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Virtual screening and modeling of physico-chemical properties of COX-2 inhibitors similar to celecoxib using neural network

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Background and Aims: COX-2 selective inhibitors such as celecoxib, rofecoxib and valdecoxib are currently used to reduce inflammatory response. There is still a need to develop more potent COX-2 inhibitors. This study was conducted to introduce new structures with more affinity to COX-2 enzyme.
Methods: Data mining of structures with 80% similarity to celecoxib was done using PubChem at NCBI database. The PDB file of COX-2 enzyme (6COX) bound to SC-558 reference ligand obtained from RCSB PDB website. The relationship between physico-chemical properties of compounds and their activities compared using neural network modeling. Docking of ligands to SC-558 site of COX-2 performed with leadIT software (version 2.1.0 BioSolveIT, GmbH, Germany) and the interaction energy of different compounds was obtained. IC50 value of selected compounds identified using *in vitro* screening against COX-2 enzyme.
Results: Our screening approach identified 5000 molecules similar to celecoxib from the PubChem database. 24 compounds had energy scores better than the 6COX bound co-crystallized ligand SC-558. The ligands were docked within the binding pocket forming interactions with Leu352, Phe518, Met522, Val523, Ala527 and Ser353. Visual inspection suggested similar orientation and binding mode for compounds with SC-558 ligand.
Conclusions: These findings potentiated the neural network modeling and computational approach for discovery of novel anti-inflammatory compounds with higher activity and low toxicity compared to general COX-2 inhibitors.

Keywords: COX-2 inhibitors; Celecoxib; Artificial neural network; Virtual screening