TESTING OF 2-PHENYLIMINOTHIAZOLE DERIVATIVES FOR COMPLIANCE WITH "DRUG LIKENESS" CONCEPT

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Introduction. Pre-experimental research methods in silico successfully used at various stages of the search and optimization of the structures of biologically active compounds. «The rule of five» Lipinski is one of such methods. This method is based on the calculation of physical and chemical parameters that determine bioavailability of investigated molecules and prediction of their drug-like properties.

Aim. The aim is testing of eleven synthesized 2-[4-aryl(alkyl)-5-aryl(alkyl)-2-phenyliminothiazole-3-yl]-1-morpholylethane (Figure I) and 3-[4-aryl(alkyl)-5-aryl(alkyl)-2-phenyliminothiazole-3-yl]-1-morpholylpropane derivatives (Figure II) for compliance with «The rule of five» Lipinski. The molecules that do not comply specified parameters will not be subjected for the further pharmacological screening.

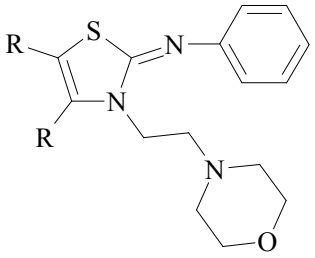

Figure I

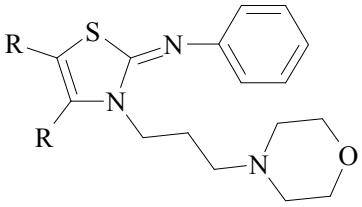

Figure II

Materials and methods. Such drug-like parameters as molecular weight, partition-coefficient, number of hydrogen bond donors and acceptors have been calculated by using online version of Molinspiration software, and molar refraction - by using ACD/Labs software.

Results and discussion. According to the the results of calculation of drug-like properties, tested substances have the following average values of physical and chemical parameters: molecular weight – 371.14, partition-coefficient – 5.34, molar refraction – 116.82, number of hydrogen bond donors and acceptors - 0 and 5, respectively.

Analysis of the results showed that determined drug-like properties are in the range of permissible values for six of the eleven test compounds. Two test compounds have one deviation and three compounds have two deviations from «The rule of five» Lipinski.

Conclusions. Eight from eleven synthesized compounds comply with requirements Lipinski and can be recommended for experimental biological tests.