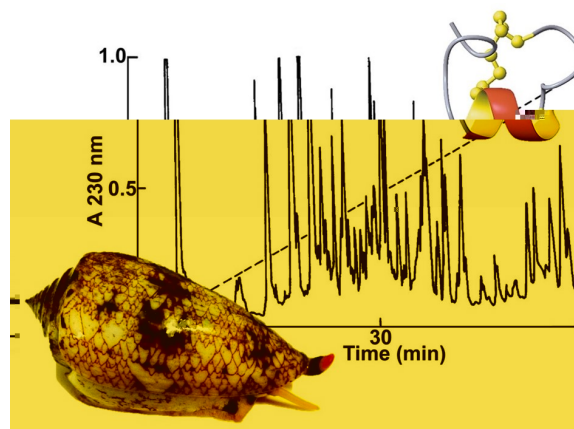


Disulfide rich peptides from predatory cone snails: synthesis, pharmacology and therapeutic potential



Cone snails are predatory marine gastropods that produce potent venom to prey on worms, molluscs or fish, and to defend against predators. Cone snail venom is a complex cocktail of various compounds, from small molecules to large proteins and enzymes. Yet, small disulfide rich peptides, called conotoxins, largely dominate the composition. These conotoxins mostly act on the transmission of the nervous signal, targeting very specifically membrane receptors, such as ion channels, GPCRs and transporters. They can therefore be used as probes to understand the physiological and molecular mechanisms of nerve transmission, but they have also been shown to have therapeutic applications for humans. For instance, the venom of the magician cone (*Conus magus*) has led to the discovery of the Prialt (Ziconotide), an analgesic more potent than morphine. Prialt is a synthetic version of omega-conotoxin MVIIA, which blocks a subtype of calcium voltage gated ion channel known as Cav2.2. Given that more than 800 species have been described, each producing between 50 and 200 major conotoxins and more than 20 pharmacological targets have been identified, the potential for discovery is truly exceptional. I will illustrate here, through several examples, the remarkable diversity of sequences, structures and pharmacologies offered by these conotoxins.



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