Curr Drug Discov Technol 2021;18(6):e130921187100.

Molecular Modelling Studies on Thiazole-Based α-Glucosidase Inhibitors Using Docking and CoMFA, CoMSIA and HQSAR

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PMID: 33092511

DOI: 10.2174/1570163817666201022111213

Abstract

Aims and objectives: The biological dataset was retrieved from two series of α-glucosidase inhibitors synthesized by Rahim et al. and Taha et al. and consisted of a total of 46 (forty-six) α- glucosidase inhibitors.

Methods: The α-glucosidase inhibitory IC_{50} values (μM; performed against α-glucosidase from Saccharomyces cerevisiae) were converted into negative logarithmic units (pIC_{50}). The CoMFA and CoMSIA models were developed using 37 as a training set, and externally validated using 9 as a test set. The CoMFA models MMFF94 were generated, ranging from 3.4661 to 5.2749 using leave-oneout PLS analysis cross-validated correlation coefficient q^2 0.787, a high non-cross-validated correlation coefficient r^2 0.819, with a low Standard Error Estimation (SEE) 0.041, F value 1316.074 and r^2 pred 0.996.

Results: The steric and electrostatic fields contributions were 0.507 and 0.493, respectively. The CoMSIA model q^2 0.805, r^2 0.833 was attained, (SEE) 0.065, F value 520.302 and r^2 pred 0.990. Contribution of steric, electrostatic, hydrophobic, donor and acceptor fields was 0.151, 0.268, 0.223, 0.234, 0.124, respectively.

Conclusion: The HQSAR model of the training set exhibits a significant cross-validated correlation coefficient q^2 0.800 and non-cross-validated correlation coefficient r^2 0.943.

Keywords: CoMFA; CoMSIA; HQSAR; docking; pharmacophore mapping; α-glucosidase inhibitor..