

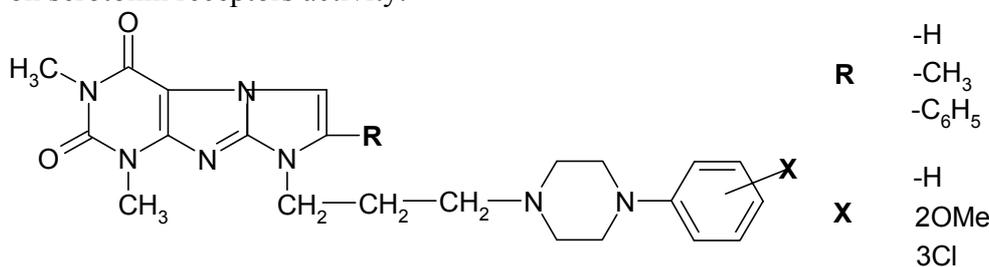
ARYLPIPERAZINYLALKYL DERIVATIVES OF IMIDAZO[2,1-F]THEOPHYLLINE AS CNS RECEPTOR LIGANDS*

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Arylpiperazines with an amide moiety are one of the most frequently investigated classes of 5-HT_{1A}/5-HT_{2A} receptor ligands. Although the terminal amide fragment significantly affects binding of 1-arylpiperazine derivatives for serotonin receptors, its role is not clear yet [1]. In our earlier attempt to find new 5-HT_{1A}/5-HT_{2A} receptor ligands, a series of arylpiperazinylalkyl derivatives with a complex terminal part based on the theophylline moiety had been synthesized. In the majority of the obtained compounds with pyrimido[2,1-f]theophylline fragment, high ($K_i < 50\text{nM}$) or very high ($K_i < 10\text{nM}$) 5-HT_{1A} receptor affinity and diversified pharmacological profile were observed[2,3]. The most potent for serotonin receptors were compounds with double bonds at annelated six member ring at 7,8 position of theophylline [4].

On the basis of the above data, we have synthesized the new tricyclic theophylline derivatives with five member ring, with double bond, annelated at 7,8 position and with arylpiperazinylpropyl substituent at N8 position, to study the influence of ring size and the presence of double bond, the kind of the substituent at N4 position of arylpiperazine moiety on serotonin receptors activity.



The newly synthesized compounds in a form of water-soluble hydrochlorides have been tested *in vitro* for their 5-HT_{1A} and 5-HT_{2A} receptor affinities. Pharmacological *in vivo* studies directing to CNS receptor profile of the synthesized compounds are in progress.

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