ЕҢБЕК ҚЫЗЫЛ ТУ ОРДЕНДІ
«Ә. Б. БЕКТҰРОВ АТЫНДАҒЫ
ХИМИЯ ҒЫЛЫМДАРЫ ИНСТИТУТЫ»
АКЦИОНЕРЛІК ҚОҒАМЫ

ҚАЗАҚСТАННЫҢ ХИМИЯ ЖУРНАЛЫ

ХИМИЧЕСКИЙ ЖУРНАЛ КАЗАХСТАНА

CHEMICAL JOURNAL of KAZAKHSTAN

АКЦИОНЕРНОЕ ОБЩЕСТВО
ОРДЕНА ТРУДОВОГО КРАСНОГО ЗНАМЕНИ
«ИНСТИТУТ ХИМИЧЕСКИХ НАУК
им. А. Б. БЕКТУРОВА»

3 (63)

ИЮЛЬ – СЕНТЯБРЬ 2018 г.

ИЗДАЕТСЯ С ОКТЯБРЯ 2003 ГОДА

ВЫХОДИТ 4 РАЗА В ГОД

АЛМАТЫ
2018

542.951.3+547.512

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ESTERS OF CYCLOPROPANECARBOXYLIC ACID DISPLAYING ANTI-INFECTIVE ACTIVITY

Abstract. A number of esters of cyclopropanecarboxylic acid of N-alkyl naphthyloxypropynylpiperidines antimicrobial activity have been studied in relation to the archival strains of microorganisms. The activities of the given preparations have been assessed *in vitro* in relation to *Bacillus subtilis* ATCC 6633, *Escherichia coli* ATCC 25922, *Salmonella enterica* ATCC 14028 and *Staphylococcus aureus* ATCC 6538-P, among which hydrochloride of 1-methyl-4-[3-(naphth-1-yloxy)prop-1-in-1-yl]-4-cyclopropanecarbonyloxypiperidine has displayed the greatest activity in relation to the archival strain of *Bacillus subtilis* ATCC 6633 in the concentration of 250 μg/ml.

Esters of cyclopropanecarboxylic acid of N-methyl phenoxypropynylpiperidine and phenyl ethinylpiperidine have displayed antimicrobial activity *in vitro* in relation to all seven strains of microorganisms, used in the experiment: *Escherichia coli* ATCC 25922, *Escherichia coli* ATCC-BAA-196, *Klebsiella pneumoniae* ATCC 10031, *Klebsiella pneumoniae* ATCC 700603, *Staphylococcus aureus* ATCC 6538-P, *Staphylococcus aureus* ATCC-BAA-39, *Candida albicans* ATCC 10231.

Hydrochloride of ester of N-benzylpiperidine-4-ketoxime of cyclopropanecarboxylic acid has a bactericidal activity in relation to the strains of the testing cultures of *Eshirichia Coli1257* and *Staphylococcus aureus 209-P*.

Key words: cyclopropanecarbonylchloride, piperidine, esters, antimicrobial activity.

Despite of a huge arsenal of available medicines, the problem of searching of new highly efficient medicinal preparations remains topical. This is stipulated by the lack or insufficient efficiency of medicinal preparations for treatment of certain diseases; side effects of certain medicinal remedies; their validity period limitations [1].

Based on the analysis of the scientific and patent literature the authors [2] point out, that the search of new synthetic medicinal preparations is mainly carried out in three directions:

1) modification or further development of the existing biologically active matrices;

2) molecular design of the structures, including the fragments of natural compounds;

3) molecular design of completely new classes of organic compounds, mainly of the heterocyclic series.

At present, the creation of innovative medicinal preparations include the obtaining of new chemical products and synthesis of pharmacologically active

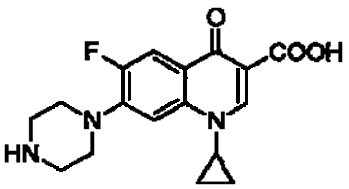
metabolites or their isomers. The development of modern medicinal forms with improved pharmacokinetic properties and new drug delivery means, creation of multicomponent biotechnological or bioengineered preparations and medicines.

