

## Influence of presence of aromatic ring(s) at position 5 of hydantoin on activity of potential 5-HT<sub>7</sub>R ligands

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Search for new antipsychotic medications is required scientific approach, since many patients show incomplete response to currently available treatment. The most important is finding new drugs with reduced side effects such as metabolic abnormalities, QTc prolongation, cognitive and motor dysfunctions.

Recently published studies indicate that blockade of 5-HT<sub>7</sub>Rs displays e.g. an antidepressant-like activity, anxiolytic-like effect and improvement of reference memory. Hence, design, synthesis and evaluation of new molecules with high affinity towards 5-HT<sub>7</sub> receptor is promising strategy for future effective CNS diseases treatment.

Our previous studies, allowed to obtain series of 14 novel hydantoin derivatives with attractive activity to above-mentioned receptor ( $3 \text{ nM} < K_i < 79 \text{ nM}$ ). Compounds with the most interesting properties were chosen for further modifications. This work is continuation of mentioned studies and is focused on evaluation how presence/absence of aromatic ring(s) in position 5 of hydantoin influences on activity. Within the research, 9 compounds (5-methyl-5-phenylhydantoin, 5,5-diphenylhydantoin and 5-methyl-5- $\alpha$ -naphthylhydantoin derivatives were synthesized and evaluated, while synthesis of 6 compounds more is ongoing (5,5-dimethylhydantoin and 5-methyl-5- $\beta$ -naphthyl hydantoin derivatives). However, for the time being, the most favourable, regarding 5-HTRs affinity, seems to be 5-phenyl-5-methylhydantoin moiety.

[1] Nikiforuk A. *CNS Drugs*. 29 (2015) 265.

[2] Bieńkowski P., Dudek D., Samochowiec J. *Psychiatr. Pol.* 49 (2015) 243.

[3] Handzlik J. et al. *Eur. J. Med. Chem.* 78 (2014) 324.

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