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Pharmacophore modeling, and 3D-QSAR studies of 2- benzanilide derivatives as Isocirate lyase (ICL) inhibitors

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Isocitrate Lyase (ICL) is one of the most important targets in the treatment of Mycobacterium tuberculosis. In this study, different scaffolds of ICL inhibitors are used to build a pharmacophore model. The pharmacophore is generated with the use of DISCOtech module of Tripos SYBYL 1.2x. seven molecules are selected on the basis of structural diversity and 8 different models are generated. Model 2 was considered as the best model as it has highest score than other models. Model 2 has four features including two donor site, one aromatic and one aliphatic site. The pharmacophore modelling was followed by 3D QSAR modelling. The best CoMFA model with 39 training set molecules was obtained with the internal validation value(q2) of 0.642 and conventional coefficient of 0.993. in addition to steric and electrostatic fields observed in CoMFA, CoMSIA also represents hydrophobic, hydrogen bond donor and hydrogen bond acceptor fields. CoMSIA model was cross validated and the cross validation co efficient value obtained is 0.660. both model are validated by external set of ten compounds and gave satisfactory prediction (r2 pred) of 0.615 and 0.601 respectively. The pharmacophore based 3D QSAR approach provides significant insights that can be used to design novel, potent and selective ICL inhibitors.

Biography

Author is currently pursuing M.Pharm at Nirma University, Ahmedabad, India. She is currently working on Homology modelling of Mycobacterium tuberculosis targets and Computer aided drug designing.

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