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Article *in* International Journal of Peptide Research and Therapeutics · July 2023

DOI: 10.1007/s10989-023-10557-8

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International Journal of Peptide Research and Therapeutics (2023) 29:83
https://doi.org/10.1007/s10989-023-10557-8

Peptides from Animal Venom and Poisons

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Venoms are not uncommon biochemical weapons that only a few species possess. It is estimated that 220,000 animal species produce venom, corresponding to approximately 15% of all animal species. Animal venom and poisons can be found in almost all habitats that spiders, scorpions, snakes, amphibians, hymenopteran insects, marine invertebrates, anemones, or jellyfishes inhabit. Animal venom and poisons are species-specific biococktails of dozens or even hundreds of bioactive molecules (Oliveira et al. 2022), which have arisen through positive evolutionary processes that enable animals to improve predation efficiency, to defend and deter competitors (Schendel et al. 2019).

Given the extensive range of animal toxins documented in the literature, especially peptides, animal venoms and poisons can be considered as an abundant source of chemical structures for utilization in the development of novel drugs (Morsy et al. 2023). The molecular diversity and medical significance of venom and poisons have long attracted scientific interest, driven both by the toxic mechanisms of envenomation and by their pharmacological potential. These toxins exhibit a wide range of pharmacological activities and have a high degree of diversity (Diniz-Sousa et al. 2023). In fact, they can interact with a multitude of molecular targets, including enzymes, transmembrane receptors, cell membranes, and ion channels, leading to the destabilization of vital physiological systems in victims or prey (Zheng et al. 2023). Consequently, many components of venom exhibit hemotoxic, myotoxic, and/or neurotoxic effects, among others. Numerous toxins isolated from venom have shown significant therapeutic potential, including activities such as antitumor, antimicrobial, anticoagulant, or analgesic effects (Chan et al. 2022). With the refinement of methods for the isolation and characterization of peptides, it is possible to identify pharmacological targets and thus several mechanisms of envenomation at the molecular level (Fig. 1). Advances in venom research are directly related to technological progress in processes and chromatographic materials that have improved venom fractionation techniques, as well as the quantification and structural determination methods, which allow for detailed analyzes of the compositions of toxins and their biochemical properties.

The characterization of peptide toxins has allowed the development of effective drugs that have been approved by regulatory authorities such as the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for clinical use. Such peptides are capable of binding specific cellular and molecular targets in various pathologies (Vyas and Vaidya 2009). Important examples of these are the snake venom peptides that inspired the development of captopril (Capoten®), an antihypertensive drug, and tirofiban (Aggrastat®) and eptifibatide (Integrilin®), which are used to treat coagulopathies (Diniz-Sousa et al. 2023). Furthermore, peptides derived from the venom of bees, snakes, and snails have led to the development of potent analgesics: apitoxin (Apitox®), cobratide (Ketongning®), and ziconotide (Prialt®), respectively. Additionally, peptides found in the saliva of leeches and lizards have been used in the development of bivalirudin (Angiomax®), an anticoagulant, and exenatide (Byetta®), used in the treatment of type 2 diabetes mellitus (Fig. 2) (Oliveira et al. 2022).

Integrated multi-omics technologies have revolutionized how scientists discover toxins present in venoms and generate insights to explore their pharmacological potential (Dalal et al. 2020) (see Fig. 3).

Genomic and transcriptomic techniques enable information to be extracted from DNA and RNA and, through the use of high-throughput DNA and RNA sequencing

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Published online: 28 July 2023

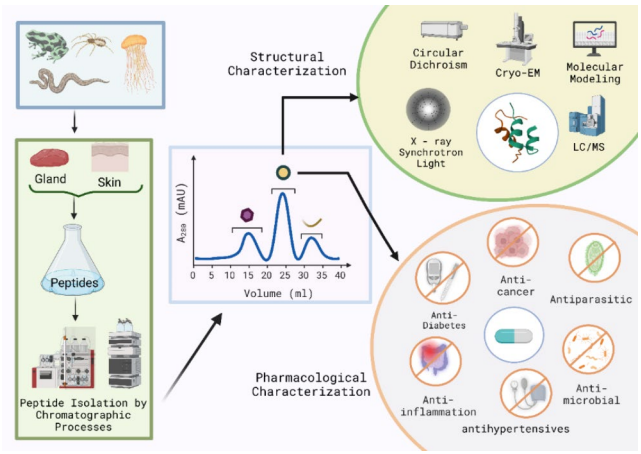

Fig. 1 Traditional strategies for obtaining peptides from glands and animal skins. The peptides are isolated by chromatographic techniques and, subsequently, their structures and pharmacological properties are determined in vitro. Figure created with BioRender.com (2020) (https://app.biorender.com/biorender-templates)

