

Evidence of rattlesnake crotalphin effects on tetrodotoxin-sensitive Na channels of mouse dorsal root ganglion neurons

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Crotalphine is an analgesic peptide identified in the venom of the South American rattlesnake *Crotalus durissus terrificus*. Although its antinociceptive effects are well documented, its direct mechanisms of action are still under investigation. The aim of the present work was to study the action of the crotalid peptide on the sodium channel subtype NaV1.7, a genetically validated pain target. To this purpose, the effects of crotalphine were evaluated on the tetrodotoxin-sensitive Na current of dorsal root ganglion neurons of adult mice, using the whole-cell patch-clamp configuration, and on the cell viability, using the propidium iodide fluorescence and trypan blue assays. The results show that 18.70 μM of peptide were necessary to inhibit 50% of the Na current, the blocking effects occurring without any marked change in the current activation and inactivation kinetics and voltage-dependencies. In addition, a crotalphine-induced increase in leakage current amplitude of approximately 150% and a maximal decrease of 28% of cell viability were detected in the presence of 50 μM of peptide. Taken together, these results point out, for the first time, the effectiveness of crotalphine to act on the NaV1.7 channel subtype, directly and/or indirectly by affecting cell membrane integrity. This mechanism of action could contribute to the peptide analgesic properties.

Keywords: crotalphine, electrophysiology, pain.
