PO-13

8-AMINO-7-PHENYLPIPERAZINYLALKYL-PURINE-2,6-DIONES AS SEROTONIN RECEPTOR LIGANDS

Grażyna Chłoń-Rzepa[a], Paweł Żmudzki[a], Maciej Pawłowski[a], Beata Duszyńska[b], Andrzej J. Bojarski[b], Małgorzata Zygmunt[c], Barbara Filipek[c], Małgorzata Dybała[d]

[a] Department of Pharmaceutical Chemistry, Jagiellonian University, Medical College, 9 Medyczna St, 30-688 Kraków, Poland,

[b] Department of Pharmacology, Polish Academy of Sciences, 12 Smętna St., 31-343 Kraków, Poland,

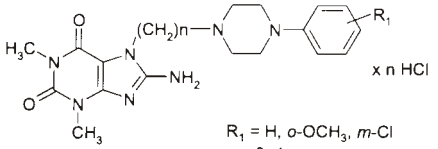
[c] Department of Pharmacodynamics, Jagiellonian University, Medical College, 9 Medyczna St, 30-688 Kraków, Poland,

[d] Department of Cytobiology and Histochemistry, Jagiellonian University, Medical College, 9 Medyczna St, 30-688 Kraków, Poland

It is well known that central serotonergic receptors play an essential role in a number of psychiatric disorders such as anxiety, depression or schizophrenia.

Our chemical and pharmacological studies in the group of 1,3-dimethyl-3,7-dihydropurine-2,6-dione derivatives showed that some compounds are potent serotonin receptor ligands[1, 2]. Among them the 7-phenylpiperazinylalkyl-8-alkoxy-1,3-dimethyl-purine-2,6-dione derivatives with a differently substituted phenyl ring (*o*-OCH_3, *m*-Cl) were the most interesting ones . It was found that the selected compounds were highly active 5-HT_{1A} (K_i = 11-19 nM); 5-HT_{2A} (K_i = 23-57 nM) and 5-HT_7 (K_i = 51-83 nM) receptor ligands [3].The most active compounds tested in behavioral models showed potential anxiolytic and antidepressant activities[3].

As a continuation of our research we designed and synthesized of new 8-amino-1,3-dimethyl-7-phenylpiperazinylalkyl-purine-2,6-dione analogues.



R_1 = H, *o*-OCH_3, *m*-Cl
n = 3, 4

The earlier obtained by multistep procedure 1,3-dimethyl-7-phenylpiperazinyl-alkyl-8-dibenzylamino derivatives were deprotected yielding final products. For binding studies the free bases were converted into water soluble hydrochloride salts.

The structures of the new compounds were confirmed by examination of their ^{1}H-NMR, MS, UV spectra as well as by elemental analyses.

The new analogues are under evaluation for their affinities for 5-HT_{1A}, 5-HT_{2A} and 5-HT_7 receptors. The most active derivatives will be tested in *in vivo* behavioral models.

[1] M. Pawłowski, G. Chłoń, J. Obniska, A. Zejc, S. Charakchieva-Minol, M.J. Mokrosz: Il Farmaco, 2000, 55, 461-468

[2] G. Chłoń, M. Pawłowski, B. Duszyńska, A. Szaro, E. Tatarczyńska, A. Kłodzińska, E. Chojnacka-Wójcik: Pol. J. Pharmacol., 2001, 53, 359-368

[3] G. Chłoń-Rzepa, P. Żmudzki, P. Zajdel, A.J. Bojarski, B. Duszyńska, A. Nikiforuk, E. Tatarczyńska, M. Pawłowski: Bioorg. Med. Chem., 2007 (prepared to publication)