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**Research Paper**

# Evolutionary Context of Venom in Animals

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## *Abstract*

*Venom is a biological substance produced by an organism that contains molecules ("toxins") which interfere with physiological or biochemical processes in another organism, which has evolved in the venomous organism to provide a benefit to itself once introduced to the other organism. The venom is produced and/or stored in a specialized structure and actively transferred to another organism through an injury by means of a specialized delivery system (Arbuckle, 2017a)*

*This paper aims to provide an overview of the diversity of venom and and also a set of evolutionary principles which are particularly applicable here. There has been substantial variation in the definition of "venom" and "venomous" in the literature, so this is discussed first with the aim of giving a definition which encompasses a number of important features of venoms. Toxins are essential components in the prey and defense system of different animals ranging from microbes (prokaryotes) to unicellular eukaryotes(protozoans) to multicellular eukaryotes. The orphan toxin OrtT of E.coli reduces growth during stringent reactions.*
*(Islam et al., 2015)*
*The cytotoxicity of fresh water ciliated protozoan is because of natural toxin* ***Climacostol.*** *Polyketides is highly diverse group of toxins in dinoflagellates and possess biological activities like haemolysis, mycotoxicity and cytotoxicity Protists produce secondary metabolites that play a role in antipredation and alleleopathy****.*** ***Opistoporins*** *are pore-forming peptides in spiders, parabutoporin, acysteine free pore forming peptide are found in the venom of scorpions. Beetles (Dysticidae) use potent paralytic venoms to quickly incapacitate prey in their aquatic environment.Xibalbanustulumensis is the only crustacean known to produce neurotoxic venom*
*In gastropods, Genus Conus is well studied and the venom produced by them is called* ***conotoxin****, containing hundreds of small cysteine rich peptides. In cephalopods, the toxicity of venom is attributed to biogenic amines, including tyramine, histamine, acetylcholine, octopamine, and serotonin. The evolution of venom delivery system in extant reptiles is seen in two lineage the advanced snakes and the helodermatid lizards (gila monsters and beaded lizards). The snake venom leads to different type of toxicity including neurotoxicity, cytotoxicity or nephrotoxicity. The venom in lizards of genus Heloderma is a mixture of saliva and venom which is toxic. Most of the amphibian species produces toxins in granular gland of their skin. The defence-evoked venom contains paralytic toxins.*

***Keywords***
*Diversity; Ecology; Function; Terminology; Variation*

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## I. Introduction

Throughout history, venomous creatures have intrigued and frightened humans, likely since the earliest days of our existence. Scientists have extensively researched these creatures over the past few centuries. Often the words- toxin, venom and poison are interchangeably used, but there is a fine distinction among them. Venomous organisms, use the toxic secretion primarily for predation (or attack), but can also use it in case they are attacked (even if inadvertently), characterizing an active defense. Differently, poisonous organisms, most times, make use of their toxins only for defense (against predators and, in some cases, also against microorganisms).(Jared et al., 2021)

The phylogenetic relationship between different venoms and animals possessing those venoms is understudied, but these are necessary to understand the selection pressures and therefore drivers of venom evolution. Therefore, this article aims to provide a review of the diversity of, and the principles fundamental to the evolution of venoms.

## Etymology of Venom

In ancient the perception of venom by Egyptian and Mesopotamian ismalevolent demons(Weinstein, 2015),rejuvenation concept was also found in Gilgamesh epic (2100BCE).As Shedding of skin considered as rebirth.In the mid thirteenth century the term 'venom' was introduced and was derived from a Latin word **venimen** meaning vulgar and this. The word venenum is used because it rushes in the veins (vena).

"Toxic" originated in the 1660s from the French word "toxique" and ultimately derived from the Latin word "toxicus," meaning "poisoned." The Latin word "toxicum" means "poison" and comes from the Greek "toxikon (pharmakon)," which translates to "poison for use on arrows." The Greek word "toxikon" is a neuter form of "toxikos," which pertains to arrows or archery and is related to the word "toxon," meaning "bow." The word "toxon" likely has its roots in a Scythian term that also made its way into Latin as "taxus," meaning "yew." According to linguist Watkins, the Iranian word "taxša," meaning "bow," may also be a possible source, originating from the Proto-Indo-European root "*tekw-," meaning "to run, flee." "Toxic" became a noun in 1890 and "toxic waste," referring to either "toxin" or "chemical or radioactive waste," dates back to 1888 in medicine

## Evolution of Venom

As briefly touched on in the preceding section , venoms are often considered to function in predation or defense (Edström, 1992a), with some literature giving additional mention to the use of venom in competition (Casewell et al., 2013a)). However, the true diversity of venom functions is broad but somewhat masked by such short and simple statements. This is not surprising because venom, as defined above, should provide many different potential benefits, and the evolution of diverse animal ecologies opens the door for a wide range of venom functions. Consequently, this section will highlight the diversity of venom functions found in animals as this directly relates to the selection pressures driving the evolution of venoms.

One key point to bear in mind is that different animals use venom for different purposes and one animal can also use certain venom for different purposes. For instance, evolution of snake venoms is primarily driven by their use in predationWüster, 2009) , but that does not prevent their use as a very effective antipredator defense often with devastating consequences for the person or other animal bitten ((Boyer et al., 2015);(Mackessy, 1988a);(Mackessy, n.d.). In addition to this example of co-opting venom for another purpose than its main driver, some animals have specifically evolved a "dual-purpose" venom systems which include separate predatory and defensive components, such as cone snails (Dutertre et al., 2014a) and scorpions (Inceoglu et al., 2003)

## Predation

A predatory function for venom is arguably the most common primary driver of venom evolution (see phylogenetic distribution of venom functions in(Casewell et al., 2013a). It is also the main function of venom in many of the better-known lineages of venomous animals such as snakes, spiders, and mccuescorpions. Nevertheless, there are various ways in which venoms can be used to aid predation.

The most direct is also the most obvious – incapacitating prey to allow the venomous predator to consume it Note that the function here is to incapacitate prey, not necessarily to kill it. Killing prey would usually require more venom than incapacitation, which is unlikely to be favored by evolution since venom is energetically expensive to produce ((McCue, 2006);(Morgenstern & King, 2013)) and incapacitated prey is just as beneficial as killed prey for consumption. That is not to say that killing prey as a standard predatory tactic is not common, in fact many mechanisms for incapacitation may kill with more time, but that killing is not an essential part of predatory venom functions. This is reflected in the toxicological effects of many predatory venoms, which typically cause two main classes of symptoms in prey: interfering with nerve action causing paralysis (and often death later) and altering blood and blood vessels causing blood loss and associated shock. For example, ant-specialist spiders (Zodarion) are capable of predating prey much larger than themselves by using paralyzing venom (Pekár et al., 2014a), without the need to actually kill the prey before consumption. Furthermore,(Fry et al., 2009) demonstrated that the Komodo monitor (Varanus komodoensis) inflicts a deep wound with recurved, serrated teeth and uses its venom to quickly induce loss of consciousness in prey via the onset of shock. The same authors also suggested that the extinct Varanus priscus probably used a similar strategy.

