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Snake Antivenom and Chemistry Behind the Mode of Action in Saving Human Lives as Well as in The Synthesis of Life Saving Drugs for Mankind: A Short Review

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ABSTRACT

The World Health Organization (WHO) in 2017, classified snake envenomation as a high-priority neglected disease and highlighted its severe impact to mankind. More than 2.7 million poisonous bites have been recorded annually, resulting in approximately 100,000 deaths and created many more disabilities. The basic treatment for snake envenomation is to administer specific antivenoms tailored to the snake species involved, and supportive care. In this study, I would emphasize the mode of action and chemistry behind the applications of antivenoms for mankind and also how different snake antivenoms may be successfully employed for medicinal purposes. Snake antivenoms contain bioactive peptides and enzymes that show therapeutic potential for conditions such as arthritis, asthma, cancer, chronic pain, infections and cardiovascular diseases. Despite many challenges, the future of snake venom-based treatments appears promising for addressing complex medical conditions.

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Introduction

In India and South Asian countries along with African continents, especially in rural and village areas, July-September months are vulnerable and time to take safety measures and precautions because every year there are many reported cases of deaths due to snake bites, though research study says in our country, only 10% of the snakes are poisonous while remaining others are nonpoisonous in nature. The primary causes of death in these months in our rural areas and villages is due to two reasons as found in my research study.

i) Still there is a lack of awareness about "Do's & Don'ts" when a snake bite is there and still people wants to adopt local expertise rather than taking the snake bite patient to a nearby health centre or hospital.

ii) The delay occurs during this process leads to deuteriation of the patient and eventually death results. While the patient could have been saved if diagnosed that the snake bite was within half an hour and would have been taken to nearby hospital. As per the directives of "Health & family Welfare" Department, Government of India, all the states in our country are nowadays have sufficient stock of "Antivenoms". Our country experiences a high incidences of snakebite, in the rural areas and the monsoon season is particularly high-risk period. States like Bihar, Jharkhand, West Bengal, Madhya Pradesh, Odisha, Uttar Pradesh, Andhra Pradesh, Telangana, Rajasthan, and Gujarat are identified as having the highest number of snakebite deaths. Within these states, the rural areas, particularly those where agricultural activities are basic medium for family income are most vulnerable.

What is "Antivenom" and how does it work?

Antivenoms are immunobiological preparations composed of specific immunoglobulins or immunoglobulin fragments that bind to and inactivate toxins present in venom, represent one of the most traditional and common uses of snake venoms [1]. Antivenom, also known as antivenin, is a specific treatment for venomous bites or stings. It's a biological product made of antibodies that neutralize the toxins in venom. These antibodies are typically harvested from the blood of animals like horses or sheep that have been injected with venom and then purified for therapeutic use. Antivenom is crucial for treating venomous snakebites, spider bites, and other envenomation's. Antivenom works by using antibodies to neutralize the toxins in snake venom. These antibodies are produced by animals like horses or sheep, which are injected with small amounts of venom, prompting their immune systems to create antibodies. These antibodies are then harvested and purified to create the antivenom, which is injected into the snakebite patient to bind to and neutralize the venom components in patients. The animal's immune system responds by producing "Antibodies" that specifically target and bind to the venom components. The antibodies are harvested from the animal's blood and purified, resulting in "Antivenom". When injected into a snakebite victim, the antivenom antibodies bind to the venom toxins in the bloodstream, neutralizing their effects and preventing further damage. Antivenom can reverse some of the harmful effects of the venom, such as bleeding or nerve damage, but it's most effective when administered soon after the bite. Essentially, antivenom acts as a "decoy" for the venom, binding to it before it can interact with the body's tissues and cause damage. The antibodies in the antivenom act like a "lock and key", specifically binding to the venom's toxins and preventing them from interacting with the body's cells and tissues. The effectiveness of antivenom is greatest when administered soon after the bite, as it can prevent the venom from causing further

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damage. While antivenom doesn't reverse the damage already done by the venom, it can stop the venom from causing further harm and allow the body's natural healing processes to work. Prompt administration of antivenom is crucial because it cannot undo the damage already caused by the venom. However, the use of animal-derived antivenoms is not without risks; they can provoke hypersensitivity reactions due to their foreign protein content, leading to potentially life-threatening conditions such as severe anaphylaxis. Additionally, antivenoms are often expensive and their availability is limited in many regions [2,3]. Thus, there is a critical need for innovative approaches to improve the efficacy, safety, and cost-effectiveness of antivenoms, which could significantly enhance treatment outcomes for snakebite victims, offering better treatment outcomes for patients affected by snakebites. Thus, there is a critical need for innovative approaches to improve the efficacy, safety, and cost-effectiveness of antivenoms, which could significantly enhance treatment outcomes for snakebite victims, offering better treatment outcomes for patients affected by snakebites.