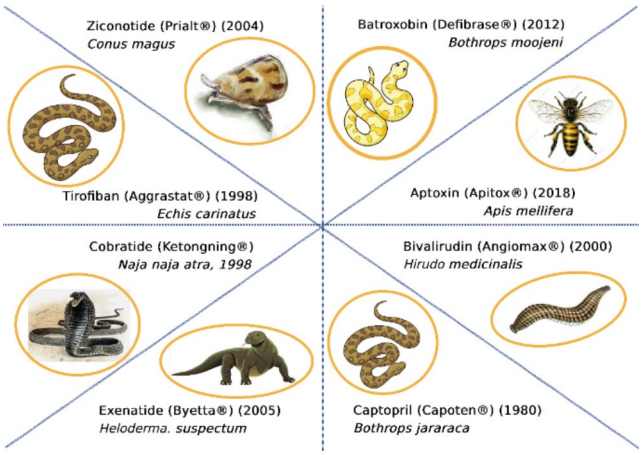

Fig. 2 Some of the drugs that have been developed from animal peptides and approved by the FDA and EMA for clinical use. Figure created with BioRender.com (2020) (https://app.biorender.com/biorender-templates)

technologies, functional genetic information can be determined (Banshidhar et al. 2023). This information is translated in the cell into peptides, functional proteins, enzymes, and other molecules. Proteomics employs sensitive methods to identify specific proteins within complex venom cocktails. In the case of enzymes, metabolites are formed during their catalytic activity, as intermediate or even final cell products. Metabolomics detects their role as fuel, signaling, stimulatory, or inhibitory molecules. The integration of traditional methodologies, computational methods, and "*omics*" techniques modernized the techniques and strategies for drug discovery, accelerating the process of finding novel prototypes derived from peptide toxins found in animal venom (Silva and Antunes 2023). However, experts unanimously agree that our knowledge of biodiversity, especially in relation to animal venom, remains limited. The rapid growth of human populations and environmental changes have played an important role in the extinction of many venomous species. Consequently, we are losing a vast amount of chemical information that could potentially lead to the development of drugs for treating various diseases that affect humanity (Guimaraes et al. 2014).

Although venoms serve as important sources of bioactive peptides for the inspiration and synthesis of new leading molecules with pharmacological activity, it is important to note that they are inherently toxic substances. To use them as pharmaceuticals, their structures must undergo chemical modifications to mitigate toxic effects and enhance stability and bioavailability. The process of developing new drugs from toxins is complex and requires significant investment in terms of time and money, without guaranteeing success, especially during clinical phases II and III.

This collection demonstrates how venom peptides interact specifically in our cellular components, with very precise effects, and why they are a vast source of inspiration for potential new drugs that target high-incidence diseases, such as cancer and neurological pathologies, for which the efficiency of existing drugs continues to be limited.

To address this pressing issue, the primary objective of the collection "Peptides from Animal Venoms and Poisons" in the International Journal of Peptide Research and Therapeutics (IJPRT) (https://link.springer.com/collections/fgiaadjagh) is to compile a wide range of articles focusing on the exploration of peptides with pharmacological potential.