The substances, containing in their structure as fragment of cyclopropane, are considerable interest for the both organic chemists and biochemists. A three-membered saturated carbocycle is a structural element with a huge synthetic potential, stipulated by a high voltage energy (~ 27,5 kcal/mol) of an unusual type of carbon-carbon bonds, called the “banana bonds”. By their nature, they are intermediate between σ- and π-bonds, due to which cyclopropane derivatives enter into various reactions of cycle opening and extension, as well as the reactions of cycloaddition [3, 4].

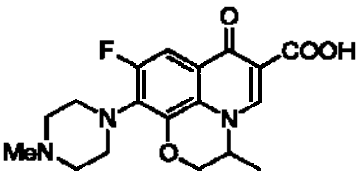
Many natural and synthetic compounds containing as cyclopropane fragment with a simple functionality, possess a wide spectrum of biological properties [5], ranging from enzyme inhibition to insecticidal, antifungal, herbicidal, antimicrobial, antibiotic, antibacterial, antitumoral [6] and antiviral, antiestrogenic, agonistic properties. The studies in the field of biosynthesis and metabolism of cyclopropane derivatives provide the information, which is required for the development of new medicinal preparations [7]. Heterocyclic compounds, possessing a cyclopropyl group as a substituent, are of special interest [8-10].

Being present in animals, plants and microorganisms or temporarily appearing upon primary and secondary metabolism, they provide convenient biological probes for mechanistic studies, and make it possible to develop new medicinal preparations.

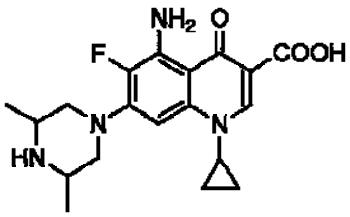
In terms of medical use, it is noteworthy, that eight of the two hundred best-selling pharmaceutical preparations are the compounds, containing a cyclopropane fragment [5]:



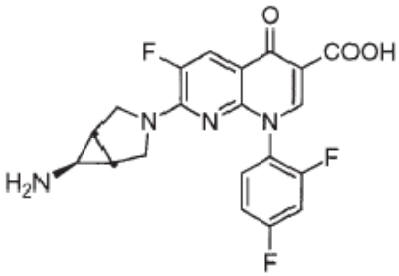
Ciprofloxacin



Ofloxacin



Sparfloxacin



Trovafloxacin

Thus, cyclopropane-containing antibacterial agents, such as ciprofloxacin CPFX, ofloxacin OFLX, sparfloxacin SPFX and trovafloxacin, are members of the principal class of broad-spectrum antibacterial medicinal preparations, and are widely used for the treatment of patients.

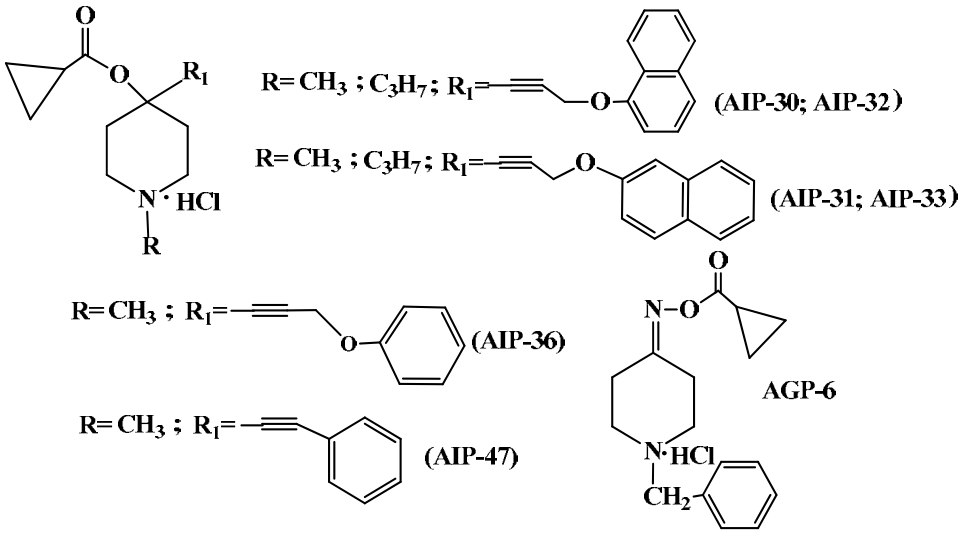
A piperidine ring is the ubiquitous structural feature of many alkaloid natural products and medicine candidates. Watson P.S. et al. [11] believe, that thousands of piperidine compounds have been mentioned in clinical and preclinical studies for the last decade. Nevertheless, the variety of functional and substituent structures, found in the piperidine targets, and the generally accepted concept, that the biological properties of piperidines strongly depend on the type and location of substituents on the heterocyclic ring.

