

Lacosamide is a Novel Antinociceptive and Antiepileptic Drug with a Dual Mode of Action

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Lacosamide is an investigational drug that has demonstrated positive results in Phase III trials of neuropathic pain and epilepsy. Preclinical studies have shown neuroprotective effects of lacosamide both in animal models and in-vitro. Electrophysiology and proteomics experiments have identified two likely modes of action for lacosamide.

Electrophysiology experiments performed in mouse neuroblastoma cells indicate that lacosamide reduces sodium-channel availability by selectively enhancing slow-inactivation. Enhancing slow-inactivation is thought to raise channel-activation thresholds, reducing pathophysiological neuronal hyperexcitability. This mechanism is different from that of anesthetic and other antiepileptic agents, which non-selectively block the sodium channel pore and/or enhance fast- and slow-channel inactivation.

A second mechanism of action may occur via the binding of lacosamide to collapsin-response mediator protein 2 (CRMP-2), a phosphoprotein that is involved in neuronal differentiation and axonal out-growth (processes that are maladaptive in the pathophysiology of pain and epilepsy). The interaction of lacosamide with CRMP-2 may underlie the apparent neuroprotective effects of lacosamide, since CRMP-2 appears to be important for mediating neuroprotection from excitotoxic insult and apoptosis.

The dual mode of action of lacosamide represents two novel mechanisms for the treatment of neuropathic pain and epilepsy. Based on current studies, it is proposed that selective enhancement of slow-inactivation of sodium channels may underlie the immediate effects of lacosamide. Further characterization of the interaction with CRMP-2 may help to explain its role in lacosamide's symptomatic and disease-modifying effects.