Computational screening of pharmacokinetics and toxicity of isothiourea derivative containing morpholine fragment

Batura Yu.D., Yeromina H.O., Ieromina Z.G.

Medicinal chemistry department

National University of Pharmacy, Kharkiv, Ukraine

annerem2012@gmail.com

For well over a decade, *in silico* prediction of ADME-Tox properties of compounds has represented the cornerstone of drug development and discovery. The significance of *in silico* ADME-Tox modeling has also become more apparent as these properties are increasingly being evaluated at an earlier stage of the drug development process. *In silico* ADME-Tox prediction allows to facilitate the appropriate selection of candidate drugs by pharmaceutical companies prior to expensive clinical trials. Early assessment of ADME-Tox properties can minimize the time and cost of screening and testing by identifying the strongest candidates for development and rejecting those with a low probability of success. The ultimate goal of *in silico* modeling of ADME-Tox properties is to predict the *in vivo* disposition behavior of potential drug molecules in the human body by assembling all kinetic processes into one inclusive model.

In view of the above, *in silico* ADME-Tox modeling were performed to predict the pharmacokinetics and toxicity of new isothiourea derivative containing morpholine fragment, namely 1-morpholino-2-[2-oxo-2-(2,4,6-trimethylphenyl)ethyl]-3-phenyl-isothiourea.

The theoretical molecular descriptors have been calculated using PreADMET software package, which is a web-based application for predicting ADME data and building *drug-like* and *lead-like* compounds. This program can calculate about 955 molecular descriptors including physicochemical, constitutional, electrostatic, geometrical and topological indices.

Pre ADMET pharmacokinetic studies indicate that tested 1-morpholino-2-[2-oxo-2-(2,4,6-trimethylphenyl)ethyl]-3-phenyl-isothiourea has a favorable parameters of pharmacokinetic profile: compound is suitable for oral administration and has a high ability to be absorbed through the human intestine, is unsuitable for transdermal administration, because the compound slightly penetrate the skin; is able to be metabolized in the liver and has an ability to inhibit P-glycoprotein transport.

Pre ADMET toxicity studies show that 1-morpholino-2-[2-oxo-2-(2,4,6-trimethylphenyl)ethyl]-3-phenyl-isothiourea has no carcinotoxicity, has a medium risk of manifestation of cardiotoxicity and has a mutagenic potential.

Based on the results obtained, new isothiourea derivative containing morpholine fragment is perspective substance for further experimental studies.