Chemical Composition of Snake Venom

Snake venom is a complex mixture, not a single chemical, primarily composed of "Proteins and peptides". These proteins can be enzymatic or non-enzymatic and account for the majority of the venom's dry weight. Inorganic salts, amines, carbohydrates, metal ions and lipids are the remaining portion. **Enzymes:** Snake venom contains various enzymes, such as proteolytic enzymes (which digest proteins), phospholipases (which degrade lipids) and hyaluronidases (which help venom spread). **Non-enzymatic proteins and peptides:** These include toxins that affect the nervous system (neurotoxins), blood clotting (hemotoxins) and muscle tissue (myotoxins). **Other components:** Snake venom also contains inorganic cations (like sodium, calcium, potassium and magnesium), small amounts of zinc, iron, cobalt, manganese and nickel, as well as nucleosides, carbohydrates and lipids.

Toxin types: Different types of toxins are found in snake venoms, including neurotoxins, hemotoxins, and myotoxins. The specific composition of venom varies between snake species and even within the same species based on factors like age, diet and geographic location. This variation leads to differences in the type and severity of symptoms caused by different snakebites. **Neurotoxins:** These toxins can block nerve impulses, leading to paralysis or respiratory failure. Examples include alpha-neurotoxins found in elapid venoms. **Phospholipases A2:** These enzymes can disrupt cell membranes and cause muscle damage or inflammation. **Metalloproteinases:** These enzymes can break down connective tissue and blood clots, contributing to tissue damage and bleeding. **Hyaluronidase:** This enzyme increases the permeability of tissues, allowing venom components to spread more easily.

Bradykinin-potentiating peptides: These peptides can lower blood pressure by interfering with the renin-angiotensin system. **Three-finger toxins (3FTx):** Found in the venom of king cobras, some 3FTx are potent neurotoxins. So, chemical research reveals that "Snake venom" is a complex cocktail of proteins, peptides and other molecules that act synergistically to cause a wide range of effects on prey or predators. Understanding the chemical structure and composition of snake venom is crucial for developing effective "Antivenoms" and for studying the

evolution and function of these complex biological weapons. Neutralizing anti-venoms, which are immunobiological preparations, composed of specific immunoglobulins or immunoglobulin fragments that bind to and inactivate toxins present in venom, represent one of the most traditional and common uses of snake venoms [4].

Types of Antivenom

Antivenom can be *monospecific*, targeting the venom of a single snake species, or *polyspecific*, targeting a range of venoms from different species found in a specific geographic area. New research developments on "Antivenom & its greater success rate" in treating snake bite patients shows that more "efficacy" of antivenom is found if the antivenom is synthesized from a region/state where the incident of snake bite has happened. A Kolkata based research group studies (May 2025) has already proved it in "Sundarban" area of West Bengal. Usually, the hospitals are receiving the "antivenoms" synthesized from various laboratories of "Chemical Biology" which are from different parts of our country. Recent formulations developed from the venoms of various Republic of Korean pit viper species [(KR20220170290 (A)] [5] have shown effective antidote properties for neutralizing snakebite effects. Advances in antivenom development are focused on enhancing neutralization efficacy, safety, and selectivity to meet the urgent need for effective treatments for snakebite envenomation. Creating novel formulations is essential for improving therapeutic outcomes by increasing efficacy, minimizing side effects, and addressing challenges such as stability and specificity. By innovating new antivenom agents, we can significantly enhance treatment options for snakebite victims, ultimately reducing morbidity and mortality associated with envenomation [3,6,7].

Extraction of Venoms from Snakes

Snake venom is primarily extracted in laboratories through a process called "milking," where venom is manually expressed from the snake's venom glands. This involves stimulating the glands to release venom into a collection container. Alternatively, researchers are developing methods to produce venom in lab-grown snake venom glands, potentially offering a more sustainable and scalable source. Snake venom can be collected in two ways: "dead collection" and "live collection". "Dead collection" is a special destructive method of cutting off the venom glands from the head after the snake is put to death by anesthesia. Snake venom extraction is a dangerous job but it is essential for research and antivenom production which are for ultimately beneficial for mankind.

