Research article
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Constitution of molluscs venom and its therapeutic possibilities (*Phylum: mollusca*)

Abstract

Molluscs are marine animals that protect themselves in shells or live freely. Some are poisonous, causing serious human poisoning and even deaths due to the neurotoxic action of substances called conotoxins, which induce the blockage of synaptic receptors and cause myorelaxant muscular paralysis, causing respiratory arrest between forty minutes and five hours after contact. The objective of the manuscript was to verify the constitution of mollusk venom and its therapeutic possibilities (Phylum: Mollusca). The present work uses the reference of bibliographical research, understood as the act of inquiring and seeking information on a given subject, through a survey carried out in national and foreign databases, to detect what is consensus or controversial. The articles in indexed scientific research, book scientific chapters, these banks, university dissertations, national and international scientific articles, scientific journals, documents, and the academic and scientific journals available online, ResearchGate, HAL, SSRN, Scielo, and Qeios.

Keywords: neurotoxic, predatory, radula, substances, therapeutic

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Introduction

Characteristics of phylum mollusca

The animal has a wide, tubular extension that can be stretched and extends far beyond the edge of the shell, being used in its food, after firing its radula, connected to venom glands, like a poisoned harpoon *Conus* Linnaeus, 1758, is a genus of predatory marine gastropod molluscs belonging to the family Conidae of the subclass Caenogastropoda and order Neogastropoda Linnaeus, 1758 when describing its first species in his Systema Naturae; notably *Conus marmoreus* Linnaeus, 1758 (Gastropoda: Conidae), its type species. Its geographic distribution mainly covers the Earth's tropical oceans, with many species in the Indo-Pacific region (Figure 1).[1-3]

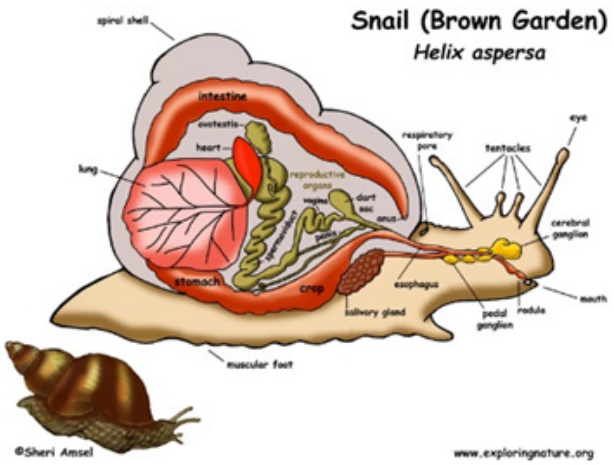

Figure 1 Phylum Mollusca: Internal and external morphology.

Sources: https://www.exploringnature.org/db/view/Mollusca-Gastropods-Bivalves-Cephalopods and Page ID: 1086, IP: 162.202.25.231

Its columellae do not have columellar folds, the external lip is quite thin and the opening is usually narrow, following the outline of the columella and its siphonal canals do not stand out from the shape of the shell. These molluscs have a soft periostracum covering their shells, and some have a small operculum. Molluscs are soft-bodied invertebrate animals that, for the most part, have protective shells. Some species, such as octopuses and slugs, do not have a shell; and in others, such as squid, the shell is internal and reduced (Figure 2).[3-5]

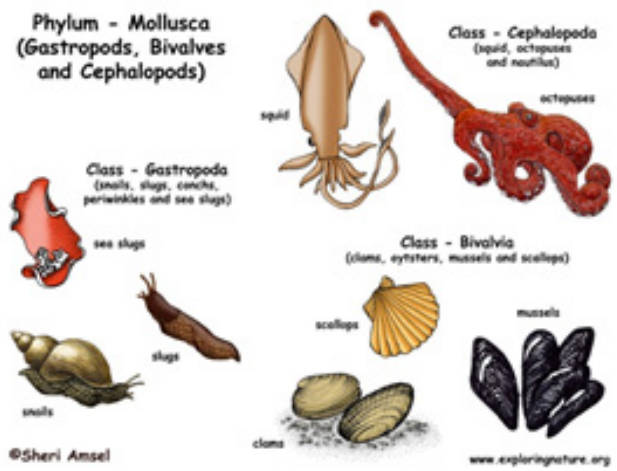

Figure 2 Systematics of Phylum Mollusca.

