

A CRITICAL REVIEW ON THERAPEUTIC USE OF SNAKE VENOM

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ABSTRACT

Snakes are the most despised animals in the world. Ample narrations about snakes are available in *Brihatrayee*. Snake venom, though greatly feared, is a natural biological resource, containing several components that could be of potential therapeutic value. The therapeutic use of snake venom is mentioned since ancient time for different diseases. It is well known that snake venom is complex mixture of enzymes, peptides and proteins of low molecular mass with specific chemical and biological activities. Snake venom contains several neurotoxic, cardiotoxic, cytotoxic enzymes, nerve growth factor, lectins, disintegrins, haemorrhagins and many other different enzymes. These proteins not only inflict death to animals and humans, but can also be used for the treatment of thrombosis, arthritis, cancer and many other diseases. An overview of various snake venom components that have prospects with the advent of biotechnology, the efficacy of such treatments has been substantiated by purifying components of venom and delineating their therapeutic properties Snake venom toxins contributed significantly to the treatment of many medical conditions. This paper will focus on certain snake venom components and their applications in health and disease, diagnosis and treatment.

Key words: Snake venom, toxins, therapeutic, enzymes.

INTRODUCTION

Snake venom is highly modified saliva. It is a clear and viscous fluid^[1] which contains zootoxins that facilitates the immobilization and digestion of prey, and defends against a threat. Snake venom, though greatly feared, is a natural biological resource, containing several components that could be of potential therapeutic value. It is injected by unique fangs after a bite but some species are also able to spit^[2]. The snake venom when injected then it is poisonous but when it is consumed orally then it is not poisonous. The wise physician should treat the patient of oral poisoning by snake bite. There is nothing to

commensurate with poison to neutralize the poison^[3]. Now many researches are done on snake venom. This thing is very well known by our ancient *Acharyas* that's why they use snake venom for the therapeutic purposes. Application of snake venom toxins in health and diseases have been mentioned in folk-medicine^[4]. Snake venom shows activity against various experimental pathology, animal studies such as cancer^[5&6], stroke^[7], neural trauma, Alzheimer's disease, Parkinson's disease^[8], Anti-arthritis activity.

“Ironically, the properties that make venom deadly are also what make it so valu-

able for medicine,” Jennifer Holland writes for National Geographic. “Many venom toxins target the same molecules that need to be controlled to treat disease. Venom works fast and is highly specific. Its active components — those peptides and proteins, working as toxins and enzymes – target particular molecules, fitting into them like keys into locks”^[9].

Thousands of animals are venomous — from snakes, scorpions, spiders, and bees to lizards, octopuses, fish, and snails. Out of these snakes venom is important. Researchers still haven’t studied or unleashed all the medicinal properties of snake venoms. Snake venom is seething with various toxins, proteins, molecules, and enzymes that could potentially be used to treat diseases.

Aim & Objectives:-

To study the therapeutic uses of snake venom.

Material and Methods:-

References of snake venom and its therapeutic use has been collected from *Ayurveda* texts as well as from modern text and internet. All the data were compiled, analysed and discussed through and in depth understanding of therapeutic use of snake venom which is mention in *Ayurveda* and modern science.

Table 1: Constituents of Snake venom

Non-Enzymatic Fractions	Enzymatic Fractions	Other coagulation factors
Neurotoxic polypeptide (NT)	Phospholipase A	Haemorrhagins
Cobravenom cardiotoxin	Proteases	Exo and endopeptidases
Crotalid neurotoxin	Amino acid esterases	Phosphatases
Crotalid neurotoxin		Lamino Acid Oxidases
		Hyaluronidase
		Acetyl choline esterases

Other substances in venom

Many small components like acetyl choline may be present in some snake venoms for inflicting immediate pain at the sight of injection. High concentration of Acetyl choline

Physical character of Snake venom^[10]

Colour of snake venom clear and viscous fluid of amber color, yellow color or straw color, The color of sea snake venom is colorless. The viscosity of extracted venom shows seasonal variation. Winter venom is smaller in quantity & more viscous when compared with that obtained in summer season. It is acidic reaction and specific gravity of ranges from 1.030 to 1.070.

