PP7

Non-basic 5-HT$_6$ Receptor Ligands

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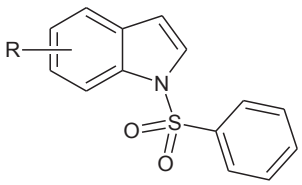
Recently a progress has been made in finding new non-basic ligands of serotonin receptors – mainly 5-HT$_6$ subtype. Until recently it was believed that only compounds with a basic nitrogen atom can act as aminergic receptor ligands. The discovery of the non-basic ligands has changed the longstanding views in medicinal chemistry. This phenomenon has been recently studied and some hypotheses were formulated, [1,2] but the mechanism of non-basic ligands-receptor interaction is still unclear.

As a part of our study on 5-HT$_6$R the consistent series of indole derivatives has been designed in an attempt to describe the interactions of non-basic ligands in the binding pocket. Following the examples of literature ligands with 1-(phenylsulfonyl)-1H-indole fragment and basic nitrogen atom, their counterparts with reduced and/or removed basicity were synthesized.



R = 1-methylpiperazinyl, 1-acetylpiperazinyl, 1-(2,2,2-trifluoroethyl)piperazinyl, 1-piperidinyl

The 5-HT$_6$, 5-HT$_{2A}$, 5-HT$_7$ and D$_2$ receptor affinities for all the synthesized compounds were assessed in radioligand binding experiments. The structure-affinity relationships and results of molecular modelling experiments are discussed.

[1] Ivachtchenko A. V. et al. *J. Med. Chem.* 54 (2011) 8161.

[2] Van Loevezijn A. et al. *J. Med. Chem.* 54 (2011) 7030.

Acknowledgements

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