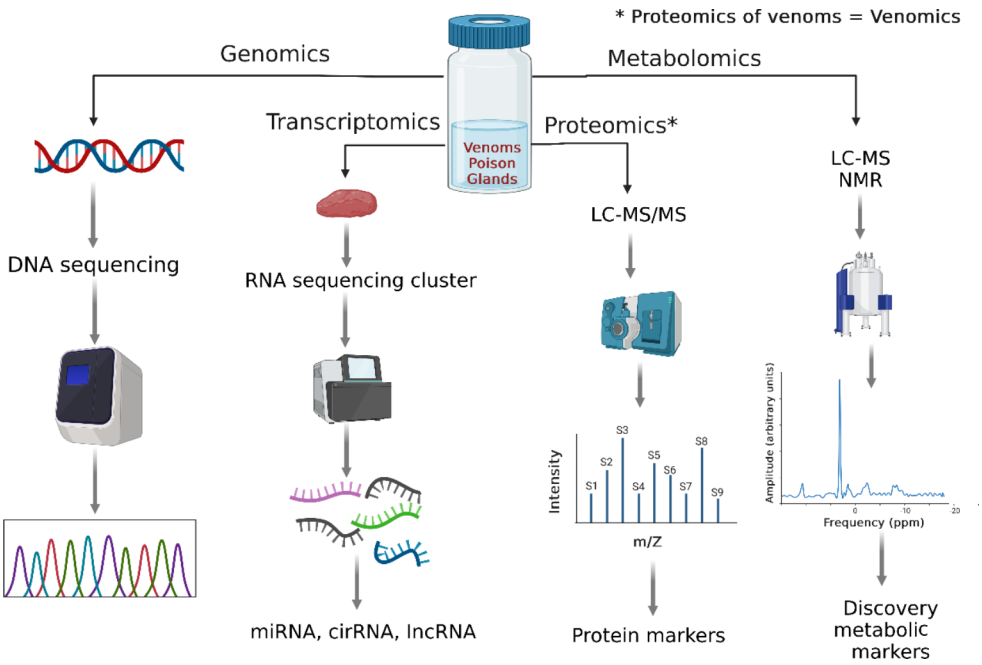

Fig. 3 Representative scheme of the *"omics"* processes: Genomics, Transcriptomics, Proteomics, and Metabolomics. Figure created with BioRender.com (2020) (https://app.biorender.com/biorender-templates)

References

Banshidhar; Pandey S, Singh A et al (2023) The potentialities of omics resources for millet improvement. Funct Integr Genomics 23(3). https://doi.org/10.1007/s10142-023-01149-2

Chan YW, Tan KY, Tan CH (2022) Preclinical assessment of VPEAV, a new trivalent antivenom for elapid snakebite envenoming in the Philippines: proteomics, immunoreactivity and toxicity neutralization. Toxicon 220:106942. https://doi.org/10.1016/j.toxicon.2022.106942

Dalal N, Jalandra R, Sharma M et al (2020) Omics technologies for improved diagnosis and treatment of colorectal cancer: technical advancement and major perspectives. Biomed Pharmacother 131(110648). https://doi.org/10.1016/j.biopha.2020.110648

Diniz-Sousa R, Caldeira C, Pereira SS et al (2023) Therapeutic applications of snake venoms: an invaluable potential of new drug candidates. Int J Biol Macromol 238(124357). https://doi.org/10.1016/j.ijbiomac.2023.124357

Guimaraes CL, Moreira-Dill LS, Fernandes RS et al (2014) Biodiversity as a source of bioactive compounds against snakebites. Curr Med Chem 21(25):2952–2979. https://doi.org/10.2174/09298673113206660295

Morsy MA, Gupta S, Dora CP et al (2023) Venoms classification and therapeutic uses: a narrative review. Eur Rev Med Pharmacol Sci 27(4):1633–1653. https://doi.org/10.26355/eurrev_202302_31408

Oliveira AL, Viegas MF, da Silva SL et al (2022) The chemistry of snake venom and its medicinal potential. Nat Reviews Chem. https://doi.org/10.1038/s41570-022-00393-7

Schendel V, Rash LD, Jenner RA, Undheim EAB (2019) The diversity of venom: the importance of behavior and venom system morphology in understanding its ecology and evolution. Toxins (Basel) 11(11). https://doi.org/10.3390/toxins11110666

Silva L, Antunes A (2023) Omics and remote homology integration to decipher protein functionality. Methods Mol Biol 2627:61–81. https://doi.org/10.1007/978-1-0716-2974-1_4

Vyas SP, Vaidya B (2009) Targeted delivery of thrombolytic agents: role of integrin receptors. Expert Opin Drug Deliv 6(5):499–508. https://doi.org/10.1517/17425240902878002

Zheng H, Wang J, Fan H et al (2023) Comparative venom Multiomics reveal the Molecular Mechanisms driving adaptation to Diverse Predator-Prey Ecosystems in closely related Sea Snakes. Mol Biol Evol 40(6). https://doi.org/10.1093/molbev/msad125