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ANTIDEPRESSANT- AND ANXIOLYTIC-LIKE EFFECTS OF NEW DUAL 5-HT1A AND 5-HT7 ANTAGONISTS IN ANIMAL MODELS AND PORSOLT TEST AUTOMATION

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ABSTRACT

The aim of this study was to further characterize pharmacological properties of two phenylpiperazine derivatives: 1-2-[2-(2,6-dimethlphenoxy)ethoxy]ethyl-4-(2-methoxyphenyl) piperazynine hydrochloride (HBK-14) and 2-[2-(2-chloro-6-methylphenoxy)ethoxy]ethyl-4- (2- methoxyphenyl) piperazynine dihydrochloride (HBK-15) in radioligand binding and functional in vitro assays as well as in vivo models. Antidepressant-like properties were investigated in the forced swim test (FST) in mice and rats. Anxiolytic-like activity was evaluated in the four-plate test in mice and elevated plus maze test (EPM) in rats. Imipramine and escitalopram were used as reference drugs in the FST, and diazepam was used as a standard anxiolytic drug in animal models of anxiety. Our results indicate that HBK-14 and HBK-15 possess high or moderate affinity for serotonergic 5-HT2, adrenergic $\alpha 1$, and dopaminergic D2 receptors as well as being full 5-HT1A and 5-HT7 receptor antagonists. We also present their potent antidepressant-like activity (HBK-14—FST mice: 2.5 and 5 mg/kg; FST rats: 5 mg/kg) and (HBK-15—FST mice: 1.25, 2.5 and 5 mg/kg; FST rats: 1.25 and 2.5 mg/kg). We show that HBK-14 (four-plate test: 2.5 and 5 mg/kg; EPM: 2.5 mg/kg) and HBK-15 (fourplate test: 2.5 and 5 mg/kg; EPM: 5 mg/kg) possess anxiolytic-like properties. Among the two, HBK-15 has stronger antidepressant-like properties, and HBK-14 displays greater anxiolytic-like activity. Lastly, we demonstrate the involvement of serotonergic system, particularly 5-HT1A receptor, in the antidepressant- and anxiolytic-like actions of investigated compounds. During conference session vision-based methods of FST automation will be also presented.

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