Sources: https://www.exploringnature.org/db/view/Mollusca-Gastropods-Bivalves-Cephalopods and Page ID: 1086, IP: 162.202.25.231

The body organization of mollusks involves three basic parts: foot, visceral mass, and mantle. The foot is a structure that helps the animal move, dig, and attach itself to the substrate. The visceral mass is the region where the animal's internal organs are located. The mantle, in turn, is a fold of tissue that covers the visceral mass, being responsible for producing the shell in those Molluscs that have it. The mantle also forms the so-called mantle cavity, which is the place where the digestive, excretory, and genital systems open. It is also in the mantle cavity where the gills are located (Figure 3).[5-8]

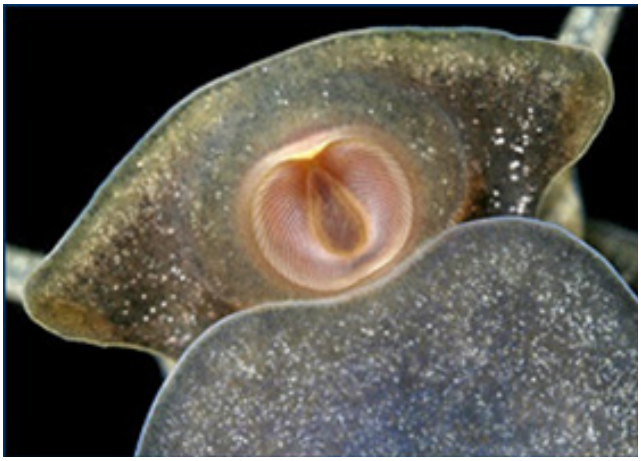

Figure 3 Radula of the sinistral pond snail the freshwater sinistral pond snail (*Physella* sp.) scrapes algae from the glass with its radula, the two "toothy" arcs you can see lining the mouth.

Source: Photos of cuttlefish, California Trivia, Giant Squid, sinistral pond snail radula and eggs.

Objective

The objective of the manuscript was to verify the constitution of mollusk venom and its therapeutic possibilities (Phylum: Mollusca).

Methods

The present work uses the reference of bibliographical research, understood as the act of inquiring and seeking information on a given subject, through a survey carried out in national and foreign databases, to detect what is consensus or controversial. The articles in indexed scientific research, book scientific chapters, these banks, university dissertations, national and international scientific articles, scientific journals, documents, and the academic and scientific journals available online ResearchGate, HAL SSRN, Scielo, and Qeios.

Characteristics of poisonous

Molluscs are marine animals that protect themselves in shells or live freely. Some are venomous and can cause death in humans, such as octopuses of the genus *Hapalochlaena* Robson, 1929 (Cephalopoda: Octopodidae) blue-ringed octopus, and gastropods of *Conus* Linnaeus, 1758. Common octopuses *Octopus* sp. also produce neurotoxins and the various species of *Conus* present in Brazil are being studied. Still, all are carnivorous and use conotoxins for hunting, although the potency or consequences of these poisons for humans are not known.[8-12]

Serious human poisoning and even deaths due to the neurotoxic action of substances called conotoxins, which induce the blockage of synaptic receptors and cause myorelaxant muscle paralysis, causing respiratory arrest between forty minutes and five hours after contact.[12-14]

These animals partially bury themselves in the sand during the day, before hunting their prey at night. This prey may consist of worms, other molluscs, and fish. Snails are a rare cause of poisoning among divers and shell collectors in the Indian and Pacific Oceans. The snail injects its venom through a harpoon-like tooth when handled aggressively. The venom can cause temporary paralysis which, on rare occasions, is fatal. Research with marine animals demonstrated the existence of hemolytic, cytotoxic, neurotoxic, neuromuscular paralyzing, and cardiotoxic activity in the isolated substances (Figure 4).[14-16]

