SYNTHESIS AND ANTITUBURCULOSIS ACTIVITY OF SOME DERIVATIVES OFAMIDES 2- (BENZOYLAMINO)(1-R-2-OXO-1,2-DIHYDRO-3*H*-INDOLE-3-YLIDENE)ACETIC ACID

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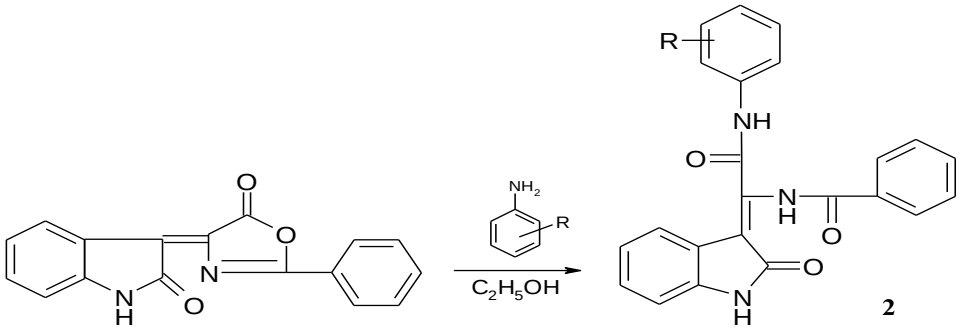
Introduction. Derivatives of (1-R-2-oxo-1,2-dihydro-3,2-indol-3-ylidene)acetic acid have proven themselves as compounds with high antibacterial and nootropic activity. And their di- and trifluoro derivatives, as potential compounds with antituberculous activity.

Aim. Therefore, difluorosubstituted amides of 2-(benzoylamino)(1-R-2-oxo-1,2-dihydro-3H-indole-3-ylidene)acetic acid derivatives as objects for research of antituberculous activity have been chosen.

Material and methods. Synthesis of compounds was carried out by aminolysis of azlactone 2-benzoylamino-(2-oxo-1,2-dihydro-3H-indole-3-ylidene) acetic acid in a mixture of dimethylformamide or ethanol (scheme 1):

Scheme 1



1 **2**

R=2,4-F; 2-F; 4-F; 2,4-CH_3; 2,4-OCH_3, isoniazid.

The structure of synthesized compounds have been confirmed by PMR-spectroscopy and X-ray diffraction analysis.

Studies on antituberculous activity were performed in vitro. As a test substance have been chosen N-[(1Z)-2-[(2,4-difluorophenyl)amino]-2-oxo-1-(2-oxo-4)-1,2-dihydro-3*H*-indole-3-ylidene)ethyl]benzamide, and as a test culture strain $H_{37}Rv$ of *M. tuberculosis*. The strain sensitivity was investigated to six concentrations of the substance - 15, 50, 100, 150, 200, 300 mg/cm^3 by seeding mycobacteria on a nutrient medium containing a certain amount of the drug. Duration of observation - 60 days.

Results and discussion. At concentration of the substance ≥ 150 mg/cm^3, growth of the test culture was slowed down, but at the end of the observation period, in all the test tubes, insignificant growth of the colonies of mycobacteria was observed. Analysis of the results of microbiological studies showed that, with an increase a concentration of the substance up to 300 mg/cm^3, the growth of colonies *M. tuberculosis* strain $H_{37}Rv$ is inhibited.

Conclusions. But since, the high concentrations of N-[(1Z)-2-[(2,4-difluorophenyl)amino]-2-oxo-1-(2-oxo-4)1,2-dihydro-3*H*-indole-3-ylidene)ethyl]benzamide (≥300 mg/cm^3) can cause acute toxicity, their use in in vivo studies will be inappropriate.