The search for new compounds with antimicrobial and virucidal activities, including those capable to induce reversion of medicine susceptibility, is related to a priority direction in the field of development of new anti-infective medicinal preparations. The importance of the scientific research, despite the availability of a wide range of antibacterial medicinal remedies, is associated, first and foremost, with the high adaptability of pathogenic organisms to the medicinal preparations, including antibiotics [12-14].

This work is a continuation of the studies in the synthesis of new antibacterial medicinal preparations in a series of piperidine-containing derivatives of cyclopropanecarboxylic acid [15, 16].

The compounds with the codes AIP and AGP have been studied for an antimicrobial activity. The results of the biological tests are presented in tables 1-3. The research model includes the required minimum of tests with different degrees of sensitivity *in vitro* [17]. The research scheme has been implemented in accordance with the current methodical recommendations, approved by the State Pharmacological Committee of the Republic of Kazakhstan [18].

Study of a biological activity. The compounds with the codes AIP-30, AIP-31, AIP-32, AIP-33 have been studied for an antimicrobial activity in relation to the archival strains of microorganisms, the activities of these preparations have been assessed *in vitro* in relation to *Bacillus subtilis* ATCC 6633, *Escherichia coli* ATCC 25922, *Salmonella enterica* ATCC 14028 and *Staphylococcus aureus* ATCC 6538-P:



As it is seem from the results presented in table 1, the compounds AIP-30 and AIP-31 [19-20] possess an antimicrobial activity in relation to all strains of microorganisms, used in the experiment. The compounds AIP-30 and AIP-31 display antimicrobial effects to different extents, AIP-30 has displayed the greatest activity in relation to the archival strain of *Bacillus subtilis* ATCC 6633 in the concentration of 250 μg/ml. Streptomycin has been active in relation to the gram-negative strains of microorganisms (*Escherichia coli, Staphylococcus aureus, Salmonella enterica*), and its efficiency in relation to *Bacillus subtilis* makes up only 50-60%.

Table 1 – Antimicrobial activity of AIP-30 - AIP-33

Strain / Code of the compound	MIC, μg/ml			
	Bacillus subtilis ATCC 6633	*Escherichia coli* ATCC 25922	*Staphylococcus aureus* ATCC 6538-P	*Salmonella enterica* ATCC 14028
AIP-30	250	250	1000	500
AIP-31	250	500	1000	1000
AIP-32	1000	–	–	–
AIP-33	500	2000	–	–

The compound AIP-32 [21] possesses an antimicrobial activity in relation to the archival strain of *Bacillus subtilis* ATCC 6633 in the concentration of 1000 μg/ml.

The compound AIP-33 [22] possesses an antimicrobial activity in relation to the archival strain of *Bacillus subtilis* ATCC 6633 in the concentration of

500 μg/ml, and it displays an activity in relation to *Escherichia coli* in the high concentration of 2000 μg/ ml.

Thus, it has been established, that AIP-32 displays a selective antimicrobial activity to the one type of the archival strains, and AIP-33 – to the two types of the archival strains, used in the experiment.