Venom has also been considered to aid in predation after prey consumption by increasing the speed of digestion with proteolytic toxins. This is most commonly discussed in snakes because viper venoms often have relatively high proteolytic activities and because some of the earlier studies demonstrating an effect of venom on digestion were carried out using Crotalusatrox rattlesnakes (Thomas &Pough, 1979). Recent studies, such as(Mccue, 2007), have failed to find an effect on digestion in Crotalusatrox, which has been used to call into question whether increased digestive performance can be a function of venom. However, (Mccue, 2007) conducted experiments at higher temperatures (25–30 C) that did not produce a large effect in(Thomas &Pough, 1979) – the latter authors found that venom was more important in digestion at lower temperatures (15 C). This, combined with some evidence of improved digestive efficiency conferred by the venom of some other species, such as Andrallusspinidens bugs (Zibaee et al., 2012), suggests that such a function cannot be completely discounted in studied taxa and is certainly a plausible function that has not been well studied in most venomous animals.

Finally, parasitism represents another predatory (in the broad sense) function of venoms in some Blood-feeding parasites such as ticks and vampire bats often produce anticoagulant venoms that facilitate prolonged feeding by maintaining a constant flow of blood, alongside other actions

(Cabezas-Cruz & Valdés, 2014a)In addition, parasitoids present an interesting situation wherein the predation is not by the organism that injected the venom but by its offspring at a later date. In Asobara parasitoid wasps, the venom acts to paralyze the host during egg laying by the wasp before killing it at a later date ((Moreau et al., 2009) – ensuring a stationary and storable food source for the larvae when they hatch. More detailed transcriptomic work on the parasitoid wasp ***Nasoniavitripennis*** has revealed that the venom of this species induces a variety of changes to gene expression in the host(Martinson et al., 2014). The venom of this wasp causes the host to enter developmental arrest and also upregulates certain antimicrobial peptides that likely help to prevent spoilage of the (live but immobile) host until the larvae hatch out and consume the host.

## Defense

Aside from predation, defense is the most common primary function for venoms, especially antipredator defense. Furthermore, as alluded to earlier in the context of venomous snakes envenomating potential predators, many (probably most) venomous species will use their venom in a defensive role even if the main role is, for example, predation. However, several groups of animals, such as bees and sea urchins, use venom primarily for defense, and many others (such as spitting cobras) regularly use venom for both defense and another function. In spite of this variation in functional importance, there are some generalities that can be made for defensive venoms when compared to predatory or other venoms.

Firstly, defensive venoms tend to be simpler in composition than predatory venoms (Casewell et al., 2013b), likely because the latter are involved in more intense arms races which generates selection for diverse and fast-evolving venoms (see later section on "(Arbuckle, 2017b)**.** Secondly, defensive venoms are more likely to have evolved to be effective at a distance, such as spitting cobras or spraying behavior of certain scorpions ((Nisani& Hayes, 2015)**.** This enables the venomous animal to defend itself while keeping away from the predator but requires chemical components which can penetrate external surfaces (mostly eyes or mucous membranes). Thirdly, defensive venoms are likely to contain toxins which interfere with fast-acting physiological processes such as nerve transmission – because lengthy delay in actions can give the predator enough time to kill the animal before the venom takes effect. Consequently, many defensive venoms contain toxins which act to cause paralysis quickly by blocking neuromuscular receptors or to target pain receptors to cause instant and intense **pain** (Bohlen et al., 2011)(Dutertre et al., 2014a); (Inceoglu et al., 2003); (Siemens et al., 2006)

Although antipredator defense is particularly well studied (and probably more important), some venoms are also known or suspected to contribute toward immune and antiparasite defense. For instance, in some social hymenopterans, the venom is spread over the cuticle of other individuals and the nest combs, and appears to reduce the prevalence of infections viaantimicrobial venom components (Baracchi et al., 2011). In others, they actively apply venom to fungus-infected groupmates which helps eliminate the fungus (Tragust et al., 2013)**.** Similarly, (Grow et al., 2015) have shown that the venom of slow loris species (Nycticebus) is effective in killing arthropods that are similar to those which parasitize them, and that lorises anoint themselves with the venom. However, it is difficult to know to what extent the venom is transferred to the microbes or parasites per se, and therefore it is debatable whether such uses would be considered as those of venom (even if the same secretions function as a typical venom in other circumstances). The alternative is to consider the same substance both as a venom and as a contact poison, depending on the use at any one time.

## Intraspecific Competition

Few venoms seem to have a prominent function in intraspecific competitive interactions, but this is known in a few mammal species, namely the platypus (Ornithorhynchusanatinus) and slow loeisspecies (Nycticebus). It is notable that both of these groups also use their venom in defense and possibly other functions but that they nevertheless use venom to a large extent for competition.

Echidnas (Tachyglossus and Zaglossus) were once thought to also be venomous and indeed possess similar glands to the platypus, but their "venom" system is highly degenerate and the secretions now seem to function in scent communication during the breeding season rather than as venom (Wong et al., 2013). Slow loris venom appears to also be used in intraspecific competition based on the frequency, patterns, and consequences of bite wounds on wild lorises as well as observations in captivity though this is less well studied than in the platypus.

## Reproduction

A potentially unique venom function is found in scorpions of the genusHadogenes. These species are extremely reluctant to use venom in either predation (relying on their pedipalps) or defense, but during courtship males will sting females in the side, which seems to produce sedative and perhaps aphrodisiac effects. Other scorpions have occasionally been seen stinging during courts hip, but similar behavioral responses are not observed, and Hadogenes also possess marked sexual dimorphism wherein males have much longer tails which facilitates this behavior. Therefore, Hadogenes represents an interesting genus for studies of sexual selection (including sexual dimorphism of venom apparatus), toxin evolution, and potentially a source of new pharmaceutical drugs given that the unique function may be associated with unique toxins. However, the venom of the genus has been extremely understudied and almost nothing is known about the details.

## Taxonomic Distribution of Venomous Animals

Venom is a trait which has evolved multiple times across the animal tree of life (Fig 1) , a testament to the myriad benifits it confers and corresponding selection pressure to originate and maintain venom systems across diverse groups of animals (Fig. 2). It should be noted that Fig. 1 is a substantial underestimate of the number of times venom has evolved in animals as it only represents broad taxonomic groups, within which venom may have evolved more than once. It is also likely that future research will uncover more

**Fig. 2 Examples of venomous animals. From left to right in each row: young huntsman spider (Heteropoda sp.), blue leg centipede (Scolopendra mirabilis), adder (Viperaberus) (row 1); unidentified**

**squid from Thailand, flat rock scorpion (Hadogenes troglodytes) (row 2); nursery web spider (Pisaura mirabilis), unidentified tick from Uganda, assassin bug nymph (Rhynocoris sp.) (row 3); stony coral (Favia sp.), cuttlefish (Sepia officinalis), unidentified wasp from Uganda (row 4); leaf-cutter ant (Atta cephalotes), beadlet anemone (Actinia sp.), Komodo monitor (Varanus komodoensis) (row 5).**
**(All photos by the author)**

groups of venomous animals because many groups are understudied and research effort is directed toward medically relevant species rather than an objective survey of animal life.

Although the focus of this chapter is on venomous animals, it is noteworthy that venom is not restricted to animals. Other groups of organisms more commonly use other forms of chemical defenses, but venom is used by taxa as diverse as plants and bacteria. For instance, plants in the family Urticaceae have stinging hairs which pierce the skin of mammals and inject pain-inducing venom which deters herbivores (Iwamoto et al., 2014). In the case of the stinging tree (Dendrocnide spp.), the pain has reported to be excruciating and has caused deaths of domestic animals and humans (Hurley, 2000). One species of bacteria, Photorhabdusluminescens, has so far been reported to have a toxin delivery system which would qualify it as truly venomous, although the diversity of bacteria and the lack of detailed study of most mean that it is likely that more examples will be revealed in the future. In P. luminescens, a "syringe protein" penetrates the cells of an insect host and transfers a toxin molecule through the pore of the "syringe" into the insect cells (Gatsogiannis et al., 2013).

