Short communication

Synthesis and 5-HT\textsubscript{1A}/5-HT\textsubscript{2A} activity of some butyl analogs in the group of phenylpiperazine alkyl pyrimido[2,1-f]theophyllines

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Abstract:
New arylpiperazines with a four-methylene spacer containing a terminal pyrimido[2,1-f]theophylline fragment (4–6) were synthesized, and their 5-HT\textsubscript{1A} and 5-HT\textsubscript{2A} receptor affinities were determined. All these compounds displayed a high affinity for 5-HT\textsubscript{1A} receptors ($K_i = 0.5–21.5 \text{nM}$), and low affinity for 5-HT\textsubscript{2A} ones. The results of in vivo experiments showed that compounds 4–6 revealed potential agonistic activity at presynaptic 5-HT\textsubscript{1A} receptors, whereas their functional activity at postsynaptic 5-HT\textsubscript{1A} sites was diversified. In fact, compounds 4, 5 and 6 behaved like partial agonists, antagonists or agonists of postsynaptic 5-HT\textsubscript{1A} receptors, respectively. The pharmacological properties of the tested compounds were discussed in comparison with those of the three methylene-analogs (1–3) described earlier.

Key words: 5-HT\textsubscript{1A} ligands, 1-phenylpiperazines, pyrimido[2,1-f]theophyllines, 5-HT\textsubscript{1A} receptor functional activity