Title: Predicting of biological targets, admet properties and QSAR studies in a series of entactogen substances of phenylethylamine class

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Abstract:
BackgroundsMany of new and formerly obscure compounds, including entactogens, have appeared on the illicit drug market. Their rapid appearance and largely unknown character put them into a legal gray area.AimsThe aim of this study was to predict an ADMET properties of selected entactogens in order to get more insights in their safety profile.MethodsEntactogens of phenylethylamine class (n = 25) were evaluated in QSAR studies using computed molecular descriptors (LogP, Mr, TPSA, V) and ADMET properties predicted by ADMET PredictorTM 8.0 (Simulations Plus, USA). Using Swiss Target Prediction software the sodium dependent serotonin or dopamine transporters and trace amine-associated receptors were revealed as targets with the highest probability for majority of these substances.ResultsThe most significant correlations were obtained between ADMET Risk vs. CYP Risk (R = 0.9997); MLogP vs. TOX hERG (cardiotoxicity) and TOX ATTP (Acute toxicity in Tetrahymena pyriformis) with R = 0.7511 and R = 0.7601, respectively. These molecules are both CYP inhibitors (1A2, 2D6) and CYP substrates (1A2, 2B6, 2C9, 2C19, 2D6 and 2E1). The following toxicological parameters were also predicted: ADMET risk 1 – 4 (codes 1A, 2C19, 2D6, Mu or Hp); CYP risk 1 - 2.72 (codes 1A2, 2D6 and 2C19) and TOX risk 0 - 3.446 with codes of mutagenicity (Mu) and hepatotoxicity (Hp). Mu was predicted for MDMEO or 1-(1,3-benzodioxol-5-yl)-N-methoxypropan-2-amine (14) and MDOH or 3,4-methylenedioxy-N-hydroxyamphetamine (15) while both Hp and Mu were predicted for MDCPM or 3,4-methylenedioxy-N-cyclopropylmethylamphetamine (18).Summary/ConclusionMDCPM was with worst toxicological profile among all investigated entactogen molecules in this study.