SYNTHESIS AND CARDIOTROPIC PROPERTIES OF THE NEW 1,3-THIAZOLE DERIVATIVES

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Introduction. Experimental and clinical trials in recent years have observed that cardiotropic drugs of metabolic type have proven clinical effectiveness. And medicines with this kind of action, such as Meldonium and L-carnitine have taken the lead in treatment regimen for cardiovascular pathologies. Having analyzed data in the scientific and patent literature, it should be noted that derivatives of 1,3-thiazole are prospective for a search of potential cardiotropic agents among them, and also they have a high pharmacotherapeutical potential.

The **aim** of this work is to obtain new biological compounds of metabolic type with a high cardioprotective activity among derivatives of 1,3-thiazole.

Materials and methods. Methods of organic synthesis; physical and physicochemical methods of analysis of organic compounds (^{1}H NMR spectroscopy, elemental analysis), the study of biological properties using standard techniques; analysis of the results obtained and their generalization, statistical methods for processing experimental data.

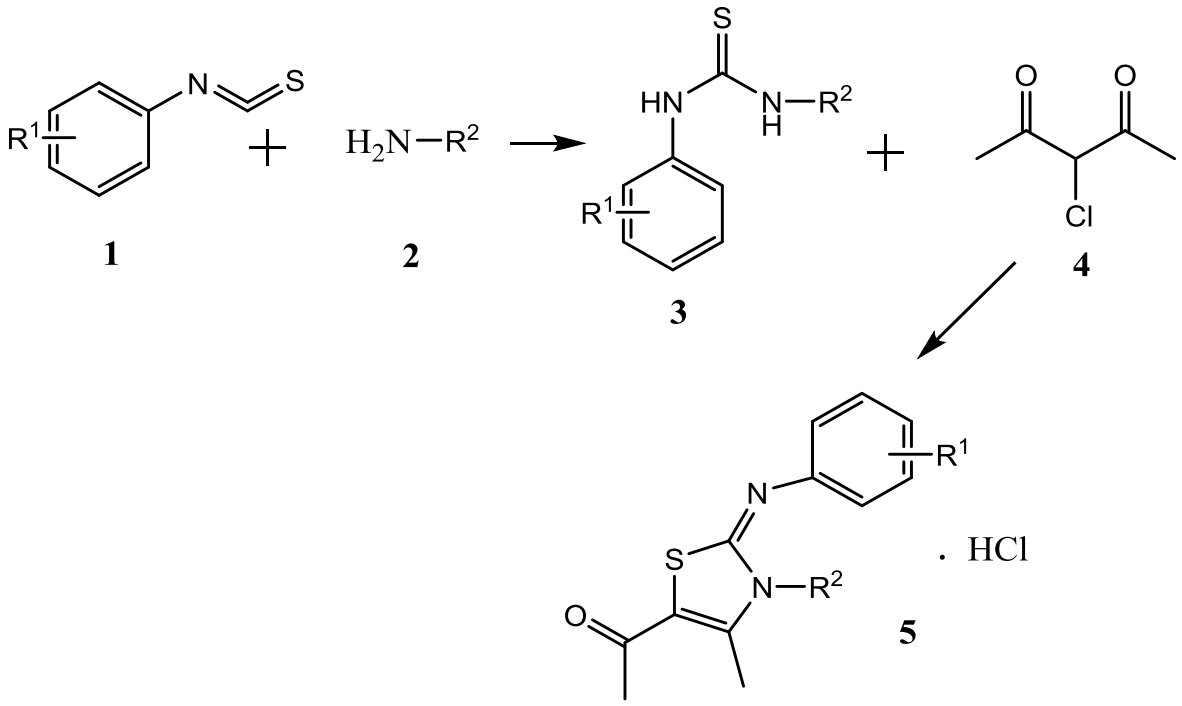
Results and discussion. In order to find new biologically active substances, the synthesis of new series of derivatives of 1-(4-methyl-2-(phenylimino)-2,3-dihydrothiazol-5-yl)ethan-1-one. has been conducted. As the initial products of the synthesis, by the interaction of substituted phenylisothiocyanates **1** and arylamines **2** the unsymmetrical thiourea solutions **3** were produced. The reaction was carried out in dry dioxan medium. The hydrochlorides of N-[4-methyl-2-R-phenyliminothiazole-3-yl]-morpholine **5** were obtained by boiling the equimolar amounts of unsymmetrical thioureas **3** with 3-chloropentane-2,4-dione **4** in Ethanol (Scheme 1). The structure and individuality of the compounds were confirmed by modern physical and chemical methods: thin-layer chromatography, elemental and ^{1}H NMR spectral analysis.

The cardiotropic action was investigated on the isolated of the thoracic aorta of laboratory mice. The effectiveness of examined compounds was compared with the negative control and the reference preparations: Meldonium and L-carnitine.

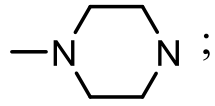
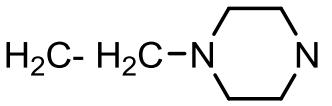
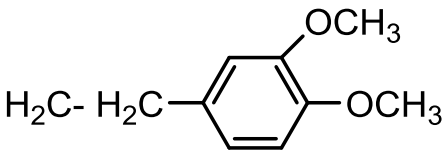
Two examined compounds at the level of reference preparations, and in some cases exceeding them, having reduced the normalized maximum rate of the contraction phase to hypoxia, which indicates the property of these compounds to

realize a decrease in the energy potential of the cardiomyocyte damaged by hypoxia.

Scheme 1



R^1 = -H, $-OCH_3$, $-CH_3$

R^2 =  ;  ; 

Conclusions. A purposeful synthesis of a new series of derivatives of 1-(4-methyl-2-(phenylimino)-2,3-dihydrothiazol-5-yl)ethan-1-one. has been carried out.

The structure and individuality of 4 compounds which have not described in the literature was confirmed by means of elemental analysis, ^{1}H NMR-spectroscopy, and thin layer chromatography.

The results of the pharmacological studies conducted of the synthesized compounds have confirmed the presence of cardiotropic properties that provides the prospectivity of the further research in this group.