[1] Deluca, H.F.; Paaren,H.F.; Schnoes, H.K. *Top. Curr. Chem*. **1979**, 83, and references there citted.

[2] Andrews, D.R.; Barton, D.H.R.; HesseR.H.; Pechet, M.M. *J. Org. Chem.***1986**, 51, 4819.

[3]Manchand, P.S.; Yiannikouros, G.P.; Belica, P.S.; Madan, P. *J. Org. Chem.***1995**, 60, 6574.

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ENANTIOSELECTIVITIES OF SOME 1,4-DISUBSTITUTED PIPERAZINES ON AMYLOSE CARBAMATE

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Chromatographic behaviour of several chiral 1,4-disubstituted piperazine derivatives with hypnotic-sedative activity has been examined on amylose tris-(3,5-dimethylphenyl)carbamate (Chiralpak AD) with hexane-isopropanol and hexane-ethanol mobile phases and the results were compared with those obtained on cellulose tris-(4-methylbenzoate) (Chiralcel OJ). On Chiralpak AD column the chiral resolution has been obtained for 10 out of 11 tested compounds whereas on Chiralcel OJ 3 compounds remained unresolved. Mobile phase influence on enantioselectivity was more pronounced on Chiralpak than on Chiralcel stationary phase. The difference between the stationary phases lies in that amylose has helical while cellulose linear structure and amylose carbamate (contrary to cellulose benzoate) may serve as hydrogen bond donor. As a result for both stationary phase types one can observe different mobile phase influence on stereoelectronic interactions between analite and stationary phase.

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8-ALKOXY-PURINE-2,6-DIONES WITH 7-PHENYLPIPERAZINYLALKYL AND 7-TETRAHYDRO-ISOQUINOLINYLALKYL MOIETIES AS 5-HT$_{1A}$, 5-HT$_{2A}$, 5-HT$_7$ RECEPTOR LIGANDS

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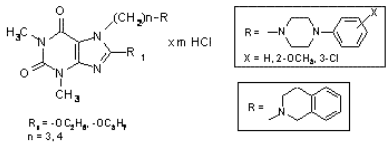
Based on our previous systematic studies on the structure-activity relationships in arylalkylpiperazine group of serotonin receptor ligands [1-3] we designed and synthesized a set of new 8-alkoxy-1,3-dimethyl-purine-2,6-dione derivatives with 7-(4-phenyl-1-pipera-zinyl)-alkyl and 7-(4-tetrahydroisoquinolinyl)-alkyl moieties. Previously obtained 1,3-dimethyl-7-(3-chloroalkyl)-8-alkoxy-purine-2,6-diones, in the reaction with appropriate piperazine derivatives and 1,2,3,4-tetrahydroisoquinoline yielded final products, which were then converted into water soluble hydrochloride salts. The purity of the compounds were controlled by TLC, the structures were confirmed by spectral (^{1}H-NMR, MS, UV), and C, H, N analyses.



The new compounds were tested in competition binding experiments for 5-HT$_{1A}$, 5-HT$_{2A}$ and 5-HT$_7$ receptors. It was found that some of 7-(4-phenylpiperazinyl)-butyl derivatives were potent 5-HT$_{1A}$, and/or 5-HT$_{2A}$ receptor ligands (K_i = 11-28 nM), and also highly active 5-HT$_7$ ligands (K_i = 75-90 nM). The compound with 7-(4-tetra-hydroisoquinolinyl)-butyl moiety was selective 5-HT$_7$ receptor ligand (K_i = 106 nM) with moderate 5-HT$_{1A}$, and low 5-HT$_{2A}$ receptor affinity. Some behavioral models demonstrated that selected compounds may be classified as partial agonists of 5-HT$_{1A}$ receptor.

References

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

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

3. P. Zajdel, A.J. Bojarski, H. Byrtus, G. Chłoń-Rzepa, J. Obniska, P. Chevallet, J. Martinez, M. Pawłowski: Biomed. Chromatogr. 17, 312, 2003.