Collection and storage of Snake venom^[11]

The venom is collected from the fangs of snake. The snake is made to bite on some object and venom is collected in glass jar. The venom can be dried to needle like crystal forms. It can be freeze dried in a container packed with ice. By this the potency of venom is kept intact.

Constituents of venom

Venom is composed of number of substances. In the snake itself it is reserved outside its circulation and physiological sphere of body, confined to venom gland and duct. So snakes also suffer from hazards of toxic effects of bite of other venomous snakes.

in mamba venom raises suspicion of immediate cardio toxic death.

There are two main types of venom:-

1) **Hemotoxins:-** Hemotoxins target the circulatory system. They prevent clotting compounds from functioning correctly, which causes uncontrollable bleeding.

2) **Neurotoxins:-** Neurotoxins target the central nervous system. They stop muscles from working, which leads to suffocation.

Therapeutic uses of snake venom (According to Modern)^[12]

The most important decision in the management of the patient bitten by a snake is whether or not given antivenom. Most commercial antivenom is of equine origin and carries a risk of anaphylactic, anaphylactoid and delayed hypersensitivity reactions. Skin testing does not reliably predict which patients will have allergic reactions to equine antivenom. False negative and false positive result may be there. Therefore, appropriate loading doses of intravenous antihistamines and cimetidine may be given in an effort to limit acute reactions. Epinephrine should be immediately available. It is almost never too late to give antivenom while signs of systemic envenoming persist, but ideally, it should be given as soon as it is indicated. Antivenom has proved effective up to 2 days after hydrophid bites and in a patient still defibrinated, weeks after bite by viperidae. In contrast, local envenoming is probably not reversible unless antivenom is given within a few hours of the bite. Intravenous route is the most effective, and it should be administered after dilution, rather than intravenous push.

Initially, the infusion may be regulated at 15-20 drops per minute. The rate can be progressively increased so that the infusion is complicated in 1-2 hours. Being with 8-10 vials and check for improvement. It is advisable to wait for 6 hours and perform investigations. If there is no significant improvement additional 5-8 vials can be given on continuing absence of improvement.

In India, antivenins are prepared from horses. Monospecific serum is prepared using the venom of a single snake. Polyspecific serum is prepared by using venom of more than one snake. This is prepared at Haffkine Institute, Mumbai and Central research Institute, Kasauli. It is in the form of a lyophilized powder of horse serum produced by immunization of horses with the venom of four snakes, namely, common cobra, common krait, Russell's viper and saw-scaled viper.

Indication for antivenom therapy may include:

Haemostatic abnormalities such as spontaneous systemic bleeding, incoagulable blood or thrombocytopenia.

Hypotension and shock, abnormal ECG or other evidence of cardiovascular dysfunction. Neurotoxicity and generalized rhabdomyolysis.

Supporting evidence of severe envenoming includes neutrophilic leucocytosis, elevated serum enzymes like creatine, phosphokinase and aminotransferases, haemoconcentration, myoglobinuria, haemoglobinuria, methaemoglobinuria, hypoxemia and acidosis.

Tender enlargement of the local lymph nodes usually indicates a systemic spread.

- It is used for research and therapeutic purposes.
- The scientific research & development with snake venom has focused on diverse physiological & biochemical processes like Coagulation cascade system, Vasoactive kinin system, Transport across cell membranes, Nerve excitation studies, Structure of phospholipids & nucleic acids.
- Therapeutically major use of snake venom is preparation of anti snake venom.
- Arvin, an active coagulant principle (amino-acid esterase) of malyanam pitviper is available for commercial use as an anticoagulant in ischemic heart diseases.

