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SYNTHESIS AND ANTITUBERCULOSIS ACTIVITY OF N-R-AMIDES 1-HYDROXY-3-OXO-6,7 DIHYDRO-3H, 5H-PYRIDO [3,2,1-IJ] QUINOLINE-2-CARBONIC ACIDS

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Introductions. The main modern problem in the treatment of tuberculosis is the rapid development of resistance of the causative agent of this dangerous infectious disease to antimycobacterial drugs. According to the World Health Organization, today, drug-resistant tuberculosis is diagnosed in an average of 7% of patients today, and may soon seriously destabilize the epidemiological situation in the world and develop into a global threat to humanity. In addition to improving preventive and diagnostic measures, today three research areas are being intensively developed, designed, if not to remove the problem of multidrug-resistant strains from the agenda, then at least to reduce its severity. The first of them provides for the development of strictly controlled schemes of intensive treatment with short courses of chemotherapy using combinations of existing drugs, significantly postponing the development of resistance to them. The second direction combines genetic studies to decipher the sequence of nucleotides in the genome of Mycobacterium tuberculosis in

order to identify genes corresponding to the mutation and, therefore, involved in the mechanisms of antibiotic resistance. In the future, this approach will make it possible to create fundamentally new means and methods for combating tuberculosis. However, at the present level of development of science, the third direction has not yet lost its significance, which is based mainly on the empirical selection of a leader structure from a series of synthesized compounds that have passed different levels of pharmacological tests.

Aim. Synthesis and study of antituberculosis activity of N-R-amides 1-hydroxy-3-oxo-6,7 dihydro-*3H, 5H*-pyrido [3,2,1-ij] quinoline-2-carbonic 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 was 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 antituberculous 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. In order to search for biologically active substances that will affect anti-tuberculosis activity, the synthesis of derivatives of N-R-amides of quinoline carboxylic acids was carried out, which is shown in fig. 1.

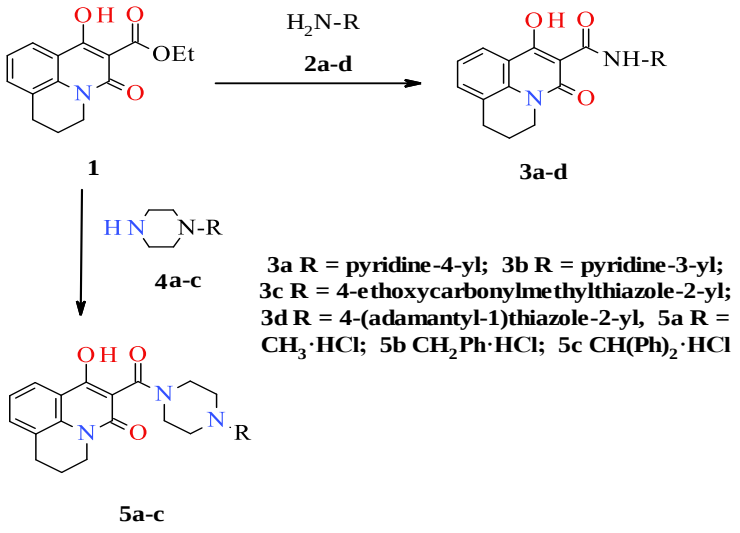

Fig. 1. Scheme of synthesis of target compounds

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 temperatures were determined, elemental analysis and 1H NMR spectroscopy were performed.

Analysis of the antimycobacterial properties subjected to microbiological screening (fig. 2) shows that compound 3a and 3c with pyridine and 4-ethoxycarbonylmethylthiazole fragments showed 100% activity in relation to the used strain. A complete loss of activity was observed in derivatives 5a-c with a 4-methoxyanilide hydrochloride fragment and a 4-R-piperazine nucleus.

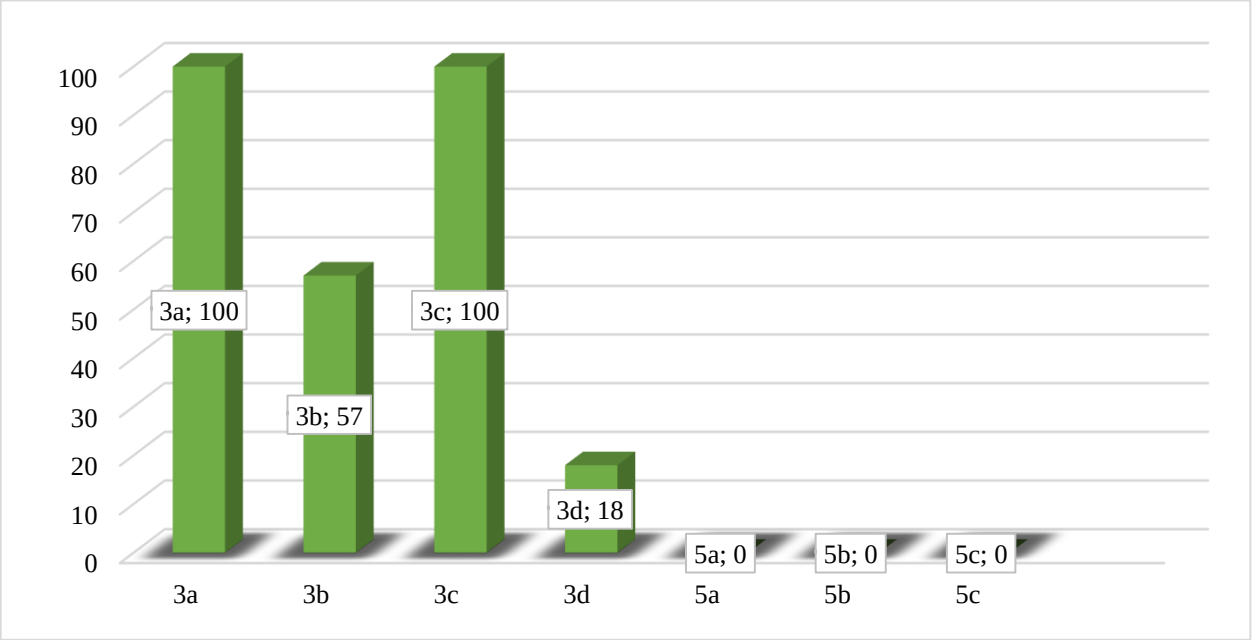

Fig. 2. Anti-tuberculosis activity of target compounds

Conclusions. A series of 1-hydroxy-3-oxo-6,7-dihydro-*3H, 5H*-pyrido [3,2,1-ij]quinoline-2-carboxylic acid heterylamides was synthesized in high yields and purity. The chemical structure of the synthesized compounds was confirmed by 1H NMR spectra and elemental analysis. Analysis of the antimycobacterial properties subjected to microbiological screening shows that compound 3a and 3c with pyridine and 4-ethoxycarbonylmethylthiazole fragments showed 100% activity in relation to the used strain. A complete loss of activity was observed in derivatives 5a-c with a 4-methoxyanilide hydrochloride fragment and a 4-R-piperazine nucleus.