**EVOLUTIONARY TREE OF VENOMOUS ANIMALS**

**Protists:** Dinoflagellates, despite being weak competitors in their ecosystems, can cause Harmful Algal Blooms (HABs). Karlodiniumveneficum, a type of dinoflagellate, produces karlotoxins that restrict the growth of other plankton in the area and prevent potential prey species from moving away.(Adolf et al., 2007)

Karenia brevis produces brevetoxins, which impact the behavior of grazers and help dinoflagellates survive.(Waggett et al., 2008)

### Cnidarians

Cnidarians, such as jellyfish, corals, and sea anemones, utilize venom for either defense or predation.(Fig. 2). This venom is produced in specialized cellular structures called nematocysts, which are equipped with a harpoon-like apparatus that can be quickly triggered upon contact and injected into prey or predators (Fautin, 2009).Within the venom of cnidarians are various neurotoxins that can induce pain and lead to swift death from respiratory paralysis .(Edström, 1992b)While most lethal envenomations from cnidarians occur in their prey, some species are also capable of causing harm to humans and other predators. Particularly intriguing is the ability of certain cnidarian predators, like nudibranch mollusks, to extract nematocysts from consumed cnidarians without triggering their discharge. These predators can then use the "stolen" venom system for their own protection by transporting the nematocysts to their own skin surface.(Greenwood, 2009)).

### Annelids

Out of the three major groups of annelid worms, only oligochaete worms (such as earthworms) lack venomous species. In contrast, blood-feeding leeches possess venom that shares functional similarities with that of other parasitic creatures. This venom contains toxins that impede blood clotting, ensuring a continuous flow of blood for extended feeding periods. The venom also suppresses pain, inflammation, and other immune responses in the host, making it difficult for the leech to be detected and removed before feeding is complete. (Hildebrandt & Lemke, 2011)

Polychaete worms, the third major group of annelids, have developed a variety of venom systems, indicating the evolution of venom in multiple lineages. Among these, bloodworms (Glycera spp.) have been extensively studied. These worms prey on other invertebrates and utilize neurotoxic venom , delivered through their jaws, to rapidly immobilize their prey . The venom can also cause a painful bite when used in self -defense (Edström, 1992a). The bite of other polychaetes, including the group referred to as "scale worms," is believed to be venomous, but knowledge of these species is limited(von Reumont et al., 2014). Apart from the polychaete species that utilize venom through their mouthparts, some, like the Amphinomida or bristle worms, have developed a venom delivery mechanism through fragile spines (modified chaetae). These spines function as a defensive apparatus that breaks off when touched, creating a wound for venom injection (von Reumont et al., 2014).The feeding habits of this worm group are centered around consuming slow-moving or sessile prey. The location and mechanism of venom delivery, combined with this feeding strategy, limit the advantages of the venom to anti-predator defense.

### Molluscs

Venom is primarily found in two of the major mollusk groups: gastropods and cephalopods (Fig. 2). Nonetheless, as mentioned in the "Cnidarians" subsection, nudibranch mollusks can repurpose the nematocysts of cnidarian prey by transferring them to their own surface for use in defense. This is an extraordinary means of sequestering chemical defenses, which typically involves extracting specific toxins or their precursors from the diet. In this case, however, the entire venom apparatus is sequestered.

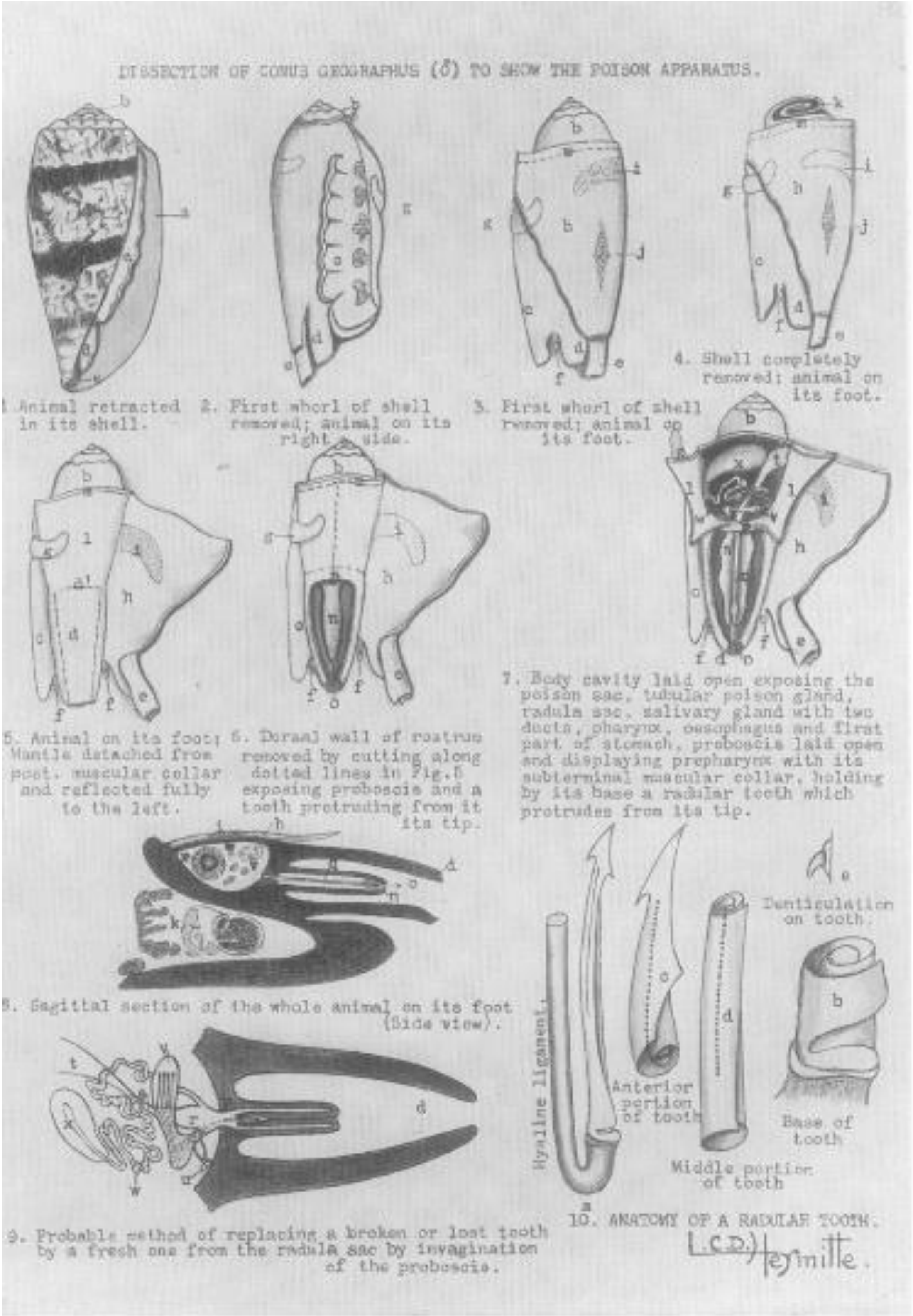
Marine gastropods, including snails, use venom primarily for predation by injecting it through a barbed “tooth” called the radula. The venom is also employed for defense, and in some species of cone snails (Conus spp.), it can cause fatal envenomation in humans and other predators. While numerous marine gastropods possess venom , the venom system of cone snails is the most extensively studied and has generated a considerable body of literature (Edström, 1992c)**;**(von Reumont et al., 2014). The venom of Conus spp. consists of potent neurotoxins that quickly immobilize fast-moving prey, like fish, through respiratory paralysis. This is particularly beneficial for slow-moving predators like snails, allowing them to access otherwise inaccessible prey. Additionally, the Conus have a venom system that serves both predation and defense, suggesting that it has undergone strong selection pressure for both functions(Dutertre et al., 2014b).A recent suggestion proposes that venom in the Conus genus first evolved in species that feed on worms as a means of defense against predatory fish, and later facilitated the transition to hunting mollusks and fish using venom for predation. However, it is uncertain whether this pattern also applies to other gastropods that possess venom(Dutertre et al., 2014b).

