MOLECULAR MODEL OF 5-HT$_7$ RECEPTOR: INTERACTION WITH ARYLPIPERAZINE LIGANDS

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Molecular model of serotonin 5-HT$_7$ receptor was constructed, based on the methodology used earlier for the 5-HT$_{1A}$ modeling [1]. The final model was selected from initial 400 models via inverse virtual screening with the use of high and low affinity compounds. The group of arylpiperazine ligands having different spacer structure was used for further model validation. It was found that conformational flexibility influences the affinity for 5-HT$_7$ and selectivity towards 5-HT$_{1A}$ [2]. The binding mode of arylpiperazine derivatives within the 5-HT$_7$ receptor is proposed. The correlation between experimental binding affinities of these compounds and FlexX docking energies is discussed. In addition, the impact of Asp$^{3.32}$ conformation on the quality of the model is investigated in comparison with analogous residue in 5-HT$_{1A}$.

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