New Product Highlights

CNS-1102: An NMDA glutamate receptor antagonist with neuroprotective activity. Exclusively available from Sigma-RBI

Cerebral ischemia causes the release of excessive amounts of the excitatory amino acid L-glutamic acid (Prod. No. G 1501), resulting in the toxic activation of several types of glutamate receptor, including the ionotropic N-methyl-D-aspartate (NMDA, Prod. No. M 3262) and α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA, Prod. No. A 0326) receptors, and subsequent necrotic neuronal cell death. Utilizing several mechanisms, blockade of glutamate receptors can ameliorate the neuronal injury associated with cerebral ischemia. One mechanism, specifically antagonizing the calcium-conducting channels associated with NMDA receptors on neurons, can block the calcium influx mediated by glutamic acid [1]. Known ligands for the NMDA receptor ion channel site include phencyclidine (PCP, Prod. No. P 3029) and MK-801 (Prod. No. M-107), both of which act as non-competitive blockers [2].

Sigma-RBI is pleased to introduce CNS-1102 (Aptiganel hydrochloride, Prod. No. C 4238), a selective, non-competitive NMDA receptor antagonist. Studies with CNS-1102 have demonstrated reduced early postischemic injury and improved perfusion following middle cerebral artery occlusion in rats, an animal model for stroke [3,4]. CNS-1102, administered 15 min postocclusion, resulted in neuroprotective effects in the cortical and caudoputaminal regions during the initial 3 hr of ischemia. Postmortem tissue analysis showed a 66% reduction in infarcted tissue as compared with untreated animals. Studies with CNS-1102 under similar experimental conditions have also demonstrated a neuroprotective effect on cerebral white matter. These results could prove useful in understanding and treating white matter ischemic changes common to elderly patients [5].

CNS-1102 was rationally designed to interact with the NMDA receptor ion channel binding site while minimizing α receptor cross-reactivity common to similar ligands such as phencyclidine [6]. Although advanced to the clinic for the treatment of acute ischemic stroke, trials were subsequently abandoned due to intolerable psychotomimetic side-effects. However, CNS-1102 is poised to be an extremely useful tool in the search for more therapeutically suitable NMDA receptor antagonists.

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References

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