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PhcrTx1, novel marine peptide acting on acid-sensing ion channels and its isolation and characterization

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Acid-sensing ion channels (ASICs) are H+-gated Na+ channels that belong to the ENaC/degenerin superfamily of sodium channels. ASICs are involved in sensory perception, synaptic plasticity, learning, memory formation, cell migration and proliferation, nociception, and neurodegenerative disorders, among other processes, therefore those molecules that specifically target these channels are of growing pharmacological and biomedical interest. Sea anemones produce a large variety of ion channels peptide toxins. However, those acting on ligand-gated ion channels, including acid-sensing ion channel (ASIC) toxins, remain poorly explored. PhcrTx1 is the first compound characterized from the sea anemone *Phymanthus crucifer*, and it constitutes a novel ASIC inhibitor. This peptide was purified by liquid chromatographic techniques, followed by biological evaluation on ion channels of isolated rat dorsal root ganglia (DRG) neurons using patch-clamp techniques. PhcrTx1 partially inhibited ASIC currents (IC50 100 nM). The N-terminal sequencing yielded 32 amino acid residues, with a molecular mass of 3477 Da by mass spectrometry. No sequence identity to other sea anemone peptides was found. Interestingly, the bioinformatics analysis of cys-pattern and secondary structure arrangement suggested that this peptide presents an inhibitor cystine knot (ICK) scaffold, which has been found in other venomous organisms such as spiders, scorpions, and cone snails. Our results show that PhcrTx1 represents the first member of a new structural group of sea anemones toxins acting on ASIC. Also, this peptide constitutes a novel template for the development of drugs against pathologies related to ASICs function.

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