The compounds with the codes AIP-36, AIP-47 have been studied for an antimicrobial activity in relation to the archival strains of microorganisms, the activities of these preparations have been assessed *in vitro* for *Escherichia coli* ATCC 25922, *Escherichia coli* ATCC-BAA-196, *Klebsiella pneumoniae* ATCC 10031, *Klebsiella pneumoniae* ATCC 700603, *Staphylococcus aureus* ATCC 6538-P, *Staphylococcus aureus* ATCC-BAA-39, *Candida albicans* ATCC 10231:

Table 2 – Antimicrobial activity of AIP-36, AIP-47

Strain / Code of the compound	MIC, μg/ml						
	Escherichia coli ATCC 25922	*Escherichia coli* ATCC-BAA-196	*Klebsiella pneumonia* ATCC 10031	*Klebsiella pneumonia* ATCC 700603	*Staphylococcus aureus* ATCC 6538-P	*Staphylococcus aureus* ATCC-BAA-39	*Candida albicans* ATCC 10231
AIP-36	1000	2000	1000	2000	2000	2000	1000
AIP-47	1000	2000	1000	HA	2000	2000	1000

As it is seen from table 2, the compound AIP-36 [23] possesses an antimicrobial activity in relation to all seven archival strains of microorganisms, used in the experiment: *Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 10031, *Candida albicans* ATCC 10231 in the concentration (MIC) of 1000 μg/ml, and in relation to *Escherichia coli* ATCC-BAA-196, Klebsiella *pneumoniae* ATCC 700603, *Staphylococcus aureus* ATCC 6538-P, *Staphylococcus aureus* ATCC-BAA-39 – in the concentration (MIC) of 2000 μg/ml.

AIP-47 [24] also displays an antimicrobial activity in relation to all seven archival strains of microorganisms, used in the experiment: *Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 10031 in the concentration (MIC) of 1000 μg/ml, and in relation to all other strains of microorganisms - in the concentration (MIC) of 2000 μg/ml.

Hydrochloride of ester of 1-benzyl-piperidine-4-ketoxime of cyclopropanecarboxylic acid with the laboratory code AGP-6 [25] has been studied for an anti-infective activity and acute toxicity. The data have been compared with the indices of streptomycin. The results of the study are presented in table 3.

The toxic dose of the preparation AGP-6 is 833.3 + 17.8 mg/kg, which is almost 4 times lower, than the toxicity of streptomycin, used as a reference. It has turned out, that the preparation AGP-6 possesses a bactericidal activity in relation to the testing cultures of *Eshirichia Coli1257* and *Staphylococcus aureus* 209-P both in the concentrations of 1% and 3%.

Table 3 – Results of the biological study of AGP-6 and streptomycin

Preparation	LD_{50}, mg/kg	Bactericidal activity in relation to			
		1 % concentration		3 % concentration	
		E. Coli 1257	*St. aureus 209-P*	*E. Coli 1257*	*St. aureus 209-P*
AGP-6	833.3+ 17.8	Growth inhibition of the microorganism the well	15 mm	Growth inhibition of the microorganism the well	25 mm
Streptomycin	213.8+ 22.61	Growth inhibition of the microorganism the well	Growth inhibition of the microorganism the well	Growth inhibition of the microorganism the well	Growth inhibition of the microorganism the well

The total assessment score of a locally irritating effect of AGP-6 on skin and ocular mucosa (cornea and conjunctiva) is equal to 3. This value is related to the 4^{th} class of chemical hazard by toxicological properties according to Methodology Guidelines 12.1105-02. Besides, slight erythema, scaling and irritation of skin have been observed for 10 days, all irritation signs disappearing completely on the 14^{th} day.

Thus, according to the instruction for the experimental (preclinical) study of new pharmacological substances, the test compounds may be used in additional studies for revealing an antimicrobial activity on a wider range of microorganisms.

Conclusion. Hydrochloride of 1-methyl-4-[3-(naphth-1-yloxy)prop-1-in-1-yl]-4-cyclopropanecarbonyloxypiperidine (AIP-30) has displayed the greatest activity in relation to the archival strain of *Bacillus subtilis* ATCC 6633 in the concentration of 250 μg/ml.

Esters of cyclopropanecarboxylic acid of N-methyl phenoxypropynylpiperidine and phenyl ethinylpiperidine, AIP-36 and AIP-47, have displayed an antimicrobial activity *in vitro* in relation to all seven strains of microorganisms, used in the experiment: *Escherichia coli* ATCC 25922, *Escherichia coli* ATCC-BAA-196, *Klebsiella pneumoniae* ATCC 10031, *Klebsiella pneumoniae* ATCC 700603, *Staphylococcus aureus* ATCC 6538-P, *Staphylococcus aureus* ATCC-BAA-39, *Candida albicans* ATCC 10231.