Can snake bite be fatal? Myths & Science

The time it takes for snakebite to be fatal varies significantly based on several factors, but death can occur within minutes to hours or even days, depending on the snake species, the amount of venom injected and the individual's health. For some of the most venomous snakes, death can occur within 30 minutes to a few hours if left untreated. Snake bites are often surrounded by myths and misconceptions that can hinder proper treatment. **Myth:** Sucking venom out of snakebite is effective. **Fact:** This is ineffective and can introduce bacteria into the wound, increasing the risk of infection. **Myth:** Tourniquets reduce envenomation. **Fact:** Tourniquets can cause tissue damage and necrosis by restricting blood flow. **Myth:** Applying ice to snakebite slows down venom spread. **Fact:** Ice can actually worsen the effects of venom and mask important symptoms. **Myth:** Young snakes



Figure 1: Extraction of snake venom.



Figure 2: Ampules of antivenom prepared from blood of immunized horses and sheep's.

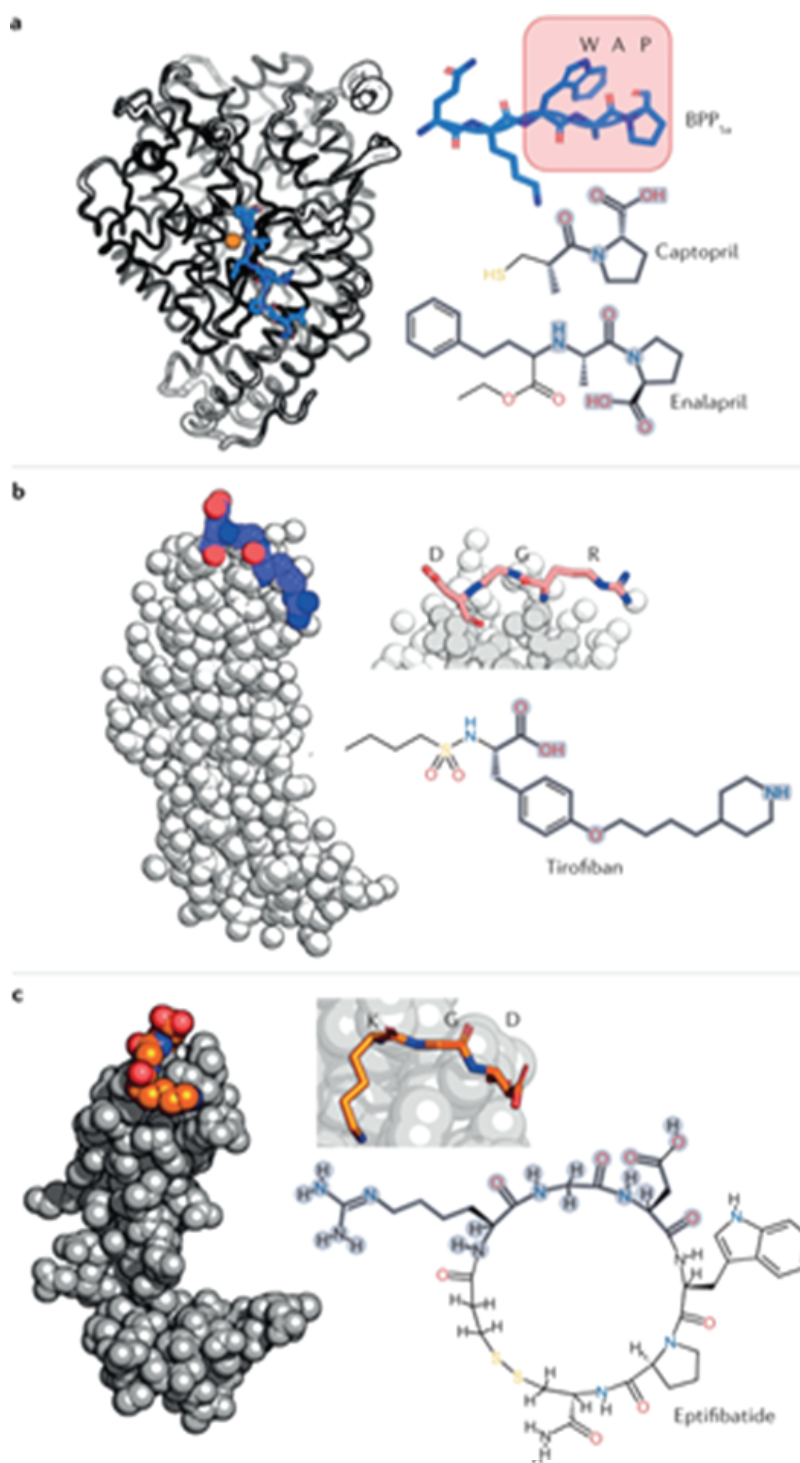


Figure 3: Chemical composition and structures of molecules present in snake venom.

are not venomous. **Fact:** Young snakes, especially young females, are often more prone to biting and can inject venom. **Myth:** Snakes will chase you if you approach them. **Fact:** Snakes prefer to avoid humans and will only bite defensively if they feel threatened. **Myth:** Snakes can be controlled by milk. **Fact:** Snakes are attracted to rodents, not milk, and the belief that they drink milk is unfounded. **Myth:** Local excision or surgical intervention is recommended for snakebites. **Fact:** These methods are no longer recommended and can increase injury and infection risk. **Myth:** Snakebite kits are effective and safe. **Fact:** Snakebite kits are often ineffective and potentially harmful.