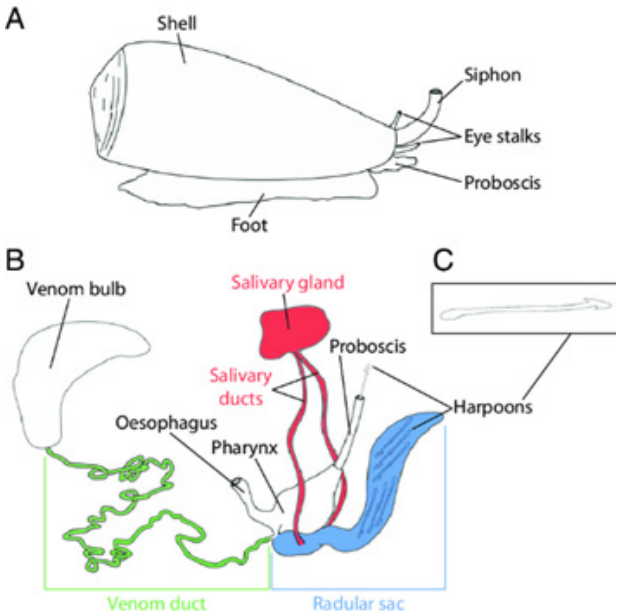

Figure 4 Macroscopic anatomy of a cone snail (A), its venom apparatus (B), and a radula tooth (C).

Source: https://www.researchgate.net/figure/Macroscopic-anatomy-of-a-cone-snail-A-its-venom-apparatus-B-and-a-radula-tooth-C_fig1_279842092.

Conus californicus Reeve, 1844 (Neogastropoda: Conidae) can cause pain, swelling, redness, and numbness at the site of the bite. Rarely, it can be followed by difficulty speaking, blurred vision, muscle paralysis, respiratory failure, and low blood pressure. North American octopus bites are seldom serious. However, the bite of the blue-ringed octopus found in Australian waters, although painless, causes weakness and paralysis that can be fatal.[16-18]

Achatina fulica Bowdich, 1822 (Gastropoda: Stylommatophora: Achatinidae), the African snail, is a threat to public health because it can be the intermediate host of the nematode, a species of microscopic worm that can cause meningoenphalic angiostrongyliasis, a type of meningitis. In Brazil, no cases have been recorded, but care must be taken, as the snail likes vegetables, such as lettuce, cabbage, and broccoli, warning the population, who use salt to kill the snail. The venom of *A. fulica* is being tested, it is a novelty in the fight against this pest, which was introduced in Brazil by escargot breeders. As it is not a native species in the country, there are no natural predators for it. The metaldehyde poison, in the form of granules, is spread directly on the soil, close to areas infested by slugs or snails, manually or using a granulated product applicator (Coordinator: Leonardo de Freitas).[18-22]

How to protect yourself

Snails can be responsible for several diseases, such as schistosomiasis, fasciolosis, eosinophilic meningitis, and abdominal angiostrongyliasis, as long as they are infected by parasites, which is not always the case. Fruits and vegetables should be washed very well with water and then left to soak for 10 minutes, completely covered, in a mixture of 1 liter of water and 1 tablespoon of bleach. It is also important to avoid environments that have snails and clean yards and vegetable gardens that may be infested. When cleaning, it is recommended to avoid contact with the snail with your hands using gloves or a plastic case.[22-25]

It is also important to collect the eggs that tend to be half-buried. Whatever is collected must be placed in a container and submerged in a solution with sodium hypochlorite for around 24 hours. Afterwards, the solution can be discarded and the shells placed in a closed plastic bag and disposed of in the general trash. The massive proliferation of microalgae can contaminate filter-feeding animals, such as bivalve molluscs, and biotoxins can cause acute poisoning in humans. The biotoxins that cause poisoning are substances synthesized by phytoplankton, phytobenthos, or macroalgae. Biotoxins IPIA (toxins responsible for paralysis) and PSP (paralyzing shellfish poison), or paralyzing shellfish poison. It is also called neurotoxin, mytilotoxin or saxitoxin. Currently, around twenty varieties of paralyzing biotoxins are known, all with chemical properties similar to those of saxitoxin (STX) (Figure 5).[25-28]

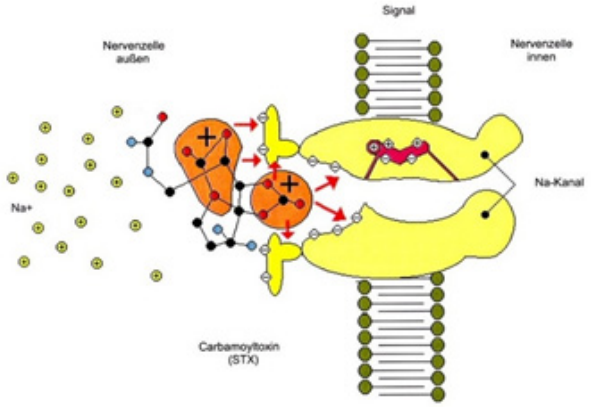

Figure 5 Model of how PSP toxins bind to the surface of excitable nerve cell membranes.

