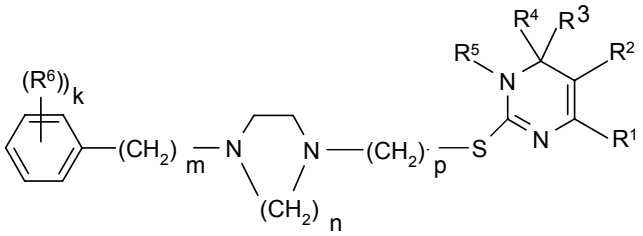
SYNTHESIS AND BIOLOGICAL ACTIVITY OF NOVEL PYRIMIDINE DERIVATIVES

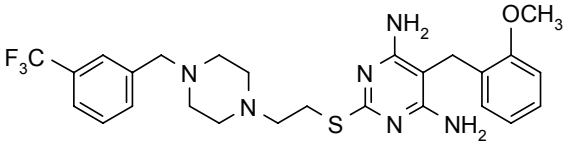
Györgyi Koványi, Lax[a], Dániel Bózsing[a], Ildikó Simonek[a], Gyula Simig[a], György Lévay[b]
István Gacsályi[b]

[a]Chemical Research Department,
[b]CNS Pharmacology Department
EGIS Pharmaceuticals Ltd., 1475 Budapest, P.O. Box 100, Hungary

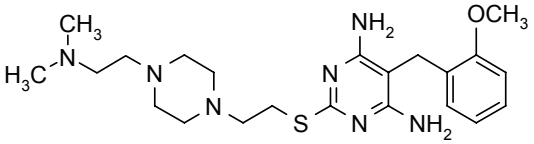
As a part of our research program new pyrimidine derivatives were synthesized **1.** These compounds were found to have high affinity for the 5-HT_{2C} receptors and some of them proved to be selective over 5-HT_{2A} receptors [1]. From our structure – activity relationship studies EGIS-8465, **2** was selected for further evaluation.



1



2



3

The very low biovailability in rats indicated high first pass metabolism of the compound. So we synthesized its analogues to avoid the enzimatic degradation. Among these molecules the "dimethyl-amino-alkyl" derivative **3** was the most effective in anxiolytic tests [2]. Synthesis and pharmacological results will be presented.

[1] WO 97/16429 patent application
[2] WO 01/00617 patent application