While the venom of certain cephalopods is also employed for defense, its primary role is in predation, with the toxins capable of inducing paralysis in prey species like crabs.(Cornet et al., 2014)The potential digestive role of venom in some species, including Octopus vulgaris , is supported by circumstantial evidence(Edström, 1992d) . The venom of blue-ringed octopuses (Hapalochlaena) contains various components, including tetrodotoxin, and they are well-known for their ability to kill humans, making them one of the few cephalopods with this capability.

### Mechanism of venom production in Molluscs

The genus Conus has been extensively studied to understand venom production. The venom is delivered through a sharp, needle-like structure called radular teeth, which are present on a retractile proboscis inside the rostrum. The prepharynx wall contracts strongly to assist the hollow tooth in injecting the venom. The radula sac is arch-shaped with two arms of unequal length, and the radular teeth are attached to it by a hyaline ligament. The teeth are spear-like, covered in spirally coiled chitin, with a barb on one side, a blade on the other, and thin hooked denticulations on half of its surface. The tooth in the radula sac cannot be used for venom injection; it must be brought to the prepharynx by breaking the hyaline ligament and anchored to the prepharynx's surface by a muscular collar. Once anchored, the tooth can tear the prey's outer layer and inject venom. The venom is stored in the poison sac, connected to a highly coiled tube, the tubular poison gland, which occupies the space of the body cavity behind the radula sac. The poison sac serves as the storage and propulsive organ, while the venom is secreted by the poison duct.(Hermitte, 1946; Prashanth et al., 2017)

The venom gland in Conus exhibits compartmentalization in order to produce peptides for both defensive and predatory purposes. The region of the gland situated near the proboscis produces venom for predation, whereas the portion near the venom duct is responsible for producing venom for defense. The composition of the peptides in the predatory and defensive venom differs(Prashanth et al., 2017).



**Centipedes**

Over 400 million years ago, the first pair of walking legs in centipedes underwent modifications to serve as pincers for injecting venom, which is a unique mechanism among venomous animals.(Dugon& Arthur, 2012) (Fig. 2). In essence, centipedes use their venomous pincers for defense rather than biting. The venom is primarily used for predation, and its evolution is likely driven by this role.(Yang et al., 2012). A complex mixture of toxins with diverse effects is present in the venom, and the effects of a centipede's pinch can be divided into two phases.(Fry et al., 2013).The venom of centipedes contains a variety of toxins with different effects, but when they pinch their prey, it results in two phases. The first phase is characterized by fast-acting but short-lived toxins that cause immediate pain, hypotension, and partial muscle paralysis. These effects contribute to quickly drive the prey into shock. In the second phase, slower-acting toxins cause pain that spreads from the pinch site, some skeletal muscle breakdown, and ultimately cardiac arrest.

**Crustaceans**

It may come as a surprise that despite the vast diversity of crustaceans, with the exception of insects, only one species has been discovered to possess venom(Von Reumont et al., 2014).The venom is found in the Xibalbanustulumensis, a remipede crustacean that resides in caves, and is composed of a paralyzing neurotoxin along with a plethora of enzymes such as proteinases. Although little is known about this venom to date, it is plausible that it has evolved to facilitate effective predation in an environment where prey has a high chance of escaping if not rapidly subdued. The scarcity of venom in crustaceans may be genuine, and the reasons behind it are still unknown, but (von Reumont et al., 2014)further study is expected to reveal more venomous crustaceans, particularly in parasitic groups.

**Arachnids**

Spiders and scorpions are commonly associated with venomous creatures, as they are among the first animals that come to mind (Fig. 2).However, the scientific literature on the toxicology of their venom has been slower to accumulate compared to their cultural impact.

The venom of Latrodectus was later identified as a-LTX, but it is not just spiders that possess venom. Other arachnids such as mites, ticks (shown in Figure 2), and pseudoscorpions also have venom. While there is limited evidence, it suggests that camel spiders (or solifugids) may also have venom.(von Reumont et al., 2014)Although the intense pain caused by their bites could be an indication of their venomous nature, there is presently insufficient information to conclusively confirm that camel spiders (or solifugids) are venomous.

Studies conducted recently have revealed a significant amount of information regarding the components of spider venom. However, many interpretations and reviews tend to heavily emphasize the medical relevance of spider venom to humans. (e.g., Sannaningaiah et al. 2014). The primary purpose of spider venoms is undoubtedly predation, enabling spiders to capture and consume much larger prey than they could otherwise.(Pekár et al., 2014b)Defensive biting is a common behavior in spiders, but only a small percentage of the approximately 50,000 species of spiders possess venom that can cause significant harm to humans. Notably, even notorious spiders like the widow spiders (Latrodectus) are known to be relatively hesitant to bite defensively.(Nelsen et al., 2014)These observations indicate that spiders mostly utilize their venom for capturing prey rather than as a defensive mechanism, and their venom typically comprises particular neurotoxins that can cause paralysis in insects.(Sannaningaiah et al., 2014)

As mentioned in the "Venom Functions" section earlier, scorpion venom is not as straightforwardly specialized into a single purpose as spider venom. It consists of two distinct components - one for antipredator defense and the other for predation.

Scorpions possess two distinct types of venom: the first type, also known as prevenom, is released initially and has a different appearance compared to the venom that is released afterwards. For example, in Parabuthustransvaalicus, the prevenom is clear, while the secondary venom is milky white.(Inceoglu et al., 2003). The first type of venom is well-suited to cause immediate and intense pain in mammals, serving as a deterrent against predators. On the other hand, the second venom type is better suited for inducing paralysis and death in insects, aiding scorpions in their predatory activities.(Inceoglu et al., 2003)The reason for this may be attributed, at least partially, to the distinct toxins present in scorpion venom that specifically target either mammals or insects(Ochola et al., 2007). Furthermore, it seems that Hadogenes, a genus of scorpions known as flat rock scorpions, has adapted its venom primarily for courtship purposes, which is a potentially distinct function of venom (see the "Reproduction" subsection in the "Venom Functions" section).

Ticks and some mites are parasitic and depend on blood for nutrition. To facilitate feeding, they employ a venom that contains a variety of toxins that interfere with blood clotting and promote blood flow(Andersen, 2010).Ticks possess venomous elements that suppress the immune reaction of their host during feeding, which helps them evade detection(Cabezas-Cruz & Valdés, 2014b).Ticks and mites can cause paralysis in their hosts by means of their venom, which is thought to prevent the host from removing the parasite before it completes its feeding(Cabezas-Cruz & Valdés, 2014b); (Tomalski et al., 1988), Similar to other blood-sucking parasites, the primary role of the venom found in ticks and parasitic mites is to facilitate their feeding behavior.

