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The Development and Validation of a Novel Virtual Screening Cascade Protocol to Identify Potential Serotonin 5-HT_7R Antagonists.

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The 5-HT_7 receptor is a well known target for the treatment of CNS disorders. In attempt to identify new potential ligands for this receptor, we performed a multistep virtual screening (VS) based on two-dimensional (2D) pharmacophore similarity, physico-chemical scalar descriptors, ADME/Tox filter, three-dimensional (3D) pharmacophore searches and docking protocol. The six chemical classes of 5-HT_7R antagonists [1] were used as a query structures in double-path virtual screening scheme. The Enamine screening database [2] consisting of approximately 730 000 commercially available compounds was adopted and used in this study. The binding mode of selected virtual hits are shown in comparison to that of known antagonists [1].

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[1] Kołaczkowski M., Nowak M., Pawłowski M., Bojarski A. J.: *J. Med. Chem. 49 (2006)*, *6732.*
[2] http://www.enamine.net/