



PHYLOGENETIC SPECIFICITY OF *CONUS* NEUROPEPTIDES

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The venom of the predatory cone snails (*Conus*) contain a diverse set of biologically active peptides. In addition to the major toxins used to incapacitate or paralyze prey, many other neuroactive peptides have been found in all species examined. Although certain class of toxins are found in related species, each species has a unique set of peptides.

Seven α -conotoxins (inhibitors of acetylcholine receptors), 11 ω -conotoxins (blockers of voltage sensitive calcium channels), and 3 conantokins (inhibitors of N-methyl-D-aspartate receptors) have so far been isolated from five *Conus* species. The conotoxins are small basic peptides ranging from 13 to 29 amino acids long with 2 to 3 disulfide bonds. On the other hand, conantokins are very acidic peptides containing 4 γ -carboxyglutamates and no cysteine residues. Presumably these peptides are targeted to receptors and ion channel of their prey and natural enemies but they can also recognize some targets in other vertebrates.

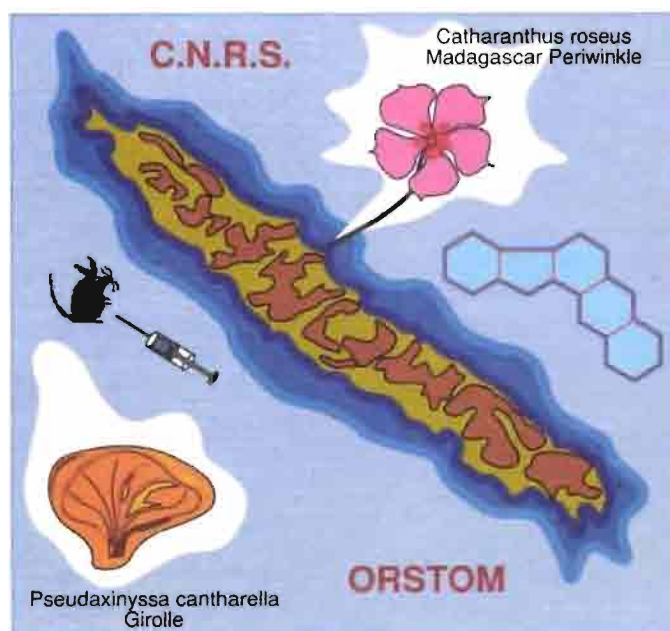
The α -conotoxins from *Conus geographus* and *Conus magnus* cause paralysis when injected intraperitoneally in fish, frog, chicks and mice but two of the α -conotoxins from *Conus striatus* affect only the fish neuromuscular junction at a comparable dose. The ω -conotoxins are also very effective in paralyzing fish but they affect only certain subtypes of calcium channels in the mammalian central nervous system. Thus, instead of causing death when injected intracranially, the ω -conotoxins produce a very characteristic shaking symptom in mice and rats. Conantokins induce behavioral symptoms dependent on the developmental stage of mice: they cause sleep in two-week old mice and hyperactivity in mice greater than three week old. In fish they produce depressed activity.

Structure-activity comparison of naturally occurring and synthetic analogs of α -conotoxins, ω -conotoxins and conantokins indicate the importance of certain residues in the recognition of target molecules in the different species. The homologous set of peptides from *Conus* venoms are now used as biochemical probes for receptors and ion channels.

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