Pseudoscorpions are among the least studied arachnids that possess venom. Their venom-delivery system is incorporated into their pedipalps, which feature a "venom tooth" at the tip, connected to a duct leading to the venom gland. Due to the limited research on the subject, very little is currently known about the venom of pseudoscorpions. However, it appears to aid in predation and may be a crucial factor that allows them to target relatively large prey. Envenomated insects have been observed to become paralyzed within seconds and die within minutes.(von Reumont et al., 2014)In addition, certain species of pseudoscorpions participate in group hunting of relatively big prey, such as beetles and millipedes. This type of hunting may require multiple individuals to utilize their venom to immobilize the prey effectively.(von Reumont et al., 2014)

**Insects**

Venom is present in various types of insects, serving as a means of predation or defense. Insects such as true bugs, beetles, hymenopterans, lepidopterans, fleas, and flies have venom. In blood-feeding insects like fleas and mosquitoes, the venom includes toxins that prevent blood clotting, ensuring a continuous blood flow while also minimizing inflammatory and other host responses(Andersen, 2010); (Ribeiro et al., 2004). These effects are similar to those observed in other venoms that facilitate feeding in parasitic creatures. As a result, blood-feeding species have undergone significant convergence in this regard(Andersen, 2010)).

Insects possess a wide range of predatory and defensive venoms, which are thoroughly examined in available literature. Venomous predation, apart from blood-sucking flies and fleas, is seen in true bugs, beetles, and hymenopterans(Fig. 2). As mentioned earlier in the "Predation" section of the "Venom Functions" segment, parasitoid wasps employ venom in their predatory behavior. However, various non-parasitic wasps and ants also use venom to immobilize their prey. The majority of ant families use venom, and it is speculated that predation is the primary driving force behind the evolution of venom in ants(Aili et al., 2014).Wasps and ants use their venom to swiftly immobilize and/or kill their prey through the use of paralyzing neurotoxins. Afterward, the food is typically transported back to the nest, where it is consumed in both solitary and social species. However, some solitary ants may choose to feed on the prey at the location where it was found.

Bugs serve as an intriguing instance of venomous insects due to their unique feature of possessing piercing and sucking mouthparts. (Fig. 2).

As a result of possessing piercing and sucking mouthparts, carnivorous (or blood-feeding) bugs are ideal candidates for utilizing venom as their mouthparts are structurally suited for venom delivery. Additionally, the requirement to consume liquid food mandates that bugs liquefy their insect (or, in some cases, vertebrate) prey before ingestion. Consequently, numerous bug venoms contain paralytic or immobilizing toxins in addition to digestive components.(Zibaee et al., 2012)

Despite the considerable diversity of beetles, which possess an extensive array of chemical defenses and a few venomous species, venom use in this group appears to be either infrequent or insufficiently researched. Nonetheless, some groups, like the predaceous diving beetles (Dysticidae), utilize potent paralyzing venoms to promptly subdue prey in their aquatic habitat, which can include sizeable prey like fish and amphibians(Formanowicz, 1982). Beetles with venomous properties also exhibit a range of venom delivery systems, which may involve the mandibles or other atypical mechanisms. For example, the long-horned beetle species Onychocerusalbitarsis has evolved its antennae into a sharp and pliable system for venom injection, primarily used to incapacitate prey.(Berkov et al., 2008)

Insect venom is commonly used for defense, although the evolution of venom for this purpose is thought to be primarily found in social hymenopterans and lepidopterans. Social wasps, bees, and ants often have venom with multiple components that cause discomfort or pain to predators. Certain species such as bullet ants and fire ants have venom that can cause extremely intense pain . ( Aili et al ., 2014); (Edström, 1992d). Additionally, due to the fact that the evolution of defensive venom typically occurs in social hymenopterans, it is common for predators to receive multiple stings, which serve to amplify the severity of the symptoms experienced.

While adult Lepidoptera, including butterflies and moths, have various toxic defenses, venom is limited to their caterpillar stages. In addition, within this group, venom is exclusively used as a defensive strategy since most species are herbivorous, and no venom has been reported in carnivorous species. (see (Pierce, 1995) for a review of carnivorous caterpillars). Caterpillars typically have a venom system that involves delicate hairs that can easily break upon contact, allowing venom to be transferred from associated glands or specialized secretory cells(Carrijo-Carvalho &) Chudzinski-Tavassi, 2007) and (Carrijo-Carvalho & Chudzinski-Tavassi, 2007); (Edström, 1992a). Although the venom of caterpillars is not well understood, it is known to cause immediate pain and intense irritation upon contact. Some species have even been reported to interfere with the blood systems of animals as large as humans, leading to fatal envenomations.(Carrijo-Carvalho & Chudzinski-Tavassi, 2007).

**Echinoderms**

Echinoderms, such as starfish and sea urchins, have developed venom solely for defense purposes. Since sea urchins are herbivorous grazers and starfish feed on sessile or slow-moving organisms, there is little or no additional benefit to be gained from using venom for predation. Although other starfish may possess venom, they have not been thoroughly researched, and only the crown-of-thorns starfish (Acanthasterplanci) has been identified as utilizing venom from dorsal spines for defensive purposes. When envenomated by this species, individuals may experience a broad range of symptoms, including intense pain, irritation, vomiting, hemolysis, and a reduction in central nervous system activity.(Lee et al., 2014)Many species of sea urchins have specialized structures called pedicellaria on their dorsal surface , which contain a venom apparatus .(Edström, 1992d)Sea urchins have specialized structures known as pedicellaria on their dorsal surface which contain a venom apparatus. These small structures have three claws, each containing a venom gland that transfer venom to predators. The exact function of the venom against natural predators is poorly understood, but it is known to act primarily as a neurotoxin . The most well -known species , Toxopneustespileolus, is capable of causing respiratory difficulties in humans .(Edström, 1992d)In addition, numerous sea urchin species possess lengthy spines that can readily break through the skin of predators. However, only a handful of these species seem to possess venom glands associated with their spines, with others relying on provocation directly from the injuries(Injury to Human Tissues from Sea Urchin Spines - ProQuest, n.d.).

The body surface of Acanthasterplanci, also known as the crown of thorns starfish, is covered with numerous venomous spines. Additionally, a lethal factor has been identified in their venom, which is a basic glycoprotein with hemorrhagic and myonecrotic activities..(Shiomi et al., 1988)

Brittle stars also have venom used for feeding. For example, Ophiomastixannulosa can induce paralysis and even death in small animals.

Toxopneustespileolus, a sea urchin species, doesn't have spines like other sea urchins, but it has tiny pedicellariae that carry venom, causing paralysis. Sea cucumbers have white cuvierian tubules, which are sticky threads that can be discharged to shoot out poison, leading to paralysis and death of small prey animals.(James, 2010)

### Fish

Fish venom is an area of study that has received little attention. Fish possess venom delivery mechanisms such as spines, barbs, teeth, and fangs, yet the majority of fish venom is used for defensive purposes.( Smith W.L., Stern J.H., Girard M.G., Davis M.P. *Evolution of Venomous Cartilaginous and Ray-Finned Fishes.* Oxford University Press; Oxford, UK: 2016 ) (Fish venom). Fish species use spines as their venom delivery system, although the morphology of the spines can vary considerably across species. For instance, stingrays have flat and serrated spines while stonefish have needle-like spines. The venom of fish species is still relatively unexplored and exhibits a high degree of variation, but typically contains powerful neurotoxins that can cause severe pain and respiratory paralysis. This suggests that fish venom is mainly used for defensive purposes(Smith & Wheeler, 2006).

