As seen from the established microbiological regulations comparison in both standards are focused to determination of water fecal contamination. Amount of indicators in the Ukrainian normative document results from the characteristics of water sources in our country and that is rational.

Dejneka S.Y., Svizhak V.K., Chornous V.O.*

SEARCH OF SUBSTANCES WITH ANTIMICROBIAL PROPERTIES AMONG THE DERIVATIVES OF 2,4-DISUBSTITUTIVE 3-(1-ARYL-IMIDAZOLE-5-IL)PROPEN-1-IONS AND PROPANE-1-IONS

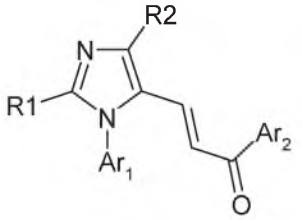
Department of Microbiology and Virology
*Department of Medical and Pharmaceutical Chemistry**
Higher State Educational Establishment of Ukraine
«Bukovinian State Medical University»

The problem of resistance to antibiotics is one of the most serious threats of the global health care [Wellington E. M. H. et all., 2013; Laxminarayan R. et all., 2013; Leibovici L. et all., 2016]. Antibiotic resistance can become a global cause of mortality in case new effective antibiotics are not found and supplied adequately [Amábile-Cuevas C.F., 2015]. Scientists from many countries focuse their attention on the necessity to search new antimicrobial means, as only few new antibiotics are synthesized a year, while the rate of resistance to them increases very fast [Spellberg B. et all., 2013; Sengupta S. et all., 2013]. For example, since the beginning of this century no more than 5 new antibiotics have been synthesized, that is rather unfavourable statistics considering the rates of resistance development of microorganisms to them.

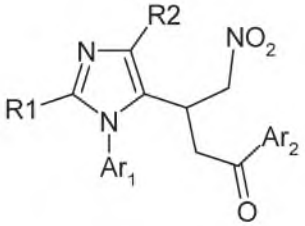
One of the ways out is to intensify the elaboration and introducing new antimicrobial drugs [Feshchenko Yu.I., 2009]. Therefore, the search of new antibiotics and modification of those already known with the aim to improve them is one of the main directions of modern medicine [Todosiychuk T.S. et al., 2011].

To study *in vitro* antimicrobial activity of new derivatives of 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propen-1-ions and 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propane-1-ions.

To study antimicrobial properties 17 new derivatives of 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propen-1-ions and 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propane-1-ions were selected with the following general formula:



derivatives 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propen-1-ions



derivatives 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propane-1-ions

Their antimicrobial properties were studied by means of common methods of two-time series dilution in a liquid nutrient medium and detection of minimal bacteriostatic and fungistatic concentrations (MBsC, MFsC), minimal bactericidal or fungicidal concentrations (MBcC, MFcC) of compounds concerning reference strains of gram-positive bacteria (*Staphylococcus aureus* ATCC 25923), gram-negative bacteria (*Escherichia coli* ATCC 25922) and yeast-like fungi (*Candida albicans* ATCC 885-653).

A part of the derivatives of 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propen-1-ions was not found to reveal any antimicrobial properties. For example, both minimal bacteriostatic or fungistatic (MBsC, MFsC) and bactericidal or fungicidal (MBcC, MFcC) concentrations of 2653, 2661 and 2664 compounds concerning reference-strains of gram-positive bacteria (*Staphylococcus aureus* ATCC 25923), gram-negative bacteria (*Escherichia coli* ATCC 25922) and yeast-like fungi (*Candida albicans* ATCC 885-653) are more than 1000 mcg/ml. At the same time, the compounds 2001 and 2654 reveal moderate antibacterial and antifungal properties – their MBsC and MFsC are on the level of 250 mcg/ml, MBcC and MFcC - 500 mcg/ml. It should be noted that the rest of the compounds (2652, 2663 and 2810) do not possess antibacterial properties concerning *Staphylococcus aureus* ATCC 25923 (minimal bactericide concentrations of the compounds indicatedare more than 1000 mcg/ml), but they demonstrate a moderate antimicrobial activity concerning *Escherichia coli* ATCC 25922 and/or *Candida albicans* ATCC 885-653 (MBsC and MFsC are on the levels of 250 mcg/ml, MBcC and MFcC - 500 mcg/ml).

Higher antimicrobial activity was found in the derivatives of 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propane-1-ions as compared to the derivatives of 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propen-1-ions. Thus, minimal bacteriostatic concentration of the examined derivatives of 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propane-

1-ions concerning gram-positive bacteria (*Staphylococcus aureus* ATCC 25923) was 62,5 – 250 mcg/ml. A little less antibacterial action of these compounds was found concerning *Escherichia coli* ATCC 25922 (MBsC for the majority of compounds is on the level of 125-250 mcg/ml). The compounds examined revealed lower anticandidosis activity – minimal fungistatic concentrations of the compounds concerning *Candida albicans* ATCC 885-653 were from 125 to 500 mcg/ml. Minimal bactericidal and fungicidal (MBcC, MFcC) concentrations of the examined compounds concerning reference-strains were in the majority of cases on the level of 125-1000 mcg/ml.

