Serotonin 5-HT_6 Receptor Antagonists for the Treatment of Cognitive Deficiency in Alzheimer's Disease

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Supporting Information

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1. Computational models of the complexes between representative compounds (4, 17, 27, 31, 50, 56, 65, 71, 75) and the 5-HT$_6$R. MODELLER v9.7[1] was used to build a homology model of human 5-HT$_6$R (Uniprot code P50406) using the crystal structure of human 5-HT$_{1B}$ (PDB code 4IAR)[2] as template. Compounds **4, 17**, **27**, **31**, **50**, **56**, **65**, **71**, **75** were docked into the receptor model using the Autodock Vina tool.[3] All docking solutions were visually inspected and the poses in which the protonated amine of the ring forms an ionic interaction with D3.32 and the HBA group hydrogen bonds N6.55 were energy minimized. Computer simulations were performed with the GROMACS 4.6.3 simulation package,[4] using the AMBER99SB force field as implemented in GROMACS, and the general Amber force field (GAFF) and HF/6-31G*-derived RESP atomic charges for the ligands. This procedure has been previously validated.[5]

2. References

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