### Amphibians

Toads use a passive mode of defense against predators, as their poisoning only occurs when the aggressor attacks and bites and comes into contact with the toxins via oral mucosa. (Mailho-Fontana et al., 2018)

Toads produce a venom containing a mixture of compounds such as steroids, biogenic amines, andproteins. These low-molecular-weight substances can rapidly cross the oral mucosa and enter the bloodstream, affecting the cardiovascular system by increasing blood pressure or heart contraction. The composition of the venom varies among different species of amphibians. For example, bufonid toads of the genus Bufo contain high levels of indole alkylamines, while leptodactylid frogs have phenolic amines and hylid frogs of genus Phylomedusa have various vasoactive peptides. Batrachotoxins found in some frogs can depolarize nerves and muscles by specifically opening sodium channels, but the sodium channels of Phyllobates species are insensitive to batrachotoxin.[2].

During predation, the teeth of some species, such as S. annulatus, may release venom through the secretion that covers their surface. The groove around the upper jaw appears to play a role in evenly distributing the venom during a prolonged bite that compresses the glands in the labial area.[3](Mailho-Fontana et al., 2020)

C. greeningi and A. brunoi possess toxic skin secretions along with a delivery mechanism, which makes them venomous. Their skin toxins can be dangerous even in small amounts and can be introduced into a wound caused by the head spines, thus these frogs can use their skin toxins as venoms against potential predators.[4](Jared et al., 2015)

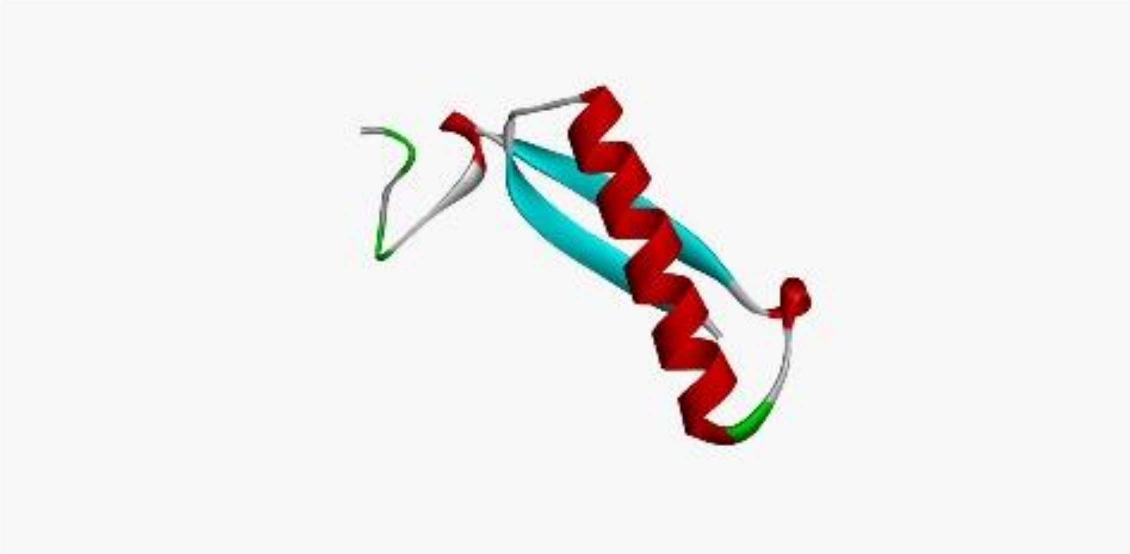
#### ***Drugs for the treatment of toad envenoming.***

**PROPRANOLOL** - to treat toad envenomation, propranolol (a non-selective ß-adrenergic antagonist) is given at a dose of 5 mg/kg intravenously, with a repetition after twenty minutes if necessary to control cardiac fibrillation.

**ATROPINE**, a muscarinic antagonist, is administered at a dose of 0.04 mg/kg to reduce salivation and lung secretions.

**PENTOBARBITAL SODIUM** a short-duration barbiturate, is given at a dose of 30 mg/kg to allow orotracheal intubation and washing of the mouth with water to reduce the venom present in the mucous.

In addition to these, drugs such as oxytetracycline, chloramphenicol, analgesics, spasmolytic drugs, multivitamins, sodium bicarbonate to wash the oral cavity, diphenylhydantoin, phenoxybenzamine, a-adrenergic antagonist, and acepromazine have been reported to help in the treatment of toad envenomation. Propranolol and atropine are considered the most efficient drugs for the treatment of toad envenomation today.(SAKATE & OLIVEIRA, 2000)



***3D computed image showing the structure of Sauvagine***

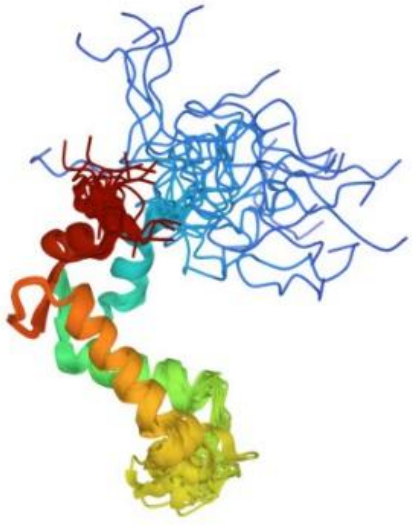
**Squamate Reptiles**

Extensive research has been conducted on reptile venoms, surpassing the amount of study on venoms from any other venomous creature. As a result, there have been numerous books dedicated to this topic. e.g., (Boyer et al., 2015); (Mackessy, 2021), largely focused on molecular toxicology and clinical implications. Previously it was believed that venom had evolved multiple times in snakes and once in Heloderma lizards. However, recent research suggests that venom actually evolved only once, early on in the lineage that includes snakes, Heloderma lizards, and Varanus monitor lizards. This group has been given the name "Toxicofera." (Fry et al., 2015)(Fig. 2). It is important to acknowledge that some writers have disputed this notion and argue that the conventional perspective of venom having multiple origins in reptiles is accurate. For additional discussion on this matter, readers can refer to the chapter written by (Zancolli et al., 2019) in this publicationIf we assume that venom indeed originated only once, then several lineages have abandoned venom due to adaptations that reduce its benefits. As almost all squamate (snake and lizard) venoms are primarily used for predation, the reasons for the loss of venom tend to be associated with alternative methods of capturing and overpowering prey, such as constriction, or different diets, like eggs or leaves, that do not require subduing. Since venom is closely linked to predation, the diet is usually the main factor that influences the variation in squamate venoms.(Daltry et al., 1996).