- It is useful in purification of extremely labile antihemophilic factor.
- Snake venom toxin was developed to treat high Blood Pressure.
- Medicine derived from haemotoxin is used to treat heart attack.
- Use of snake venom in breast cancer.
- Medicines derived from neurotoxins are used to treat brain injuries, strokes and diseases.
- Use of snake venom as an analgesic agent.
- Use of snake venom in medicine to treat diseases from chronic pain to cancer.
- Two venom based medication, carbotoxin and nyloxin were marketed for the treatment of pain.
- Venom of viper a russelli, a heat stable compound has been identified, which was found to produce cardio-respiratory modulation in animal. With a possible application in the cardio-respiratory related pathological condition.
- The antinociceptive activity of the venom was dose and time dependant and persisted

after neutralization with a specific antivenin.

- The Indian cobra *Ophiophagus hannah* venom induces immunomodulatory and haemopoietic stimulant activity.
- Snake venom components and their applications in biomedicine.^[13]

Activity of snake venom^[14]

1. Fibrinolytic and fibrinolytic activity of snake venom.
2. Cardiotonic antiarrhythmic activity of snake venom.
3. Antineoplastic activity of snake venom.
4. Antiparalytic activity of snake venom.
5. Anti arthritic activity of snake venom.

Method of collection of Sarpavisha:-

A hooded serpent which is stimulated and enraged, and once it emits fumes by its mouth then it should be made to bite several times on a piece of meat tied to the tip of a stick. The physician, after analyzing the strength of the poison and strength of the patient should administer the powder of the above meat to that patient suffering from poisoning¹¹.

Table 2: Therapeutic uses of Sarpavisha in Ayurveda^[15]

Sr. No	Disease	Ingredients
1	<i>Jirna jwara</i>	<i>Lodhra</i> [<i>symplocos racemosa</i>], <i>chandan</i> [<i>santalum album</i>], <i>vacha</i> [<i>acorus calamus</i>], <i>shankaraghrita</i> , <i>visha</i> mix with <i>madhu</i> and milk.
2	<i>Jirna jwar, prameha, twacharoga</i>	<i>Nikumbha</i> [<i>baliospermum-montanum</i>], <i>Danti</i> [<i>baliospermum-montanum</i>], <i>Triphala ghrit</i> , <i>madhu</i> & <i>visha modak</i> .
3	<i>Jirna jwar,</i>	(<i>visha</i> + <i>karki</i>) <i>kwath</i> + <i>Viisha</i> .
4	<i>Raktapitta</i>	<i>Visha</i> , <i>Muleheti</i> [<i>glycyrrhiza glabra</i>], <i>rasna</i> [<i>pluchea lanceolata</i>], <i>khus</i> [<i>vetiveria zizanioidis</i>] (drink by rice water)
5	<i>Dushit vrana- paka & vedana</i>	<i>Rasouna</i> , <i>bhargi</i> , <i>vishwavuti</i> , <i>mansaparni</i> [<i>teramanus labialis</i>], <i>lepa</i> is applied .
6	<i>Hikka</i>	<i>Mishri</i> , <i>visha</i> [<i>aconitum ferox</i>], <i>bargad</i> [<i>ficus bengaliensis</i>](leaves) + <i>madhu</i> and eat.
7	<i>Vamana</i>	<i>Madhu</i> , <i>visha</i> , <i>khas</i> , <i>mulethi</i> , <i>tavakshar</i> , <i>haldi</i> , <i>kudeki chal</i> . (Give vaman.)

8	Arsha-kushtha Gulma, Arma Timir, krimi, pandu, kushthaunmad, galgraha, grahabadha,	Harad+ pimappali mula+ pippali+ gajapippali+ chitrak + pushlkarmula+ kachur+ draksha + Ajamoda+ yavakshar + ajawayan+ mishri+ mulethi+ badikateri+ 1/2pal visha +1pal saindhav + Iprastha ghrita (made ghritapaka) (Drink it) Anupana = old hemanth rice .
9	Mutrakruchha	Visha+ Harad+ chitraka+ Danti + Draksha+ Haldi + Atis
10	Ashmari & Mutrajanit udavarta	Visha + Shilajatu
11	Ashmari	Gomutra + Yavkshar + Saindhav + Visha + Pashanbheda (Griend all like vajra)
12	Shulahar	Piplali mula + gomutra + visha
13	Vatajanya Andavrudhi	Erand oil + triphala + gomutra + chitraka + visha (Drink with ghee).
14	Gulma	Triphala + sarjakshar +visha
15	Plihodar, gulma	Visha + maricha + sounf + milk
16	Plihodar	Sounf + vidanga + visha + milk (drink)
17	Kushtha	Root of kathagular + visha (drink)
18	Vicharchika, Dadru, Shataru	Bhallataka+ agni samyaka + visha(masserated in cow urine)
19	Use in sterile women	Fresh juice of Bijapura + vacha + bhramhi + ghruta + visha (Drink)
20	Timira	Ghruta + madhu + sugar + visha (Anjana)
21	Shirovedana	Apamarga + mishri + visha (nasya)
22	Putinasa	Sountha + harad + visha + patha + dravanti
23	Karnashula	Sarjakshar + Saindhav + shukta + visha (insert in ear)