Source: https://www.eurobiotox.eu/science_of_toxins/24/index.html

Some species of *Dinophysis* Ehrenberg, 1839 (Dinophysales: Dinophysaceae) produce toxins that, when accumulated in bivalve molluscs above certain levels, cause the syndrome of "diarrheal shellfish poisoning", or DSP. The symptoms produced are diarrhea, nausea, vomiting, and abdominal pain. The active ingredient studied and typified to date is saxitoxin (STX), but others in this group have already been discovered, such as neosaxitoxin (neo-STX) and goniautoxins (GTX). It appears that both are transformed into saxitoxin inside the molluscs thanks to the action of bacteria and vibria, with the conversion rate being higher under aerobic conditions. All biotoxins in this group are paralyzing. In general, they are soluble in water and thermostable in acidic environments, but extremely unstable and easily oxidized in alkaline or weak acidic environments (Figures 6A-6B).[26-29]

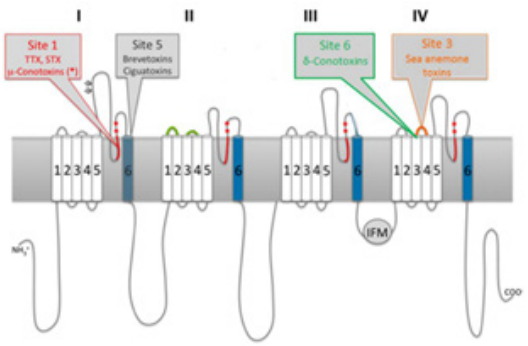

Figure 6A Sodium channel architecture and binding sites of marine neurotoxins. Cylinders represent transmembrane helices that comprise the four homologous domains. Sites targeted by marine neurotoxins are indicated by gray call-outs.

Source: https://www.mdpi.com/1660-3397/11/4/991

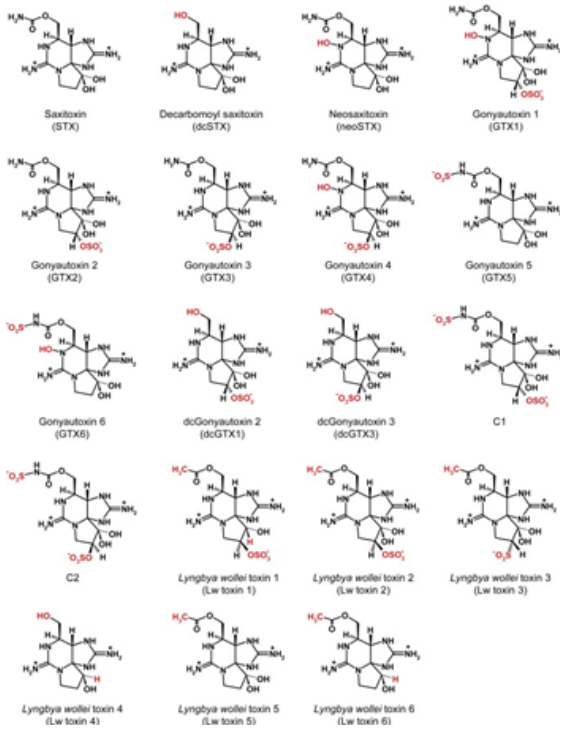

Figure 6B Saxitoxin analogues are produced by some members of different cyanobacteria genera. From Llewellyn (2006). Reproduced by permission of The Royal Society of Chemistry (http://dx.doi.org/10.1039/b501296c)

Biointoxication of mollusca

Biointoxication by Paralytic Shellfish Poisoning (PSP) or PSP-saxitoxin. Biointoxication by AZP, or azaspiracid poisoning, Biointoxication by Amnesic Shellfish Poisoning (ASP), ASP toxin domoic acid, Venerupine Biointoxication, or VSP (Venerupine Shellfish Poison), DSP toxins, PSP toxins, and ASP toxins. The answer to the problem of opioid addiction may come from a surprising source: the oceans. Scientists are studying the venom of various snails, slugs, and marine Molluscs as a non-addictive alternative to pain treatments. As they do not have resources such as teeth and arms, these marine Molluscs paralyze and capture their prey using such substances. Scientists want to use venom's anesthetic qualities to combat pain and inflammation in humans, rather than using addictive opioids (Figure 7).[27-29]

Figure 7 Shellfish poisoning.