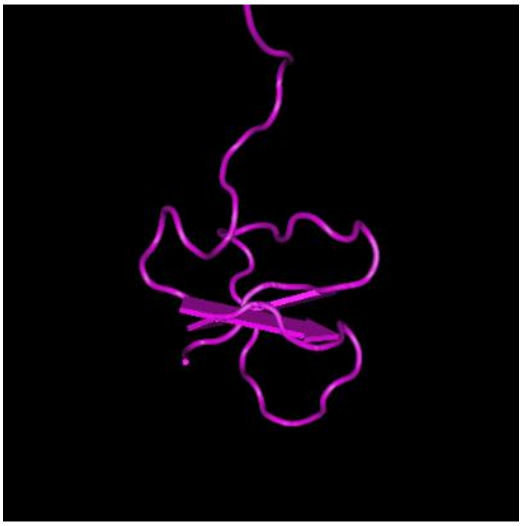
**Mammals**

Venom has evolved at least four times in mammals and probably more due to multiple origins within these four groups: platypuses, vampire bats, slow lorises, and insectivores. There is also some fossil evidence that some extinct mammals were also venomous (Fox & Scott, 2005). Therefore, venom is rare but taxonomically dispersed in mammals. Vampire bats share similar venom characteristics with other blood feeding animals, with toxins acting to maintain blood flow (via anticoagulant effects and vasodilation) and avoid disturbing (in this case waking) the host by reducing pain and inflammation (Ligabue-Braun et al., 2012)(Low et al., 2013).

. Female platypuses lose the spurs early in life and generally have a degenerate venom system; It is believed that platypus venom functions in mate competition and is used against male rivals since it is present on keratinous spurs in male platypuses and the venom glands increase in size during breeding season along with increase in venom production. Platypus venom possesses some cytolytic activity and stimulates calcium-dependent current from intracellular calcium release in cultured dorsal root ganglion cells. The venom also has protease activity and induces mast cell histamine release that may contribute to pain, vasodilation, and edema.



**NUCLEOBINDIN-2 Platypus nucleobindin 2 (ENSOANP000000 12244) is the first nucleobindin molecule identified in any animal venom. Three defensin-like peptides (DLPs) were isolated from platypus venom and sequenced - peptide called DLP-1 was created through chemical synthesis, and its structure was analyzed using NMR spectroscopy. The peptide consists of 42 amino acid residues and has a three-dimensional structurecharacterized by an anti-parallel β-sheet formed by residues 15–18 and 37–40, as well as a small 3"! helix that spans residues 10–12. The overall structure is similar tothat of β-defensin-12 and the neurotoxin ShI from Stichodactylahelianthus.**



**DEFENSIN LIKE PEPTIDE-1 (monomeric): NCBI database**
**Despite being independently derived in each lineage, the venom of the platypus is most similar to those of snakes and other reptiles in that it contains amide oxidase, WAP, protease inhibitors, and CRISP. The similarities might reflect the two taxa's more recent common ancestry compared with other well-studied venomous taxa.** (Wong et al., 2013)

There are two mammals which use venom for intraspecific competition in addition to defense: platypuses and slow lorises (Grow et al., 2015; Whittington et al., 2009)
Primates, Lorisidae use Needle-like toothcomb (incisors and canines of lower jaw) as venom delivery apparatuses used for PC, PD, IC and/or ectoparasite defence. Even though the most accepted hypothesis for venom usage in lorisidaes is using it for intraspecific competition, various other hypotheses have been proposed and a leading theory has yet not been discovered.

**Evolution of loris venom:** Mimicry among vertebrates is less common and in mammals extremely rare. slow lorises display facial markings undeniably akin to the eyespots and accompanying stripes of the spectacled cobra (Najanaja) and The dark contrasting dorsal stripe of these two species also closely resembles the body of a snake, making it seem like there is a close evolutionary relationship between snakes and lorises. Hence, it is believed that the Nycticebus mimicry evolved during a period of co-existence with Najanaja, at a time when environmental pressures would have favoured its selection. (Nekaris et al. 2013) .

These two venoms, although both are used for defense, have different effects on their victims. The venom of the slow loris causes severe pain, inflammation, and tissue damage, which may give an advantage to the male using it, or may be a side effect of the venom's multiple functions. Interestingly, the venom of the slow loris is formed by mixing two harmless fluids - brachial gland secretion and saliva - which become toxic when combined and injected through a bite. In contrast, the venom of the platypus is not as destructive as that of the slow loris, but still causes significant pain and inflammation. (Nekaris et al. 2013) and (Whittington et al. 2009)

Several groups of insectivores like solenodons, have either been demonstrated or suspected of using venom to assist predation. Shrews like Blarina and Neomys are known to be venomous, as are all of which have venom glands in the lower jaws and transfer venom to prey via a bite, and there is some evidence that other shrews are similar (Ligabue-Braun et al. 2012). Moles are also strongly suspected of being venomous as they have similar glands in the lower jaw and are known to store paralyzed worms in burrows (Ligabue-Braun et al. 2012). It seems to be generally the case for insectivores that the venom does not usually kill prey but rather immobilizes it in a live but paralyzed state, in which it is stored for later consumption.

### Evolutionary Drivers of Variation in Venoms Between and Within Species

Venoms are highly variable both between species and within a single species. The evolutionary causes of this variation will vary depending on the primary function(s) of the venom, and the extent of the variation will partly depend on any constraints acting on the system. Although this section will focus on the generation and maintenance of variation, it is worth mentioning the influence of convergent evolution in constraining diversity of toxins. Convergence is a common theme in venom evolution (e.g., Casewell et al. 2013; Fry 2015) and can be seen at two levels.

The first is at the level of individual toxins, wherein the same protein structures are repeatedly altered to function as toxins across the animal kingdom (Fry et al. 2009a, c). This is likely a consequence of a combination of similar basic protein structures being available as body proteins to many different animals, therefore the raw materials are similar before toxin evolution, and that toxin evolution by small alterations of particular physiologically active molecules is likely to be easier to achieve as the molecule is already adapted to interact with physiological systems.

The second level that convergence can be seen is in whole venoms, by which the author means that venom in some form has evolved repeatedly a large number of times across the animal kingdom (Fig. 1). This level could be extended to the consideration that venom functions have also evolved convergently throughout the animal kingdom, especially predatory and defensive venoms (but use in intraspecific competition has evolved at least in monotremes and primates).

It should also be noted that venom is an energetically expensive product (McCue 2006) as so selection would be expected to act to optimize the cost-benefit ratio of the functions for which it is used. Therefore, venom evolution has followed a complex path of diversification and convergence which has shaped the observed variation in animals.

### Interspecific Variation

The chemical composition of venom often varies remarkably between even closely related species. For predatory venoms, different species may have different diets, and this may drive divergence in the venom of each as it increases the efficacy of the venom toward that species' particular prey (Wüster, 2009)). It is highly likely that such dietary shifts are the main selection pressure driving variation in predatory venoms as there are numerous observations of venom systems degenerating (presumably to save energy) when diet changes make venom unnecessary (e.g., Fry et al. 2013).

For defensive venoms, there is little clear evidence that different predator communities drive differences in venom. However, this would be difficult to obtain for multiple reasons. Firstly, it is often unknown what the actual predator community is in a given area for a given venomous prey species. Secondly, predators are likely to be attacking multiple prey species, and perhaps multiple venomous prey species, and so attributing changes to a particular predator is difficult. Thirdly, venoms (including defensive venoms) are often effective against a wide range of predators so even if the predator community were fully replaced, the same venom may still be effective. In other chemical defense systems, it seems that the defense is readily gained but difficult to lose which suggests that there are strong and general individual benefits (Arbuckle & Speed, 2015) . Furthermore, natural enemies such as predators are expected to impose strong selection on defenses, and therefore it is likely that predators do drive variation in defensive venom, but it may be at a broader scale that is typically examined.

Competitive and reproductive venoms are so poorly understood that the drivers of their variation between (or within) species are unknown. For venoms with a reproductive function, we may expect that sexual conflict is strong as males chemically manipulate females and females may be selected to resist this.