DISCUSSION

The snake venom are complex mixture of proteins, nucleotides and inorganic ions^[1]. The therapeutic use of snake venom is mentioned since ancient time for different diseases. Apart from poison, even in other diseases where all other measures are ineffective then snake poison can be administered^[13]. Those who wish to undergo *rasayana* therapy can also be administered snake poison regularly^[13]. According to *Ayurveda (ashtangasangraha)*, it is use in many diseases such as *jirna jwar*, *prameha*, *twacharoga*, *raktapitta*, *hikka*, *vamana*, *gulm*, *arma*, *timir*, *krimi*, *pandu*, *galgraha*, *graha-badha*, *mutrakruchha*, *ashmari*, *gulma*, *plihodar*, *kushtha*, *dardu*, *vicharchika*, etc^[12]. There are 47 formulations have been mentioned in

various diseases where the snake venom is used wisely^[13]. These 47 *kalpas* are administered through different routes like through nasal route, oral route, through skin contact.

In modern medicine, various researches are going on which emphasizes therapeutic use of snake venom in various diseases.^[14] Untreated mortality of snake venom is 100%. In modern medicine it is used in cancer, heart disease^[14]. Gomes and De has defined fibrinogenolytic and fibrinolytic activity of snake venom. fibrinolytic activity, with a possibility of use in thrombosis^[15]. It has Cardiotonic antiarrhythmic activity. It has been observed that Malayan pit viper venom has blood thinning properties and could be effective in treating stroke patients. It is found that a non protein micromolecular toxin from In-

dian king cobra venom which possesses antiarrhythmic properties at microgram level¹⁵. Use of ancrod has also been reported successive in cardiac catheterization and coronary artery bypass grafting. In antineoplastic activity of snake venom, it has been showed that Indian cobra venoms cytotoxic to Ehrlich ascites tumor cells. Therapeutic use of cobra venom is in cancer and arthritis¹⁵. Rhodopsin an arg-gly-asp containing anti-platelet snake venom peptide served as an inhibitory agent in the prevention of thrombin enhanced metastasis. In antineoplastic activity of snake venom, neurotoxins from snake venoms have been utilized in different pharmacological and biochemical studies of nicotinic acetylcholine receptors (nAChR) in the neuron and neuromuscular junction^[16]. Use of snake venom toxin to identify AChR & their antibodies permitted both the purification & understanding of pathological mechanism impairing neuromuscular transmission in Myasthenia gravis^[16]. Haemotoxins, in snake venom target the circulatory system, and typically attack the body's clotting ability & muscles. But scientist has also found ways to use haemotoxins for medicine, such as treating heart attacks & blood disorder. Other drugs have been developed from neurotoxins in snake venom, which used to treat Parkinson's & brain injuries. Due to its wide use it is necessary to do researches on snake venom as a therapeutic agent

CONCLUSION

- Snake venom toxin may serve as a starting material for a drug design to combat several patho physiological problems such as cardiovascular disorder, Neurological problems, Cancer therapy.
- Very few clinical studies are available & there is need for extensive research programs to work out the above mention areas.

- More than 40 formulations of snake venom are mentioned in *Ayurveda* for management of various diseases. The efficacy and safety of such formulations should be studied hence, researches are needed in this context , to prove the potency of formulation of snake venom.

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