

The New Snake Oil – How Venomous Animals Could Save Lives

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What is venom? According to Dictionary.com, venom is defined as, “the poisonous fluid that some animals, as certain snakes and spiders, secrete and introduce into the bodies of their victims by biting, stinging, etc.” In short, the difference between poison and venom is the method of introduction to the victim, as venom (in nature) is always injected into the victim, usually through a fang, stinger, or other form of spike. However, venom harvested from venomous animals can be used in the medical field. There are many uses for the diverse forms of venom, especially snake venom, cone snail venom, toad venom, and arthropod venom.

Snakes are one of the most well-known and diverse potentially venomous animals in the world. Snakes mainly use their venom, injected through their fangs, to immobilize prey when hunting or to ward off and fight against potential predators. Snake venom is cocktails of roughly four dozen proteins and compounds, specially mixed to deal damage and cause local and systematic malfunction in cells and organs, even in small doses (microliters). There are hundreds of combinations of these proteins and compounds, making each venom type highly specialized in its effects and what it targets within the victim’s body. When attempting to convert snake venom into a state that can be used medicinally, one needs to: isolate and characterize an individual toxin, unravel its molecular structure, disclose its molecular mechanism, including the identification of the target molecule, and decipher its effects at the level of cells, organs and the entire organism. The proteins combinations within snake venom can be classified and sorted into three main categories: structure, function, and abundance. Over two dozen structures of snake venom protein combinations have been observed. Snake venom can affect numerous parts and processes in the body, such as hemostasis (blood stalling/coagulation), thrombus formation

(blood clots), blood pressure regulation, and more. Therefore, different kinds of venom can be categorized by what they negatively impact within the body. Finally, mass spectrometry-based proteomic studies and transcriptional analyses of venom glands have led to a better understanding of the diverse abundances of venom, which has been labeled venomics.

One of the major medical applications of snake venom is in the use of countering blood clots, due to venom's interaction with platelets. One of the contributing factors in a blood clot is the body's platelets moving towards and bonding with many complexes and compounds, obstructing blood flow. Medicines that counter blood clots, such as aspirin, have several side effects that can have negative effects on the body. One way to counter blood clots without the traditional negative side effects is by using snake venom as a treatment option, preventing the platelets from bonding without the existing side effects other medicines cause. Two snake venom protein families, CLRPs and disintegrins, activate or inhibit the adhesion receptors in the platelets, preventing them from unnecessarily bonding and obstructing blood flow. Snake venom also has been used as a blood coagulant, anti-coagulant, and pseudo-coagulant, depending on which combination of proteins the venom has. One successful snake venom-derived drug, captopril, is an angiotensin-converting enzyme (ACE) inhibitor used to treat high blood pressure, heart failure, and kidney problems caused by diabetes, and to reduce the risk of death after a heart attack.

Snake venom's most-promising feat is its potential in cancer treatment. It is reportedly quite easy to kill cancer cells with many snake venoms, the ones geared to kill cells at least. The issue, however, is that these venoms are also effective at killing properly functioning cells and are not properly able to distinguish between healthy and malignant cells. Due to this difficult and deadly risk, snake venom in cancer treatment has not been tested much and is slow to get any

approval on medication from the FDA. Snake venom is also able to slow and stall tumor growth and cancer spreading by blocking signals necessary for the spread of cancer. This, in theory, can give medical professionals extra time to find where in the body the tumor is without having to deal with the spread of cancer throughout the body. More testing has been done with venoms that inhibit cancer cell growth than with venoms that kill cells outright.

Another source of venom comes from a lesser-known animal, the deadly cone snail. Cone snail venom is ancient, fast-acting, and potentially lethal. Smaller varieties of cone snail's venom equate to that of a bee sting, but the stinger (tooth) on large cone snails can kill a grown man in 24 hours. Cone snail venom, especially the purple cone snail, is known for its ability to paralyze victims, and paralyze them quickly. However, some purple cone snails do not appear toxic whenever they sting someone, as if they are not in the stage of their life where they're at their most venomous, based on age or some similar factor. Due to their immobilizing abilities, variance in potency, and targeting of the nervous system, cone snail venom is a potential way to counter many medical conditions. Due to the speed at which it circulates through the body, some suggest using cone snail venom as a base for insulin introduction/circulation in diabetic patients, or for Alzheimer's treatment. Some see potential in the venom to curtail cancer in early stages, while others theorize it could be used on the brain to battle addiction. Currently on the market, it is used as an anti-inflammatory in anti-wrinkle creams. Other research uses snail venom to learn about the overlap of nervous and immune system processes and cells and turn that research into the development of a non-venom-based treatment for several types of cancer. Through tests on the brains of flies, research have also seen potential in cone snail venom in addiction treatment and Parkinson's disease treatment, due to the venom's interaction with the parts of the brain that control addiction and muscle control.

