

New Product Highlights

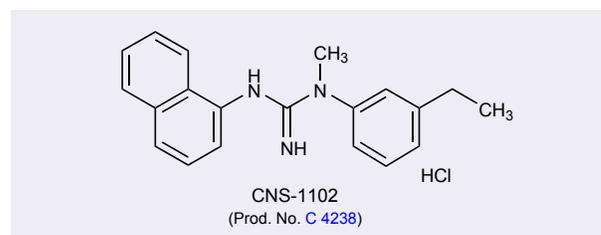
CNS-1102: An NMDA glutamate receptor antagonist with neuroprotective activity. *Exclusively* available from Sigma-RBI

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 caudoputaminial 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 σ 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

1. Lees, K.R., *Neurology*, **49**, S66-69 (1997).
2. Weiloch, T., *Science*, **230**, 681-683 (1985).
3. Minematsu, K. et al., *Neurology*, **43**, 397-403 (1993).
4. Minematsu, K. et al., *Stroke*, **24**, 2074-2081 (1993).
5. Schäbitz, W.-R. et al., *Stroke*, **31**, 1709-1714 (2000).
6. Reddy, N.L. et al., *J. Med. Chem.*, **37**, 260-267 (1994).

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