

Toxins from the Venom of Cone Snails Indigenous to the Americas

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Abstract: Cone snails are venomous, predatory marine mollusks whose venom is composed of a cocktail of neuroactive peptides (conopeptides). A wide range of neurologically-related conditions, ranging from chronic pain to epilepsy, can be treated with conopeptides; i.e., a constrained conopeptide (the ω -conotoxin MVIIA) have been developed into PrialtTM, a powerful painkiller that has been approved by the FDA in the U.S. in December 2004, which is the first drug of marine origin to receive such status. Other conopeptides undergoing clinical trials are CVIA from *C. catus*, Conantokin-G and Contulakin-G, both from *C. geographus*, ACVI from *C. victorae* and Xe2174 from *C. marmoreus*. The venom of a cone snail is species-specific and contains up to 200 different conopeptides. Their separation and characterization is a daunting task, particularly since conopeptides contain numerous post-translational modifications. Our laboratory is dedicated to the collection, isolation and characterization of conopeptides from cone snail species from the Americas (Atlantic and Panamic regions). To date, we have collected over 100 different species of Atlantic and Panamic *Conus*. We have developed a high performance separation scheme that allows the isolation of single-component fractions of conopeptides from very small quantities of crude *Conus* venom. We have developed a novel molecular characterization scheme that relies on the use nanoNMR and MS techniques to determine the covalent structure of conopeptides. We have termed this approach "Conopeptidomics", which is a comprehensive methodology for the screening of neuroactive compounds from marine sources. Through conopeptidomics, we are aimed to intensify the discovery process of marine compounds of neuropharmacological importance and evaluate their potential for drug development.