Citation: Santana NVO, Marchiori CH, Malheiro KP. Constitution of molluscs venom and its therapeutic possibilities (*Phylum: mollusca*). *MOJ Biol Med.* 2025;10(2):90–95. DOI: 10.15406/mojbm.2025.10.00247

Sources: Done by Antar Sarkar, Faculty of Fisheries, CVASU, and 2024 Slide Share from Scribd

In the Vietnam War, a considerable number of American soldiers died from *Conus* poison. At first, the animal retreated into the shell to protect itself and, a few seconds later, quickly exposed an adapted radular tooth, a true harpoon, connected to the vesicle that contains the powerful venom, and injected it, through this tooth, into the victim. The venom inoculation mechanism is very similar to that developed by snakes. Death was quick.[28-30]

Mollusk poison reality and therapeutic possibility

Most of the research has already been carried out, which consists of shellless snails. The species *Dolabella auricularia* (Lightfoot, 1786) (Gastropoda: Aplysiidae) is a source of more than 15 cytotoxic peptides known as dolastatins. These compounds showed antineoplastic activity in P388 lymphocytic leukemic cells and B16 melanoma. Dolastatin 10 inhibits tubulin polymerization, being as potent as vincristine and colchicine (Figure 8).[29-30]

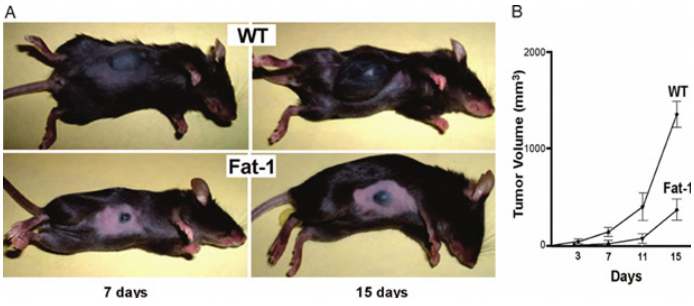

Figure 8 Tumorigenicity of B16 melanoma cells in fat-1 transgenic and WT mice. (A) Different sizes of melanomas in WT and fat-1 transgenic (FAT-1) mice at two different time points. Several 5 ᵡ 10 6 viable cells in 50 l of PBS were injected s.c. into each of 10 transgenic and 10 WT littermates (2-month-old female). On days 7 and 15 after cell implantation, animals were anesthetized briefly with isofluorane, and tumors were examined and photographed by using a digital camera. (B) Growth rates of melanomas in WT and transgenic mice. Tumor growth was monitored at the indicated time points by measuring the length, L, and width, w, of the tumor with a caliper and calculating tumor volume based on the following formula: volume σ (12). The points are mean values ↟ SD of 10 tumors (nσ10) for the WT group or of 7 tumors (nσ7) for the fat-1 transgenic group (fat-1).

Source: https://www.researchgate.net/figure/Tumorigenicity-of-B16-melanoma-cells-in-fat-1-transgenic-and-WT-mice-A-Different_fig1_6898863

Hexabranchus sanguineus Ruppell & Leuckart, 1828[31] (Gastropoda: Aplysiidae) avoids predation by feeding on chemically protected sponges. She then uses the sponge's chemicals for her defense. These substances have been observed to be powerful antifungal agents. Dactylomelin-P isolated from *H. sanguineus* Rüppel & Leuckart, 1828. (Gastropoda: Aplysiidae), inhibited the growth of gram-positive and gram-negative bacteria, including marine species. The research focuses on *Conus* spp., whose venom has protein toxins that selectively block different subtypes of calcium ion channels.[29-31]

The w-conotoxin MVIIA from *Conus magus* Linnaeus,[33] (Neogastropoda: Conidae) from the Pacific Ocean was demonstrated to be a neuroprotective agent in a mouse model of stroke. By preventing the uncontrolled release of potentially toxic levels of excitatory neurotransmitters in the brain after strokes, calcium channel blockers can limit damage to neurons. United States will develop medicines based on omega-conotoxin from *C. magus.* This substance blocks the influx of calcium into neuronal terminals and prevents neurotransmission and pain when applied topically to these locations in the nervous system (Figure 9).[29-33]

