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DESIGN OF NEW BIOLOGICALLY ACTIVE SUBSTANCES BASED ON N-(2-HYDROXYETHYL)-N'-PHENYLTHIOUREA

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Analisis of scientific and patent literature shows that iminothiazole-containing hetero-cyles are prospective biologically active substances with anti-inflammatory, antihistaminic, antimicrobial, antihypertensive activity. Iminothiazolines are also possessing interesting activities such as imuscarinomimetic, antimycotic, cell adhesion antagonists, thrombopoietin agonism, analgesic and kinase CDK1, CDK5 and GSK3 inhibition, schistosomicides, trichomonides, hypolipemic, antidiabetic and cadiotonics. They are widely used as valuable scaffolds in medicinal and combinatorial chemistry.

Thus these and other encouraging findings focused our attention on this heterocyclic system and motivated to synthesize a series of 2-[4-aryl(adamantyl)-2-phenyliminothiazol-3-yl]-ethanol derivatives as candidates for pharmacological evaluation as anti-inflammatory agents.

To achieve this purpose the first step of our work was development of the method of synthesis of substances. 2-[4-aryl(adamantyl)-2-phenyliminothiazol-3-yl]-ethanol derivatives were synthesized by Hantzsch reaction. To obtaine substances with different R-phenyl substituents in position 4 of thiazole cycle and with phenyl substituent in position 2 of thiazole cycle as initial substances were chosen substituted phenacylbromides and unsymmetric *N*-(2-hydroxyethyl)-*N'*-phenylthiourea. Structure and purity of synthesized compounds were confirmed by ^{1}H NMR and chromato-mass spectra.

The second step of our work was optimization pharmacological screening. Prospective biologically active substances were chosen using *in silico* methods and data of literature. Theoretical bioavailability of investigated molecules and prediction of their drug-like properties were tested for «The rule of five» Lipinski using ACD/Labs and Molinspiration software. Computer prognosis of toxicity and possible types of biological activity was perfomed using site: http://www.way2drug.com.

Analysis of the data obtained allowed to select substances that have a reactive functional group in their structure, probably have a low level of toxicity and probably possesses the desired anti-inflammatory activity.

The third step – evaluation of anti-inflammatory activity on model «hystamine edema» of the selected compounds synthesized was revealed their high potential to create anti-inflammatory and anti-allergic drugs.