬКОГО ДЕРЖАВНОГО МЕДИЧНОГО УНІВЕРСИТЕТУ
06, 08, 13 лютого 2023 року**

Конференція внесена до Реєстру заходів безперервного професійного розвитку,
які проводитимуться у 2023 році №5500074

Чернівці – 2023

expect that given the importance of heterocycles in the chemistry of life, they should have found application in medicine as well. This is true. Long before the development of pharmaceutical chemistry, people treated diseases using heterocyclic compounds from nature's pharmacy: leaves, fruits and bark of trees, roots and stems of herbs, extracts from insects, etc. The twentieth century is sometimes called the age of the Great Medical Revolution. One of its bright symbols, of course, should be considered β -lactam antibiotics – penicillin and cephalosporin, which have saved millions of human lives. Both of them are derivatives of heterocyclic compounds.

Conclusions. In recent years, there has been a breakthrough in solving such a difficult task as the creation of effective antiviral drugs. Of course, only a small part of what makes heterocycles interesting has been told. We should also mention the outstanding role of heterocycles in the respiratory process and energy conservation, photosynthesis, production of pesticides, dyes, heat-resistant polymers, analytical reagents and many other practically important materials. In recent years, a new rapidly developing field of science is closely related to heterocycles – supramolecular chemistry, which investigates the patterns of self-organization of molecules and their recognition by each other.

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STUDY OF ANTIMICROBIAL ACTIVITY AMONG NEW PHOSPHONIUM SALTS

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Introduction. Uncontrolled prescription of drugs with antimicrobial action contributed to the selection of resistance of pathogenic and opportunistic microorganisms to antibacterial and antiseptic drugs, which in their turn led to an increase in the role of infectious diseases caused by resistant strains of microorganisms.

The aim of the study. In connection with a wide spread of microorganisms that have acquired resistance to many antibacterial and antiseptic drugs, it is necessary to search for new substances that could be used in medicine as antimicrobial and antiseptic substances.

Material and methods. Screening of antimicrobial activity among new naphthalene-containing phosphonium salts was carried out using 5 test cultures. Experiments to determine the antimicrobial activity of new phosphonium salts were performed applying the micromethod using disposable polystyrene tablets and Takachi microtitrators.

Results. The results of studying the antimicrobial activity of the indicated compounds are shown in the table.

Table

Antimicrobial activity of naphthalene-containing phosphonium salts ($\mu\text{g/ml}$)

№ compounds	<i>S.aureus</i> ATCC 25923		<i>E.coli</i> ATCC 25922		<i>E.faecalis</i> ATCC 29213		<i>P.aeruginosa</i> ATCC 27853		<i>B.subtilis</i> 8236 F 800	
	MIC	MB _C C	MIC	MB _C C	MIC	MB _C C	MIC	MB _C C	MIC	MB _C C
1	7,8	15,6	250	500	62,5	125	250	500	7,8	15,6
2	7,8	15,6	250	500	62,5	125	250	500	7,8	15,6
3	15,6	15,6	250	500	125	125	500	>500	15,6	15,6
4	7,8	15,6	250	500	62,5	125	250	500	7,8	15,6
5	7,8	15,6	500	500	62,5	125	500	500	15,6	31,2
6	7,8	15,6	250	500	62,5	125	250	500	7,8	15,6
7	7,8	15,6	250	500	62,5	125	250	500	7,8	15,6
8	7,8	15,6	250	250	125	125	500	500	62,5	62,5
9	3,9	7,8	125	250	62,5	125	500	>500	7,8	15,6
16	3,9	7,8	125	125	62,5	62,5	500	>500	3,9	7,8

Note: MIC: minimum inhibitory concentration; MB_CC: minimum bactericidal concentration

Conclusions. These salts show the highest antibacterial activity against Gram-positive microorganisms – *Staphylococcus aureus* (*S.aureus* ATCC 25923) and vegetative cells of spore-forming bacilli (*B.subtilis* 8236 F 800). *E.faecalis* ATCC 29213 showed much lower sensitivity to the action of these compounds. Gram-negative microorganisms (*E.coli* ATCC 25922 and *P. aeruginosa* ATCC 27853) were significantly more resistant to the action of naphthalene-containing phosphonium salts. The results of our research obtained testify of the expediency of further synthesis and study of antimicrobial activity among naphthalene-containing phosphonium compounds.

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**CYTOKINES' MECHANISMS OF IMMUNOLOGICAL DISORDERS
IN CHILDREN WITH HEARING LOSS DEPENDING ON GENE POLYMORPHISM
INTERLEUKIN-4 (rs2243250)**

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Intoduction. Nowadays, about 360 million people worldwide suffer from hearing loss. Hearing loss can be caused by genetics, birth defects, certain infectious diseases, chronic ear infections, certain medications, exposure to excessive noise, etc. About 100 genes in the human body are responsible for the hearing organ formation and function. However, there are currently no guidelines for using of molecular genetic tests in the early diagnosis of deafness. The question of the impact of genetic factors on the features of the immune response depending on the type of deafness is also debatable.

The aim of the study. To evaluate some immunological mechanisms of sensorineural (SNHL) and conductive hearing loss (CHL) development in children after pro- and anti-inflammatory cytokine levels depending on gene polymorphism of interleukin-4 (IL-4, C-590T) (rs 2243250).

Material and methods. The prospective study included 102 children aged 8 to 18 years with hearing impairments, whose parents signed an informed consent to participate in the study, followed by a set of anamnestic-clinical and laboratory-instrumental examinations (otoscopy, speech audiometry, tone audiometry). Among the examined children 68 (66.7%) once had SNHL, 34 (33.3%) - CHL. The control group consisted of 30 practically healthy children. Levels of cytokines: tumor necrosis factor-alpha (TNF- α), IL-1 β , IL-4, IL-10 and IL-13 in plasma were determined by ELISA. Study of gene polymorphism of IL-4 (C-590T) performed by polymerase chain reaction. Statistical processing was performed with Statistica® 7.0 software. The differences were considered significant at $p < 0.05$.

Results. The analysis of the obtained results showed that the SNHL and CHL course in children is associated with a decreased concentration of IL-1 β in the peripheral venous blood plasma by 36.06% and 29.53%, increased of IL-4 1.69 ($p < 0.05$) and 2.68 times ($p = 0.013$) and different changes of TNF α content (increases in CHL children, reduces in SNHL cases), IL-10 and IL-13 (contrary, it increases in SNHL children and decreases in CHL subjects).

The imbalance of the immune response in children with SNHL is characterized by inhibition of cellular immunity and activation of humoral answer caused by low TNF- α and IL-1 β content in CT, TT-genotype carriers of IL-4 gene – 2.42 ($p = 0.032$) and 2.02 times ($p = 0.042$) with the anti-inflammatory IL-4 and IL-10 cytokines hyperproduction 4.4-16.45 times ($p \leq 0.005$).

In children with the TT-genotype of the IL-4 gene, CHL occurs with an increase in TNF- α by 1.69 times ($p = 0.033$) and IL-4 35.71 times ($p < 0.001$), a decrease in the level of IL-10 by 3.11-4.44 times ($p \leq 0.01$) and IL-13 – 1.66-2.72 times ($p \leq 0.026$) respectively which is generally evidence of an acute inflammatory process of a predominantly infectious nature.

Conclusions. Sensorineural hearing loss in the T-allele carriers' children is characterized by decreased activity of anti-infectious nonspecific immune defense factors, whereas conductive hearing loss course is associated with cell immune response activation (mainly) and humoral part (less) as well.