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# PRIORITY DIRECTIONS OF SCIENCE AND TECHNOLOGY DEVELOPMENT

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# SEARCH FOR PROSPECTIVE BIOLOGICALLY ACTIVE SUBSTANCES OF ANTITUBERCULOSIS ACTION IN THE SERIES OF PYRAZIN-2-YLAMIDES 1-R-4-HYDROXY-2-OXO-1,2-DIHYDROQUINOLINE-3-CARBOXYLIC ACIDS

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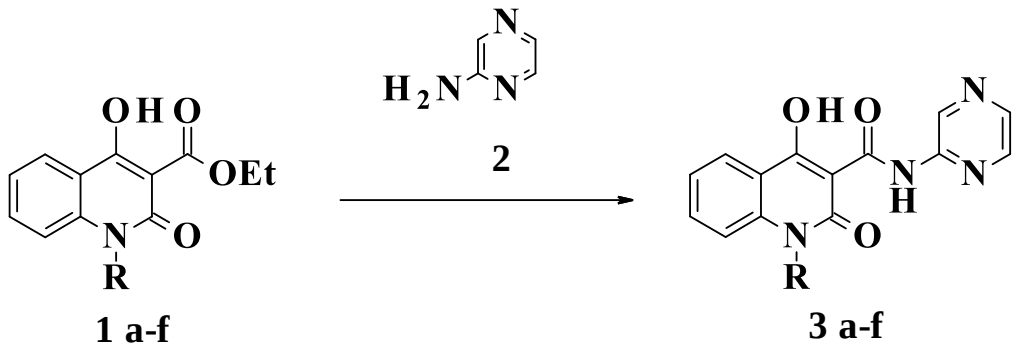
**Introductions.** The search for new biologically active substances and the creation of medicines on their basis, which, in terms of their effectiveness and safety, met the requirements of modern times as much as possible, is one of the most pressing problems of pharmaceutical science. An efficient and reliable way of solving such problems was the optimization of the first selected leading structures. It carried out by means of a purposeful chemical modification, which is simple in execution, due to which it has found wide use in various fields of science and technology, including in medicinal chemistry. Derivatives of 4-hydroxy-2-oxoquinoline-3-carboxamide, which is widespread in nature, are of particular interest in this regard. The extremely wide range of biological properties inherent in this compound and, what is especially important, the practically unlimited synthetic potential make them very convenient objects for research of this kind. The experience accumulated in this case and the identification of structural and biological regularities formed the basis of this work, which is actually a fragment and a logical continuation of a large complex study on the study of methods of synthesis, structure, chemical transformations and pharmacological properties of various 4-hydroxy-2-oxoquinoline-3- carboxamides.

**Aim.** Search for potential anti-tuberculosis drugs in the series of pyrazin-2-yl amide derivatives of 1-R-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acids

**Materials and methods.** The necessary reagents for the synthesis of the target products were obtained using standard techniques. The melting point was determined on a Kofler instrument. Elemental analysis were performed by the method of Dumas. 1H NMR spectra were recorded on a Bruker WM-360 instrument, the solvent was DMSO-d6, and the internal standard was tetramethylsilane.

The antituberculosis activity of all synthesized derivatives by in relation to Mycobacterium tuberculosis H37Rv ATCC 27294 was studied *in vitro* at a concentration of 6.25 μg / ml.

**Results and discussion.** The target products pyrazin-2-yl amides **3a-f** were obtained by thermolysis of ethyl esters of 1R-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acids **1a-f** with 2-aminopyrazine **2** on metal bath in equimolecular amounts at temperature 160ºC, which is shown in fig. 1.




**R= $C_2H_5$; , $CH_2CH=CH_2$, *i*-$C_4H_9$, $C_6H_{13}$, $C_7H_{15}$, $C_9H_{19}$**

**Fig. 1. Scheme of synthesis of target compounds**

The obtained substances are colorless crystalline substances that are soluble in DMF, DMSO, ethanol and insoluble in water.

To establish the structure and individuality of the synthesized compounds, melting point were determined, elemental analysis and 1H NMR spectroscopy were performed.

Microbiological screening revealed compounds that have pronounced anti-tuberculosis activity. It was found that the manifestation of high activity is observed starting with 1-N-butyl derivatives, that is, the activity is promoted by the elongation of the alkyl chain (fig. 2).

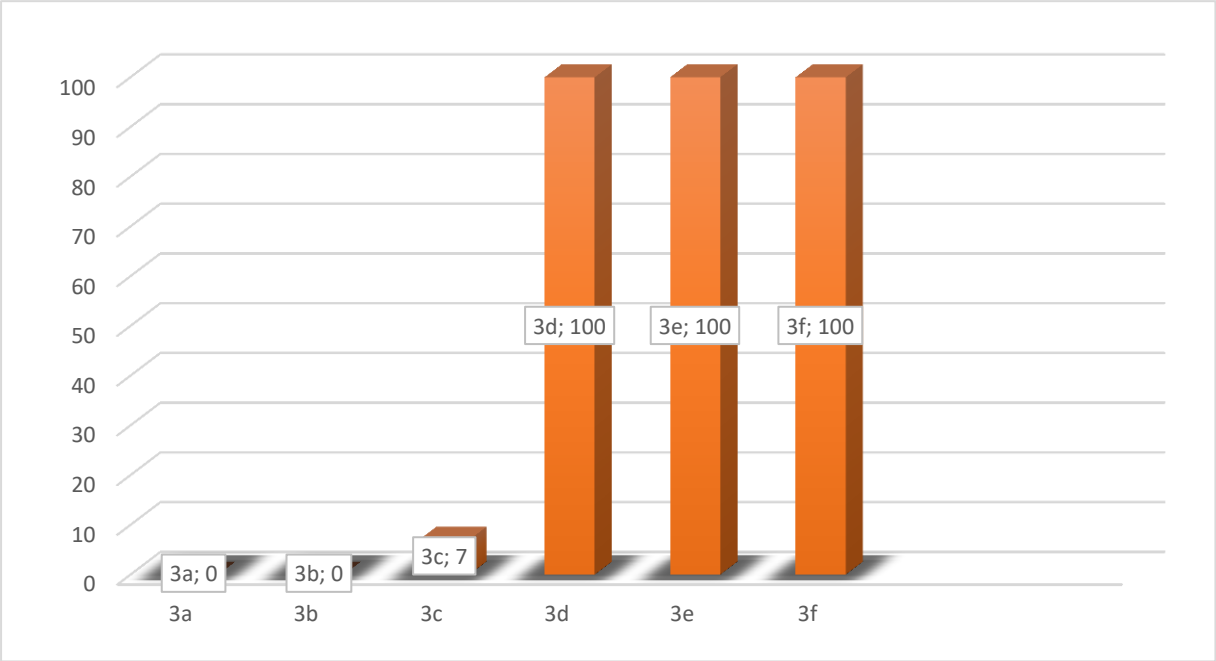



**Fig. 2. Anti-tuberculosis activity of target compounds**

**Conclusions.** In order to identify new biologically active substances of anti-tuberculosis action, a series of pyrazin-2-yl amides of 1-R-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acids was synthesized. The structures of the synthesized compounds was confirmed by 1H NMR spectroscopy and elemental analysis. Microbiological screening revealed compounds that have pronounced anti-tuberculosis activity. It was found that the manifestation of high activity is observed starting with 1-N-butyl derivatives, that is, the activity is promoted by the elongation of the alkyl chain.