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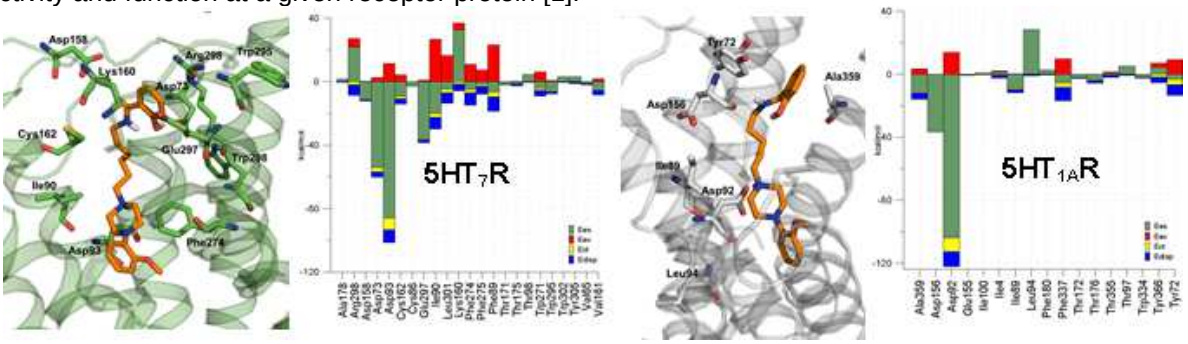
FMO/EDA study of 1-hexyl-4-(2-methoxyphenyl)piperazines as ligands of serotonin receptors

Paweł Śliwa,[a] *Rafał Kurczab,*[b] *Jolanta Jaśkowska,*[a] *Magdalena Malinowska,*[a] *Damian Kułaga,*[a] *Andrzej J. Bojarski*[b]

[a]*Faculty of Chemical Engineering and Technology, Cracow University of Technology, Warszawska 24, 31-155 Cracow, Poland*
[b]*Department of Medicinal Chemistry, Institute of Pharmacology, Polish Academy of Sciences, Smetna 12, 31-343 Cracow, Poland*

e-mail: psliwa@chemia.pk.edu.pl

Long-chain arylpiperazines (LCAP) are one of the commonly studied class of bioactive compounds due to their potential therapeutic effects caused by interactions with different subtypes of serotonin receptors. A number of studies have been aimed at examining the impact of LCAP structure modifications on the affinity, selectivity and function at a given receptor protein [1].



In this study the structure of four derivatives of 1-hexyl-4-(2-methoxypneyl)piperazine complexed with two serotonin receptors (5-HT_{1A}R, 5-HT_7R) has been investigated by means of quantum mechanical methods. The FMO/EDA analysis showed that the 2-(piperazin-1-yl)-methoxybenzene moiety of considered ligands forms very strong salt bridge between the protonated nitrogen atom of piperazine and Asp3.32, as well as hydrophobic interactions of the methoxybenzene ring with the aromatic cluster of TMH6 (Phe6.51, Phe6.52), for both studied receptors. The performed calculations can be helpful in the interpretation of the experimental results concerning the affinity to receptors, as well as they provide the reasonable binding energies and binding patterns of ligand-protein interactions.

[1] Kowalski P. et al., *Arch. Pharm. Chem. Life Sci*. 346 (2013) 339–348,

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