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# QSAR, Docking and E-pharmacophore Approach on Novel Series of HDAC Inhibitors with Thiophene Linker as Anticancer Agents

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**Abstract :** HDAC inhibitors can reactivate gene expression and inhibit the growth and survival of cancer cells. The 3D-QSAR and Pharmacophore modeling studies were performed to identify important pharmacophoric features and correlate 3D-chemical structure with biological activity. The pharmacophore hypotheses were developed using e-pharmacophore script and phase module. Pharmacophore hypothesis represents the 3D arrangement of molecular features necessary for activity. A series of 55 compounds with well-assigned HDAC inhibitory activity was used for 3D-QSAR model development. Best 3D-QSAR model, which is a five PLS factor model with good statistics and predictive ability, acquired Q2 (0.7293), R2 (0.9811) and standard deviation (0.0952). Molecular docking were performed using Histone Deacetylase protein (PDB ID: 1t69) and prepared series of hydroxamic acid based HDAC inhibitors. Docking study of compound 43 show significant binding interactions Ser 276 and oxygen atom of dioxine cap region, Gly 151 and amino group and Asp 267 with carboxyl group of CONHOH, which are essential for anticancer activity. On docking, most of the compounds exhibited better glide score values between -8 to -10.5. We have established structure activity correlation using docking, energetic based pharmacophore modelling, pharmacophore and atom based 3D QSAR model. The results of these studies were further used for the design and testing of new HDAC analogs.

**Keywords :** Docking, e-pharmacophore, HDACIs, QSAR, Suberoylanilidehydroxamic acid.
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