Consequently, we might expect that variation in venoms between closely related species using venom in reproductive interactions is much higher than otherwise expected, but this remains to be investigated.

Finally, environmental drivers of interspecific variation in venoms are understudied (excepting prey choice and availability). However, we might expect, for example, that predatory venoms may be more potent in species that hunt in environments where prey may escape out of reach unless venom takes effect especially quickly, such as in slow-moving aquatic predators or those hunting in dense habitats or where prey can escape to burrows.

### Intraspecific Variation

The same drivers of interspecific variation may also drive intraspecific differences between populations, but there are other considerations that are specific to the latter. However, many of these are not evolutionary in origin. For instance, variation in venom can be a consequence of amount of energy available to an individual for toxin manufacture, or time since last envenomation as venom supplies need to be replenished (and different toxins may regenerate at different rates).

Other causes of intraspecific variation may be a consequence of evolution. For instance, sex differences in venom may reflect sex differences in diet or predation risk (e.g., in Bothrops jararaca; (Furtado et al., 2003), in which niche partitioning between sexes leads to feeding on different prey types and consequent shifts in venom, increasing variation within the species. Similarly, age-related variation may be a consequence of diet or predation differences coupled with a smaller venom yield in smaller individuals (e.g., in Crotalus spp.; (Furtado et al., 2003); (Mackessy, 1988b). This situation allows young, and therefore small, individuals to possess a relatively more effective (e.g., higher toxicity) venom that could offset the low venom yield available to secure prey or repel predators.

Finally, in predatory venoms, prey populations or communities may change over time. This could conceivably generate selection on venomous predators to have a quick evolutionary response in their venoms, leading to increased mutation rates in venom genes compared to other genes (either in coding or regulatory regions controlling expression of different components). This situation would lead to high variation in venoms within a species, and within populations, despite the selection acting on evolvability rather than favoring the increased variation per se. Nevertheless, evidence for this scenario is currently lacking and remains a mere possibility, though if true it could provide an additional explanation for many toxins being part of multigene families.

### Antagonistic Coevolutionary Interactions Are the Common Thread in Venom Evolution

All venoms have evolved in the context of antagonistic coevolution. Despite the massive diversity of venoms, venom delivery systems, venom functions, and venomous animals, this is one key point which is applicable throughout. The antagonists may be traditional natural enemies (e.g., predator-prey, host-parasite) as in the case of predatory and defensive venoms or less traditional (in this context) such as conspecifics of the same or opposite sex as in the case of competitive or reproductive venom functions. Nevertheless, because they all represent parties with opposing interests (one side wants to envenomate, the other wants to avoid envenomation), there are implications for considerations of the evolution of venomous animals: it never takes place in isolation.

In essence, any evolutionary change in venom – whether gain, loss, or alteration – will impose selection pressure on another organism to limit or remove the benefits conferred to the venomous animal. This will both lead to diversification of the venom as the arms race forces both parties to continually adapt but also constrain the advantages that can be gained. A common example of coevolution in the context of venomous animals is venom resistance. Predators that eat venomous prey have often evolved resistance to the prey's venom to enable consumption (Drabeck et al., 2015) Similarly, prey that are eaten by venomous predators often have a high level of resistance to the predator's venom (Heatwole& Powell, 1998); In some cases, prey species are more resistant to the venom of their predators than to other venomous predators that do not eat that species – a result that would be unintuitive without an appreciation of coevolution. This concept is taken further by nudibranch mollusks which feed on venomous cnidarians but are able to not only avoid envenomation but extract the entire venom system from the cnidarian and transport it to the nudibranch's surface for its own defense (Greenwood, 2009)

### Ecological and Evolutionary Consequences of Venom (and Other Chemical Defenses)

Natural enemy interactions are expected to lead to phenotypic divergence and evolutionary diversification in organisms, as a consequence of the coevolutionary arms races that they fuel (Ehrlich & Raven, 1964). In essence, the expectation is that effective antipredator defenses should lead to a greater freedom of movement (without having to be as cautious about potential predators) and hence occupy a broader niche space. The broader niche space may allow more opportunities for diversification, and the arms race itself is predicted to generate evolutionary diversification in such scenarios (Ehrlich & Raven, 1964)) – a phenomenon known as “escape-andradiate” theory.

Note that these predictions stem from theories of defense but should apply well to venomous animals since most use venom either primarily or secondarily in defense. Unfortunately, little research effort has been focused on the evolutionary and ecological consequences of possessing venom in animals, and so this discussion will borrow from the literature on other chemical defenses. However, because the predictions are based on the interplay between the predators and the repellent nature of the defense, the response should be similar in many cases across specific forms of defense.

Higher predation risk (and correlates of higher predation risk) tends to favor the evolution of effective defenses, but the consequences to ecology and life history of the animals after the evolution of venom are less well known. Two general points are of particular interest though. The first is that chemical defense does seem to be associated with a broader niche space, as predicted above(Arbuckle, 2017b). Specifically, in musteloid mammals (a group including skunks, badgers, and otters), those that use repugnant anal gland secretions in defense had a less constrained activity period and a broader diet. The second point is that chemical defense is associated with slower life histories including such traits as longer life span (Hossie et al., 2013) – although venoms used primarily for predation did not show the same pattern of longevity, suggesting specificity to defensive venoms. This is expected based on evolutionary theories of the life history of aging that predict slower senescence and generally slower life histories in species with lower extrinsic mortality, such as from predation (Blanco & Sherman, 2005)

Few empirical tests of the prediction from “escape-and-radiate” theory, that chemically defended animals should have higher diversification rates, have been conducted. Recently, (Arbuckle & Speed, 2015) investigated this idea using amphibians and found that chemically defended lineages actually had lower diversification rates, due to an increased extinction rate. The raised extinction rate was also observed in present-day amphibians (Arbuckle & Speed, 2015), wherein chemically defended species are more likely to be threatened (based on IUCN Red List conservation status) than non-defended species. The most plausible mechanism to explain this is that because chemically defended species should have slower life histories, they should be less resilient to population declines due to slower rates of subsequent population increase.

## II. Conclusion and Future Directions

Venom has evolved frequently across the tree of life and is consequently found in many disparate groups of animals. The benefits obtained by venomous animals are most often related to enhancing prey capture or avoiding attack by predators but can include other aspects of biology such as competition and reproduction. These functions are not mutually exclusive, but all take place in the context of antagonistic coevolutionary interactions – perhaps the one comprehensive rule of venom evolution. Venom displays extensive variation both within and between species, which can be driven by various processes relating to the functions of the particular venom. Finally, the evolution of venom, especially as a defensive trait, can have important long-term consequences for the ecology, evolution, and conservation of venomous animals.

Throughout this chapter, many gaps in our knowledge have been highlighted. However, perhaps the most promising for future work falls into the following two areas. Firstly, there are many venomous animal groups which have been given very little attention, particularly among the invertebrates, and directed research into those groups would provide insights into the evolution and diversity of venom, as well as uncover novel toxins which could potentially yield a multitude of new pharmaceutical products. Secondly, the macroevolutionary consequences of venoms have been almost ignored until very recently, yet provide an opportunity to understand how venomous animals originated and how their future is likely to play out. These areas are likely to be extremely fruitful for further investigation.

Cross-References

▸A Critique of the Toxicoferan Hypothesis

▸Evolution of Resistance to Toxins in Prey

▸Mutation, Duplication, and More in the Evolution of Venomous Animals and Their Toxins

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