QSAR modeling and in silico designing of Tumor-Associated Carbonic Anhydrases XII inhibitors

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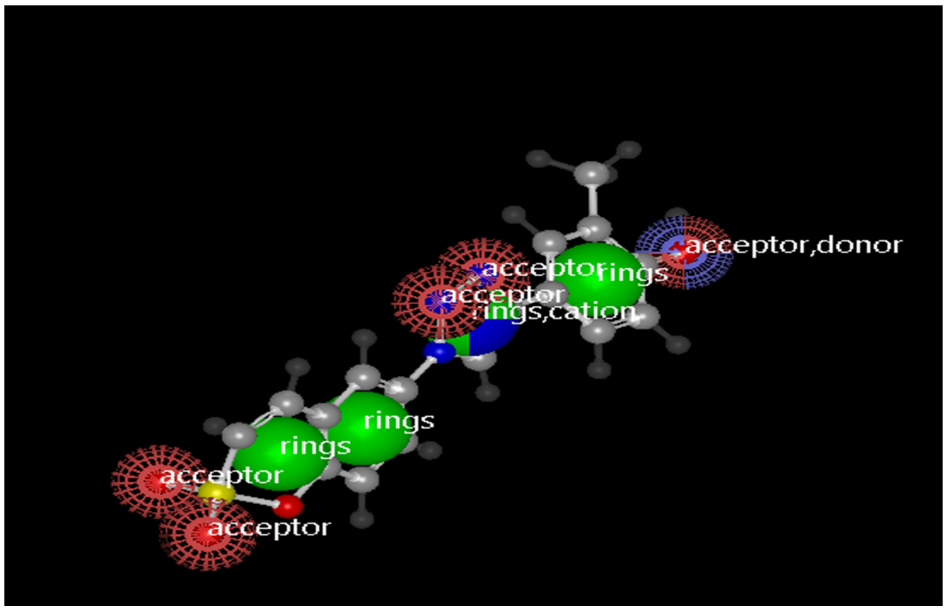

Abstract

Substituted coumarin such as sulfocoumarins (1,2-benzoxathiine 2,2-dioxides) possessing are the most important class of Potent and Isoform-Selective Inhibitors of Tumor-Associated Carbonic Anhydrases CA XII.

I have attempted to build QSAR models to explore the correlations between the calculated molecular descriptors on the pool of 16 compounds and their experimental CAXII inhibitory activities. The quality of prediction is high enough (SE =0.1291, r^2=0.98; F=212.7398, Q=0.7963). The virtual molecular fragment that lead to a significant increase of the inhibitor activity of hCA XII is C_2HN_3 , The virtual fragments , Br atom and NO_2 leads to a significant decrease of the inhibitor activity value. The innovation of this work consists in not only exploring the structural attributes of bioactive molecules but in predicting in silico the structures of twenty six new compounds which may show Tumor-Associated Carbonic Anhydrases XII (CAXII) inhibitory activity. The analogs of the lead molecule are generated by replacing selected fragments that have similar shape and electrostatics. The molecules of the prediction set include many molecules having high computed activity.

keywords: Carbonic Anhydrase inhibitors , PRECLAV, **Tumor-Associated Carbonic Anhydrases XII,** sulfocoumarins