Another ancient toxin can be found in that of Chinese toads, specifically the Bufonidae family of toads. For generations, the toxin of these toads has been used (primarily in China) as a superficial anesthetic, anodyne, antimicrobial, and cardiogenic. In more modern times, there is some use of it in treating tumors and cancer, as with other venoms. The toad's toxin is different from other animals, as it is collected through their skin, and used in a relatively raw state. Due to this, overdosing on the toxin is quite possible, causing nausea, vomiting, diarrhea, paralysis, or even death. Work is still being done on toad venom, testing its properties and makeup, and how its effects on the body can differ when stimuli (such as temperature or different chemical compounds) are applied to the toxin.

A diverse number of venomous animals fall under the category of "arthropod". This includes arachnids, like scorpions and spiders; insects, like wasps and ants; and crustaceans, like lobsters and crabs. There is only one living venomous crustacean, however, as most are non-venomous, except for the remipede *Speleonectes tulumensis*. This creature resembles a centipede and has venom that is reminiscent of the venom of a spider. Within many creatures, arthropods or otherwise, hyaluronidases can be found. Hyaluronidases are chemical catalysts found in soft connective tissues of many animals. However, a variant of hyaluronidase can be found in the venom of venomous animals as well, especially arthropods. This form of hyaluronidase has been taken from arthropods and used for multiple medical purposes and tests, when combined with drugs and medication. The combination increases the absorption rate and dispersion throughout the body of the drug, reduces swelling, reduces localized side effects, and promotes skin healing. Hyaluronidase in scorpions is difficult to isolate, but present. Its potency and condition are affected by the diet and lifestyle of the scorpion, but not directly by region. Venom hyaluronidase from spiders can be found in many spiders and shares many properties

with the already commonly used testicular hyaluronidase found in mammals. Spider hyaluronidase works especially well in catalyzing reactions with hyaluronan (the main acid hyaluronidase is involved with) but struggles with chondroitin sulfate A and has an almost absence of activity upon chondroitin sulfates B and C. Limited research has been done on centipede venom's hyaluronidase. Caterpillars and butterflies have very diverse hyaluronidase, leading to diverse effects. The hyaluronidase in social insects, such as bees, wasps, and ants, is what causes the main allergen response that humans have to bee stings. A better understanding of this hyaluronidase allows for a better understanding of how and why allergic responses are triggered, and how to counter them better.

Venom manages to succeed as a deadly weapon for highly evolved and specialized predators, a tool for scientific growth to better the world, and a cure for some of the toughest diseases and medical conditions. As the possible best option for battling cancer, a diverse list of catalysts, coagulants, and supportive compounds, a key to understanding allergens, and a potential counter for Parkinson's and other debilitating conditions, venom stands as the most high-risk and high-reward field of medical science out there. The animals are dangerous, and the venom is even more dangerous. However, the chance that a rattlesnake's venom could bring an end to breast cancer is a risk many scientists are willing to take.

Works Cited

- Balsam, J. (2018, December 6). He Saved the Largest Venomous Snake in the Americas. Now, He Hopes It Could Save Human Lives. Retrieved from <https://time.com/longform/snake-venom-cancer-research/>
- Bordon, K. C. F., Wiesel, G. A., Amorim, F. G., & Arantes, E. C. (2015). Arthropod venom Hyaluronidases: biochemical properties and potential applications in medicine and biotechnology. *Journal of Venomous Animals and Toxins Including Tropical Diseases*, 21(1).doi: 10.1186/s40409-015-0042-7
- Estevão-Costa, M.-I., Sanz-Soler, R., Johanningmeier, B., & Eble, J. A. (2018). Snake venom components in medicine: From the symbolic rod of Asclepius to tangible medical research and application. *The International Journal of Biochemistry & Cell Biology*, 104, 94–113. doi: 10.1016/j.biocel.2018.09.011
- Soniak, M. (2014, January 8). Meet the World's Only Known Venomous Crustacean. Retrieved from <https://www.mentalfloss.com/article/54168/meet-worlds-only-known-venomous-crustacean>
- Swenson. (2020, February 10). How the Cone Snail's Deadly Venom Can Help Us Build Better Medicines. Retrieved from <https://www.nist.gov/news-events/news/2017/10/how-cone-snails-deadly-venom-can-help-us-build-better-medicines>
- Venom. (2011). Retrieved from <https://www.dictionary.com/browse/venom>
- Xingping, L., Zongde, Z., Yanfang, Z., Liren, C., & Yongmin, L. (2006). Microemulsion electrokinetic chromatographic determination of bufadienolides in toad venom

and in traditional Chinese medicine. *Analytical and Bioanalytical Chemistry*, 384(5), 1254–1258. doi: 10.1007/s00216-005-0251-y