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Synthesis and pharmacological screening for novel phenoxyalkyl derivatives of 1,3,5-triazine as ligands of 5-HT6 serotonin receptor

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5-HT6 serotonin receptor is the most recently identified and cloned member of serotonin receptor superfamily. Since then, numerous studies proved 5-HT6R involvement in depression, anxiety, obesity and memory, making it a new, promising therapeutic target in treatment CNS disorders [1,2]. In a recent study it has been proved that 1,3,5-triazine derivatives feature high affinity towards 5-HT6 receptor [3]. The purpose of this research was to assess the effect on both affinity and selectivity by introducing modifications within aryl moiety as well as alkyl linker of the lead structure. Furthermore, in silico screening has been performed to predict P-glycoprotein inhibition and blood-brain barrier permeability of synthesized compounds. Among obtained compounds, two showed highest affinity (Ki < 5 nM) and selectivity towards 5-HT6 receptor.

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