It has been also shown, that hydrochloride of ester of N-benzylpiperidine-4-ketoxime of cyclopropanecarboxylic acid (AGP-6) suppresses the growth of *E. Coli1257* and *St. aureus 209-P* with low toxicity.

Thus, it has been shown, that the directed introduction of a cyclopropanecarboxylic fragment into the structure of naphthyloxypropynylpiperidine, phenoxypropynylpiperidine, phenylethynylpiperidine and N-benzylpiperidine-4-ketoxime leads to the compounds of an anti-infective activity.

REFERENCES

[1] Kubinyi G. In search for new compounds-leaders for the creation of medicines // D.I. Mendeleyev Russian Chem. J. 2006. N 2. P. 5-17.

[2] Golovko Yu.S., Ivashkevich O.A., Golovko A.S. Modern methods of searching for new medicinal remedies // Herald BSU. Series. 2. 2012. N 1. P. 7-15.

[3] Salaun J. The Chemistry of the Cyclopropyl Group // J. Wiley & Sons: New York, 1987. Vol. 1. P. 809-876.

[4] A. de Meijere, Wessjohann L. Tailoring the Reactivity of Small Ring Building Blocks for Organic Synthesis // Synlett. 1990. P. 20-32.

[5] Salaun J. Cyclopropane Derivatives and their Diverse Biological Activities // Topics in Current Chemistry. Vol. 207 © Springer, 2000.

[6] Symon A.V., Veselova N.N., Kaplun A.P., Vlasenkova N.K., Fedorova G.A., Liutik A.I., Gerasimova G.K. Shvrts VI. Synthesis and antitumor activity of cyclopropane derivatives of betulinic and betulonic acids // Bioorg. Khim. 2005. 31(3). P. 320-325.

[7] Wessjohann L.A., Brandt W. Biosynthesis and Metabolism of Cyclopropane Rings in Natural Compounds // Chem. Rev. 2003. 103. P. 1625-1647.

[8] Pokhodylo N.T., Matiichuk V.S., Obushak N.D. Methyl 3-Cyclopropyl-3-oxopropanoate in the Synthesis of Heterocycles Having a Cyclopropyl Substituent // Russ. Jour. of Organic Chemistry. 2010. Vol. 46, N 6. P. 894-897.

[9] Marradi M., Brandi A., Magull J., Schill H., A. de Meijere. New Highly Strained Multifunctional Heterocycles by Intramolecular Cycloadditions of Nitrones to Bicyclopropylidene Moieties // Eur. J. Org. Chem. 2006. P. 5485-5494.

[10] Zanobini A., Brandi A., A. de Meijere. A New Three-Component Cascade Reaction to Yield 3-Spirocyclopropanated β-Lactams // Eur. J. Org. Chem. 2006. P. 1251-1255.

[11] Weintraub P.M., Sabol J.S., Kane J.M., Borcherding D.R. Recent advances in the synthesis of piperidones and piperidines // Tetrahedron 59 (2003). P. 2953-2989.

[12] Brya L. Antimicrobial drug resistance. Orlando: Academic press, 1984. P. 450.

[13] Antimicrobial resistance surveillance in Europe 2012. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). European Centre for Disease Prevention and Control. Introduced 2013. Stockholm. P. 208.

[14] Jung Hun Lee, Kwang Seung Park, Asad Mustafa Karim, Chang-Ro Lee, Sang Hee Lee. How to minimise antibiotic resistance // J. Lancet Infect. Dis. 2016. Vol. 16, N. 1. P. 17-18 [Electronic source]. Available at: http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(15)00467-3/fulltext

[15] Akhmetova G.S., Sadyrbayeva F.M., Yu V.K., Praliyev K.D., Zhilkibayev O.T., Pichkhadze G.M., Nassyrova S.R., Imasheva Sh.O., Amirkulova M.K. Piperidine-containing derivatives of cyclopropanecarboxylic acid – potential PAS // Chem. J. of Kazakhstan. 2012. N 1. P. 118-127.

