New Product Highlights

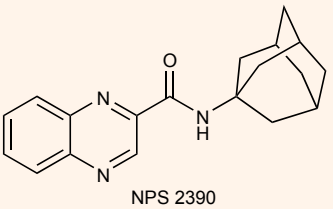
NPS 2390: A potent and selective noncompetitive Group I metabotropic glutamate (mGlu) receptor antagonist
First available from Sigma-RBI!

At present, eight G protein-coupled glutamate receptors (also referred to as "metabotropic" glutamate receptors, or mGlus) have been identified and classified into three groups referred to as Group I, Group II and Group III. These receptors are distributed throughout the central nervous system and their function is only beginning to be elucidated.

The Group I (mGlu1 and mGlu5) receptors are located both pre- and post-synaptically, signal through inositol phospholipid hydrolysis and modulate the activity of calcium and potassium channels [1,2]. The mGlu1 receptors play a role in motor learning and motor coordination [3,4], whereas mGlu5 receptors contribute to induction of long-term potentiation and associative learning [5]. There is also some indication that Group I mGlu receptor antagonists may provide neuroprotection against excitotoxic neuronal death [6,7]. Several Group I-selective antagonists have been synthesized that exhibit varying degrees of specificity and potency, such as **AIDA** (Prod. No. A-254), BAY 36-7620, **CPCCOEt** (Prod. No. C 9611), LY-367385, **MPEP** (Prod. No. M 5435), MTEP, R214127, **SIB-1757** (Prod. No. S 9186) and **SIB-1893** (Prod. No. S 9311).

Sigma-RBI is pleased to introduce **NPS 2390** (Prod. No. N 4786), a potent, selective and structurally novel, non-competitive Group I mGlu receptor antagonist. In Chinese hamster ovary (CHO)-dhfr$^-$ membranes, NPS 2390 displaced [^{3}H]-R21427 binding displaying a K_i of 1.36 nM, but failed to affect the binding of [^{3}H]-quisqualate, an analog of the endogenous ligand, glutamate, suggesting that NPS 2390 binds to sites other than glutamate on Group I mGlu receptors [8]. NPS 2390 also inhibited calcium sensing receptor-mGlu1 and calcium sensing receptor mGlu5 chimeras with IC_{50} values of 5.2 nM and 82 nM, respectively. At 30 µM, it displayed no activity at calcium sensing receptor-mGlu3 chimeras, calcium sensing receptor receptor-mGlu8 chimeras, or a range of 37 receptors, ion channels and enzymes [9].

A major challenge at present is to develop subtype-specific receptor agonists and antagonists with which to define the biological role of each group of mGlu receptors *in vitro* and *in vivo*. NPS 2390 should prove to be a useful tool for the study of these Group I mGlu receptors and their pathophysiological significance.



NPS 2390
(Prod. No. N 4786)

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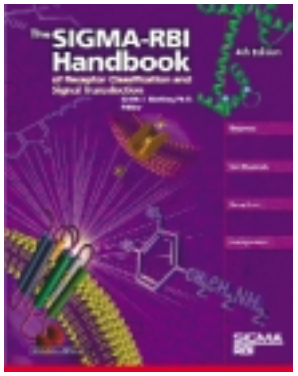

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