Chemistry of Snake Venom and its Medicinal Potential in the synthesis life saving drugs

The fascination, curiosity and fear of snakes in the world were found to mankind from ancient Egyptian time as well as the fear psychosis. Owing to their lethality, snakes have often been associated with images of perfidy, treachery and death. However, snakes did not always have such negative connotations. The curative capacity of venom has been known since antiquity, also making the snake a symbol of pharmacy and medicine. Today, there is renewed interest in pursuing snake-venom-based therapies. This mini-review will also focus on the chemical potential of venom to be exploited for medicinal purposes in the development of drugs. The mixture of toxins that constitute snake venom is examined, focusing on the molecular structure, chemical reactivity and target recognition of the most bioactive toxins, from which bioactive drugs might be developed. The design and working mechanisms of snake-venom-derived drugs are explained as understood and the strategies by which toxins are transformed into therapeutics. Also, I have tried to emphasize on the challenges in realizing the immense curative potential of snake venom and chemical strategies by which a plethora of new drugs may be achieved.

Snake venom is a rich source of bioactive molecules that hold great promise for therapeutic applications. These molecules can be broadly classified into enzymes and non-enzymes, each showcasing unique medicinal properties. For centuries, snake venoms, bile, oils, meat, fat and body parts have been used across the world to treat diverse illnesses [8]. Ancient cultures from Asia, Africa, Europe and America have described their benefits. Although snake venom is inherently toxic, it contains several peptides and enzymes with significant biological activities [9]. Among the species that have been recognized for their medical properties are cobras, vipers, pit-vipers and pythons⁸. Their venom derivatives have been used to alleviate arthritis, asthma, eczema, pain, inflammation, allergy, migraine, rheumatism, diabetes, skin disorders, cancer, heart conditions and infections [8]. Research on venom components is essential for developing targeted therapeutic strategies due to their specificity and potency [10,11]. Some of the toxins present in snake venom are three-finger toxins (3FTxs), phospholipases A2 (PLA2s), snake venom metalloproteinases (SVMPs), snake venom serine proteinases (SVSPs), cysteine-rich secretory proteins (CRISPs), L-amino acid oxidases (LAAOs), and C-type lectin-like proteins (CTLs) respectively [10]. The activity of these toxins can be grouped as *myotoxic*, *neurotoxic*, *cardiotoxic*, *anticoagulation*, *hemostatic disturbances* and *inhibition of platelet aggregation* [11]. Modern science has succeeded in isolating and studying these venoms, leading to numerous biomedical applications [12]. The focus on the primary medical indications for registered innovations include coagulation disorders/thromboembolic diseases, lung cancer, inflammation, chronic obstructive pulmonary disease, antiviral applications, Zika virus infection, hemorrhage, pain, arthritis, gout, rheumatoid arthritis, snake bites, cancer, myasthenia gravis, and hemophilia A. Despite the broad biomedical applications of snake venoms due to their compositional variability, their activities can be classified into several categories: *anticoagulant*, *cytotoxic*, *anti-inflammatory*, *antiviral*, *procoagulant*, *hemostatic*, *antinociceptive*, *cytolytic*, *thrombolytic*, *antibacterial*, and *immunogenic* respectively. Cytotoxins and polypeptides from snake venoms, such as those from *Naja atra* (CN107737333 (A)) [13] and (CN107929717 (A)) [13], show *efficacy in cancer treatment* by inducing apoptosis and cellular damage in tumor cells. The formulation with these cytotoxins and polypeptides was tested in various cancer cell lines and murine models. Snake venom-derived cytotoxins are being explored for their potential to selectively target and destroy cancer cells, offering innovative approaches to cancer therapy and highlighting their role in precision medicine [14-16]. The full medicinal scope of these toxins is still emerging.

Conclusion

In conclusion, my studies on antivenoms as lifesaving snake bite patients

as well as applications of snake venoms in the synthesis of lifesaving drugs including cancer has been described. I believe, this short review and the detailed information's in the references may provide further encouragement for the scientists to pursue research in this domain.

Conflict of Interest: Author declare that there is no conflict of interest

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