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A novel mGluR7 negative allosteric modulators

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The metabotropic glutamate receptors (mGluR) represent class C GPCRs and play significant neuromodulatory roles throughout the brain. The metabotropic glutamate receptor 7 (mGluR7) is a member of group III family that binds to protein G and inhibits the adenylate cyclase [1]. The mGluR7 has the highest CNS dentisity of all group III mGluR subtypes due to widely distribution and presence at broad range of synapses [2,3]. Many studies have shown that mGluR7 receptor is an important target for therapeutic intervention in a number of neurological and psychiatric disorders including anxiety, post-traumatic stress disorder, depression, autism, drug abuse, and schizophrenia [1-4]. In terms of discovery of new selective ligands the mGluR7 receptor is one of the most challenging of the all mGluR subtypes [4]. So far only few compounds which influence on the mGluR7 receptor are known: positive modulator - AMN082 [5], negative allosteric modulators - MDIP, MMPIP [1] and ADX71743 [6]. Therefore the discovery of highly selective mGluR7 ligands which can be used in clinical trials seems to be still the most significant challenge.
The development of novel chemical scaffold possessing activity towards mGluR7 receptor is the aim of present study. So far a variety of chemotypes were synthesized and examined *in vitro*, followed by the primary *in vivo* evaluations. The studies have shown new quinazolinone derivatives as promising mGluR7 negative allosteric modulators. Primary pharmacokinetics results demonstrated that concentration of ALX-171 in plasma as well as in brain is higher than for the reference ADX-71743 compound

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