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RESEARCH ARTICLE

Ligand recognition properties of the vasopressin V2 receptor studied under QSAR and molecular modeling strategies

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Abstract

The design of new drugs that target vasopressin 2 receptor (V2R) is of vital importance to develop new therapeutic alternatives to treat diseases such as heart failure, polycystic kidney disease. To get structural insights related to V2R-ligand recognition, we have used a combined approach of docking, molecular dynamics simulations (MD) and quantitative structure–activity relationship (QSAR) to elucidate the detailed interaction of the V2R with 119 of its antagonists. The three-dimensional model of V2R was built by threading methods refining its structure through MD simulations upon which the 119 ligands were subjected to docking studies. The theoretical results show that binding recognition of these ligands on V2R is diverse, but the main pharmacophore (electronic and π–π interactions) is maintained; thus, this information was validated under QSAR results. QSAR studies were performed using MLR analysis followed by ANN analysis to increase the model quality. The final equation was developed by choosing the optimal combination of descriptors after removing the outliers. The applicability domains of the constructed QSAR models were defined using the leverage and standardization approaches. The results suggest that the proposed QSAR models can reliably predict the reproductive toxicity potential of diverse chemicals, and they can be useful tools for screening new chemicals for safety assessment.