The examined derivatives of 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propen-1-ions and 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propane-1-ions possess moderate antibacterial and antifungal activity. Higher antimicrobial activity was found in the derivatives of 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propane-1-ions as compared to the derivatives of 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propen-1-ions. Minimal bacteriostatic concentration of the examined derivatives of 2,4-disubstitutive 3-(1-aryl-imidazole-5-il)propane-1-ions concerning *Staphylococcus aureus* ATCC 25923 was 62,5 – 250 mcg/ml, *Escherichia coli* ATCC 25922 - 125-250 mcg/ml, and minimal fungistatic concentrations of the compounds concerning *Candida albicans* ATCC 885-653 were from 125 to 500 mcg/ml.

Gavryliuk O.I., Panasenko N.V.*, Dejneka S.Y.

ANTIMICROBIAL ACTION OF 2-(1-PHENYL-3-ARYL-1*H*-PYRAZOL-4-IL)BENZO[b]QUINOLIN-4-CARBONIC ACID DERIVATIVES

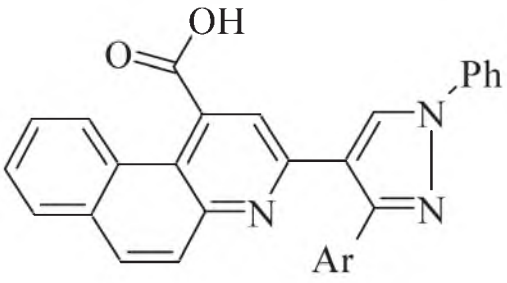
Department of Microbiology and Virology
*Department of Medical and Pharmaceutical Chemistry**
Higher State Educational Establishment of Ukraine
«Bukovinian State Medical University»

The search of new biologically active substances in a number of quinolin-4-carbonic acid (cinchonine) derivatives is a very prospective area of investigation [Dubrovin A.N. et al., 2014]. Quinolinic nucleus is a wide-spread pharmacophore fragment. Quinolin-4-carbonic acid and its derivatives were studied more carefully than any other quinolinic acids, and the compounds with different biological activity were found among them [Skrobala V. et al., 2013]. Quinoxidine is used in medical practical work as an antibacterial means, and antimicrobial activity is found in isopropylamide 2-(2,4-dinitrophenylhydrasino) cinchoninic acid [Novikov M.V., 2009].

Although despite a rather wide use of 4-quinolincarbonic acids, the potential of their studies has not been exhausted. For example, the derivatives of 2-(1-phenyl-3-aryl-1*H*-pyrazol-4-il)benzo[b]quinolin-4-carbonic acid are not studied completely.

To study *in vitro* antimicrobial properties of new derivatives of 2-(1-phenyl-3-aryl-1*H*-pyrazol-4-il)benzo[b]quinolin-4-carbonic acid.

35 derivatives of 2-(1-phenyl-3-aryl-1*H*-pyrazol-4-il)benzo[b]quinolin-4-carbonic acid were selected for the study, of the common formula:



3-[(3-aryl)-1-phenyl-1*H*-pyrazol-4-il]benzo[b]quinolin-1-carbonic acid, for example, were received in the following way. The mixture of 0,0011 mole aldehyde, 0,16 g (0,0011 mole) β-naphthylamine and 0,1 g (0,0011 mole) of pyruvic acid in 5 ml of methanol was boiled during 3 hours. The sediment obtained was filtered, washed in 5 ml of methanol and dried in the air.

To study antimicrobial properties of the compounds examined generally accepted methods of two-time series dilution in a liquid nutrient medium were used. The museum strains of gram-positive bacteria (*Staphylococcus aureus* ATCC 25923), gram-negative bacteria (*Escherichia coli* ATCC 25922) and yeast-like fungi (*Candida albicans* ATCC 885-653) were used as test-objects. The following liquid nutrient medium was used: beef-extract broth (BEB) for bacteria, and Sabouraud's peptone agar for fungi.

A number of *in vitro* experiments proved that prevailing majority (82,86 %) of the compounds examined possess antimicrobial activity. Minimal bacteriostatic concentration of the majority of derivatives of 2-(1-phenyl-3-aryl-1*H*-pyrazol-4-il)benzo[b]quinolin-4-carbonic acid is within the limits of 250-1000 mc/ml. The compounds examined manifested the concentrations indicated both concerning gram-positive *S. aureus* ATCC 25923, and gram-negative *E. coli* ATCC 25922.

The analysis of the dependence of antimicrobial activity of 2-(1-phenyl-3-aryl-1*H*-pyrazol-4-il)benzo[b]quinolin-4-carbonic acid derivatives and their chemical structure has found the following. The nature of aryl fragment substitute in the position of 3-pyrazol effects the activity of the compounds examined. The presence of