[16] Sadyrbayeva F.M., Ospanova S.I., Issayeva U.B., Akhmetova G.S., Yu V.K., Praliyev K.D. Amides of cyclopropanecarboxylic acid – potential BAS // Cluster of Conferences in organic chemistry “OrtChim”-2013. June 17-21, 2013. SPt.: Repino. P. 248-249.

[17] Instruction for experimental (preclinical) study of new pharmacological substances, Ministry of Health RF, “IIA Remedium”. M., 2000. P. 679.

[18] Preclinical studies of medicinal preparations (Methodological recommendations). Pharm. State Committee RK. Almaty, 1997. P. 22.

[19] RK Innovation patent No.29020. Hydrochloride of 1-methyl-4-[3-(naphth-1-yloxy)prop-1-in-1-yl]-4-cyclopropanecarbonyloxypiperidine, possessing an antibacterial activity // K.D. Praliyev, M.Ye. Kulmanov, A.I. Ilyin, F.M. Sadyrbayeva, G.S. Akhmetova, V.K. Yu, U.B. Issayeva, N.V. Leonova, et al.; Published 15.10.14. Bul. N 10.

[20] RK Innovation patent No.29021. Hydrochloride of 1-methyl-4-[3-(naphth-2-yloxy)prop-1-in-1-yl]-4-cyclopropanecarbonyloxypiperidine, possessing an antibacterial activity // K.D. Praliyev, M.Ye. Kulmanov, A.I. Ilyin, F.M. Sadyrbayeva, G.S. Akhmetova, V.K. Yu, U.B. Issayeva, N.V. Leonova, et al.; Published 15.10.14. Bul. N 10.

[21] RK Innovation patent No.29022. Hydrochloride of 1-propyl-4-[3-(naphth-1-yloxy)prop-1-in-1-yl]-4-cyclopropanecarbonyloxypiperidine, possessing an antibacterial activity // K.D. Praliyev, M.Ye. Kulmanov, A.I. Ilyin, F.M. Sadyrbayeva, G.S. Akhmetova, V.K. Yu, U.B. Issayeva, N.V. Leonova, et al.; Published 15.10.14. Bul. N 10.

[22] RK Innovation patent No.29023. Hydrochloride of 1-propyl-4-[3-(naphth-2-yloxy)prop-1-in-1-yl]-4-cyclopropanecarbonyloxypiperidine, possessing an antibacterial activity.// K.D. Praliyev, M.Ye. Kulmanov, A.I. Ilyin, F.M. Sadyrbayeva, G.S. Akhmetova, V.K. Yu, U.B. Issayeva, N.V. Leonova, et al.; Published 15.10.14. Bul. N 10.

[23] RK Innovation patent No.31047. Hydrochloride of 1-methyl-4-(3-phenoxypropin-1-yl)-4-cyclopropanecarbonyloxypiperidine, possessing an antibacterial activity // K.D. Praliyev, M.Ye. Kulmanov, A.I. Ilyin, F.M. Sadyrbayeva, G.S. Akhmetova, V.K. Yu, U.B. Issayeva, N.V. Leonova, O.A. Sulzhik, S.S. Kassymbekova. Published 15.04.16. Bul. N 4.

[24] RK Innovation patent No.31050. Hydrochloride of 1-methyl-4-phenylethinyl-4-cyclopropanecarbonyloxypiperidine, possessing an antibacterial activity // K.D. Praliyev, M.Ye. Kulmanov, A.I. Ilyin, F.M. Sadyrbayeva, G.S. Akhmetova, V.K. Yu, U.B. Issayeva, N.V. Leonova, A.N. Myrzabayeva. Published 15.04.16. Bul. N 4.

[25] RK Innovation patent No.29931. Hydrochloride of 1-benzyl-4-(cyclopropanecarbonyloxyimino)piperidine (SHV-6) // F.M. Sadyrbayeva, U.B. Issayeva, D.N. Narbayeva, G.S. Akhmetova, Zh. Myrzabekov, K.D. Praliyev, V.K. Yu. Published 15.06.15. Bul. N 6.