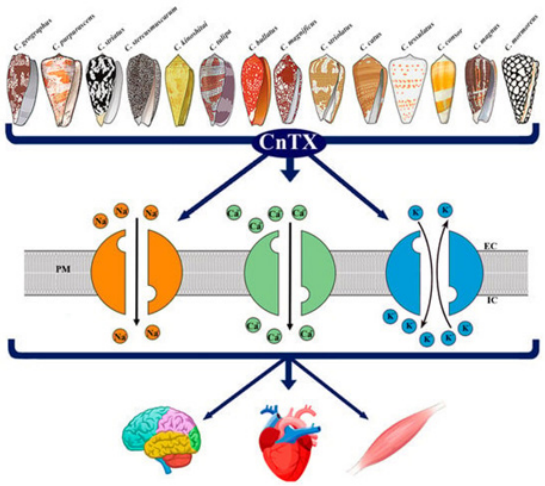

Figure 9 Representative image of CnTX bioactivity via voltage-gated ion channel modulation. *Conus*-derived toxins (CnTX) target numerous and different NaV and/or CaV and/or KV channel subtypes generating ion current fluxes through neurons of central and peripheral nervous systems as well as in heart and skeletal muscle cells. IC = intracellular compartment; EC = extracellular compartment; PM = plasma membrane.

Source: Toxins 2013, 5(2): 286-314; https://doi.org/10.3390/toxins5020286

Hapalochlaena maculosa (Hoyle, 1883)[32] (Cephalopoda: Octopodidae) has a substance that acts as a nerve impulse blocker. Ziconotide, extracted from the toxins of *Conus* spp., is used to treat chronic pain. *Perna canaliculus* (Gmelin, 1791) (Bivalvia: Mytilidae) showed anti-arthritic and anti-inflammatory activity. *Arcanflata* Reeve, 1844, and *Arca granosa* (L.,1758) (Bivalvia: Arcidae), whose shells are used in decoctions in pieces or powder form, showed good clinical results in the treatment of peptic ulcers. *Ostrea rivularis* (Gould, 1861) (Bivalvia: Ostreida: Ostreidae) clinical results in the treatment of ten cases of tuberculosis. hemostatic action of *Sepia esculenta* Hoyle, 1885, natural remedy, and *Sepiella maindroni* Rochebrune, 1884(Sepiida: Sepiidae).[29-32]

A possible weapon against neuropathic pain. History repeats itself: from poison to medicine!

The researchers were able to show the effectiveness of a peptide, derived from a-conotoxin, which can be used orally. They modified the structure of the molecule to make it somehow more solid. The peptide joins the two ends of the protein. Typically, peptides are used as oral medications because they are very unstable and degradable in the digestive system before they have done their job. The fact that the protein is circularized makes it resistant to exopeptidases, but also to endopeptidases thanks to the reinforcement of internal hydrogen bonds.[29-33]

The substance is as effective as the medicine usually administered in cases of severe pain (gabapentin), with just one-hundredth of the usual dose being administered. Its short name, a-conotoxin cVcl.l, should be kept (Researchers at the Institute for Molecular Bioscience, University of Queensland, Australia).[29-33]

The lack of this external protection (shell) led to the evolution of defense mechanisms dominated by the secretion or incorporation of bioactive chemical substances. Many have already been revealed to belong to families of proteins with L-amino acid oxidastic activity (LAAOs). The mechanisms of action of dactylomelin-P, purified antibacterial protein from ink, and the comparison of the protein composition and antimicrobial activities of inks released by two

gastropods. Dactylomelin-P is an L-amino acid oxidase capable of oxidizing L-lysine and L-arginine, with greater affinity for L-arginine. It also demonstrated that its antibacterial activity is measured by this property, with hydrogen peroxide, generated in enzymatic oxidation, having a major role in bacterial and fungal inhibition (Figure 10).[29-42]

Figure 10 Neuropathic pain is also characterized by the dysregulation of certain ion channels, receptors, and processes.

Source: Pharmaceutics 2023, 15(7), 1799; https://doi.org/10.3390/pharmaceutics15071799

Conclusion

This prey may consist of worms, other molluscs, and fish. Snails are a rare cause of poisoning among divers and shell collectors in the Indian and Pacific Oceans. The snail injects its venom through a harpoon-like tooth when handled aggressively. The venom can cause temporary paralysis which, on rare occasions, is fatal. Research with marine animals demonstrated the existence of hemolytic, cytotoxic, neurotoxic, neuromuscular paralyzing, and cardiotoxic activity in the isolated substances

Acknowledgments

None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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