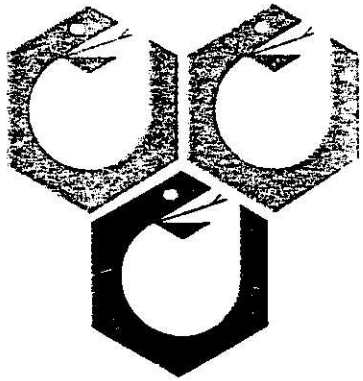

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## Structural parameters of Arylpiperazine type of ligands determining their 5-$HT_{1A}$/5-$HT_{2A}$ selectivity

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Two general strategies in design of new ligands acting at central serotonine (5-HT) receptors can be distinguished. The highly selective agents are desired pharmacological tools, whereas multireceptorial ligands are of interest from therapeutic point of view, since pathogenesis of psychiatric disorders is extremely complex and of heterogeneous nature. In both cases, a knowledge of structural features controlling affinity/selectivity for different receptors is needed.

It was found that 5-$HT_{1A}$ and 5-$HT_{2A}$ receptors are involved in severe mental disorders like schizophrenia, depression and anxiety. For many years we were engaged in structure-activity relationship studies within 5-$HT_{1A}$/5-$HT_{2A}$ receptor agents and hundreds of compounds were designed, synthesized and examined for their in vitro affinity. Based on these results structural parameters determining 5-$HT_{1A}$/5-$HT_{2A}$ selectivity ($S_{1A/2A}$) of arylpiperazine derivatives and analogues for ca.400 compounds were analyzed.

Initially, it was confirmed that 5-$HT_{1A}$/5-$HT_{2A}$ selectivity significantly depends on modifications within core system: $S_{1A/2A} < 0.1$ for 18% of 1-phenylpiperazines (PhP), 19% of *m*-Cl-PhP and 62% *o*-OMe-PhP. The influence of alkyl chain length and structure of terminal fragment on selectivity ratio were also investigated. A similar approach for literature data was used and the results compared.