Резюме

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ИНФЕКЦИЯҒА ҚАРСЫ ӘСЕРІ БАР ЦИКЛОПРОПАНКАРБОН ҚЫШҚЫЛЫНЫҢ КҮРДЕЛІ ЭФИРЛЕРІ

N-алкилнафтилокипсипропил пиперидиндердің циклопропанкарбон қышқылының күрделі эфирлерінің қатары микроорганизмдердің мұражайлы штаммдарына қатысты микробқа қарсы белсенділігі зерттелді. *Bacillus subtilis* ATCC 6633, *Escherichia coli* ATCC 25922, *Salmonella enterica* ATCC 14028 және *Staphylococcus aureus* ATCC 6538-P бойынша осы препараттардың әсері бағаланды, олардың арасында 1-метил-4-[3-(нафт-1-илокси)проп-1-ин-1-ил]-4-циклопропанкарбонилоксипиперидин гидрохлориді *Bacillus subtilis* ATCC 6633 мұражайлы штаммына қатысты 250 мкг/мл концентрацияда әлдеқайда жоғары белсенділік көрсетті.

N-метилфеноксипропинилпиперидин және фенилтинилпиперидиннің циклопропанцарбон қышқылының күрделі эфирлері тәжірибеге алынған барлық жеті микроорганизм штаммдарына: *Escherichia coli* ATCC 25922, *Escherichia coli* ATCC-BAA-196, *Klebsiella pneumoniae* ATCC 10031, *Klebsiella pneumoniae* ATCC 700603, *Staphylococcus aureus* ATCC 6538-P, *Staphylococcus aureus* ATCC-BAA-39, *Candida albicans* ATCC 10231 қатысты in vitro микробқа қарсы белсенділігін көрсетті.

Циклопропанкарбон қышқылы N-бензилпиперидин-4-кетоксим эфирінің 1% және 3% -ды гидрохлорид ерітінділері *Eshirichia Coli1257* және *Staphylococcus aureus 209-P* микроорганизмдерінің сынама-дақыл штамдарына қарсы бактерицидтік әсерге ие екендігі анықталды.

Түйін сөздер: циклопропанкарбонилхлорид, пиперидин, күрделі эфирлер, микробқа қарсы белсенділік.

Резюме

Г. С. Ахметова, У. Б. Исаева, Ф. М. Садырбаева,
К. Д. Пралиев, Н. В. Коротецкая

СЛОЖНЫЕ ЭФИРЫ ЦИКЛОПРОПАНКАРБОНОВОЙ КИСЛОТЫ
С ПРОТИВОИНФЕКЦИОННЫМ ДЕЙСТВИЕМ

Ряд сложных эфиров циклопропанкарбоновой кислоты N-алкил нафтилоксипропинилпиперидинов были изучены на антимикробную активность в отношении музейных штаммов микроорганизмов, оценены действия данных препаратов *in vitro* в отношении *Bacillus subtilis* ATCC 6633, *Escherichia coli* ATCC 25922, *Salmonella enterica* ATCC 14028 и *Staphylococcus aureus* ATCC 6538-P, среди которых наибольшую активность проявил гидрохлорид 1-метил-4-[3-(нафт-1-илокси)проп-1-ин-1-ил]-4-циклопропанкарбонилоксипиперидина в отношении музейного штамма *Bacillus subtilis* ATCC 6633 в концентрации 250 мкг/мл.

Сложные эфиры циклопропанкарбоновой кислоты N-метил феноксипропинилпиперидина и фенилэтинилпиперидина проявили противомикробную активность *in vitro* в отношении всех семи штаммов микроорганизмов, взятых в эксперименте: *Escherichia coli* ATCC 25922, *Escherichia coli* ATCC-BAA-196, *Klebsiella pneumoniae* ATCC 10031, *Klebsiella pneumoniae* ATCC 700603, *Staphylococcus aureus* ATCC 6538-P, *Staphylococcus aureus* ATCC-BAA-39, *Candida albicans* ATCC 10231.

Оказалось, что 1 и 3% растворы гидрохлорида эфира N-бензилпиперидин-4-кетоксима циклопропанкарбоновой кислоты обладает бактерицидным действием против штаммов тест-культур микроорганизмов *Eshirichia Coli1257* и *Staphylococcus aureus 209-P*.

Ключевые слова: циклопропанкарбонилхлорид, пиперидин, сложные эфиры, антимикробная активность.