**IN VIVO AND AQUATIC TOXICITY OF NITROAROMATICS, A QSAR STUDY**

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**Abstract:** Problems of toxicity pertaining to widely used nitroaromatic explosives, pesticides, etc. and of damage to living organisms and the environment still remain crucial. Therefore, the aims of present study are: (i) the application of the Hierarchical Technology for Quantitative Structure - Activity Relationships (HiT QSAR) for the evaluation of the influence of such well known pollutants as nitroaromatic compounds on their aquatic toxicity and toxicity in vivo, (ii) prediction of toxicities for new nitroaromatic derivatives, (iii) analysis of the characteristics of the substituents in nitroaromatic compounds influence on their toxicity. The 50% lethal dose concentration for rats (LD\(_{50}\)) and 50% inhibition growth concentration (CIG\(_{50}\)) for Tetrahymena pyriformis were used to develop QSAR models based on simplex representation of molecular structure. Obtained 2D QSAR PLS models are quite satisfactory (R\(^2\)=0.86–0.98; Q\(^2\)=0.71–0.95). The predictive ability of QSAR models was confirmed by usage of three different test sets (maximal and minimal similarity with training set and also random choice, taking into account toxicity range only) for any developed model (R\(^2\)\(_{\text{test}}\)=0.54–0.97). Since obtained 2D QSAR PLS models are predictive, the prediction of toxicity for new nitroaromatic derivatives (virtual screening), and the revelation of molecular fragments that promote and interfere with toxicity have been performed. The comprehensive analysis of substituent effect on toxicity and contributions of electrostatic, hydrophobic and van der Waals interactions of toxicants with the biological target was carried out. It was concluded, that non-additive substituents interference in benzene ring plays the determining role for their toxicity.

**Keywords:** SiRMS approach, QSAR, toxicity, gene expression, HepG\(_2\) cells

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