Title: Predicting of biological targets and admet properties of synthesized hydroxyurea derivatives

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Abstract:
BackgroundsA diverse cyclic and acyclic hydroxyurea derivatives were synthesized and tested on different biological acivities, i.e., the cell viability on human acute monocytic leukemia THP-1 and human acute T cell leukemia Jurkat cell lines, as well as on antibacterial activity against three E. coli strains, i.e., a strain susceptible to antibiotics, a strain resistant to macrolide antibiotics and a strain resistant to aminoglycoside antibiotics.AimsThe aim of this study is to evaluate the potential biological targets and to predict ADMET properties of investigated hydroxyurea derivatives in order to get more insights in their pharmacological and safety profile.MethodsPotential biological targets were evaluated using Swiss Target Prediction (www.swisstargetprediction.ch) while ADMET properties were computed using ADMET PredictorTM 8.0 (Simulations Plus, USA).ResultsThe results of biological targets evaluation of the most active compounds revealed: the muscleblind-like protein 1, 2 and 3 as potentional targets of N1-benzyloxy- N2-p-(carboxylic acid)phenyl urea (6), the P2X purinoceptor 1 with poor probability of N1-hydroxy-N2-p-(carboxylic acid)phenyl urea (12), different carbonic anhydrases (1-7) of N1,N2,N3-trihydroxybiuret (14) and the fatty-acid amide hydrolase 1 of 1-(N-benzyloxycarbamoyl)benzotriazole (1). These molecules are either CYP 2E1 and CYP 1A2 substrates or CYP 1A2 inhibitors. ADMET Predictor analysis predicted ADMET risk between 1 to 7, CYP risk between 0 to 2 and TOX risk between 1 to 5.Summary/ConclusionA variety of biological targets of investigated hydroxyurea derivatives as well as predicted ADMET properties have indicated on a high toxic potential of these compounds.