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**TITLE: THERAPEUTIC VALUE OF SNAKE VENOM -INCHING TO THE  
LONGITUDINAL EXTENT: A PROSPECTIVE STUDY**

**Poonam Bhojak<sup>1</sup>, J.G.Mitti<sup>2</sup>, M.C.Patil<sup>3</sup>**

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## THERAPEUTIC VALUE OF SNAKE VENOM -INCHING TO THE LONGITUDINAL EXTENT: A PROSPECTIVE STUDY

<sup>1</sup> Poonam Bhojak, <sup>2</sup>J.G.Mitti, <sup>3</sup>M.C.Patil

<sup>1</sup> MD Scholar, <sup>2</sup>Assistant Professor, <sup>3</sup> HOD, Department of Rasashastra  
DGMAMC, RGUHS, Gadag, Karnataka, India

### ABSTRACT:

*Sarpa Visha* has been traditionally utilized by the practitioners of Indian system of medicine from time immemorial. It is that which causes complication & may be death in living being, yet due to its composition it has become an area of interest in India & other parts of the world as well. Recently, the drug development area has caught an eye due to the constituency of *Sarpa Visha*. It has been discovered that the very compounds that make venom work, may also prove useful in the treatment of several human disorders and diseases. In Ayurvedic literature many formulations have been explained which contain *Sarpa Visha* viz *Suchikabharana Rasa, Ardhanarishwara Rasa, Mrtasanjeevani Rasa etc.* for the management of ailments like *Sannipata roga, Visuchika, Swasakrchra Tivra shwasa, Pralapa, Badhirya, Mookata* etc. The present paper discusses the therapeutic importance of *Sarpa Visha*, the recent advances in the drugs derived from it & how this *Visha* not only restores health but also builds the human body to fight from chronic illness.

### Keywords:

Ailments, Ayurvedic literature, Chronic illness, Krshnasarpavisha, Management.

## INTRODUCTION

### Correspondent:

**Dr. Poonam Bhojak**

MD Scholar

Department of Rasashastra

DGMAMC, RGUHS,

Gadag,

Karnataka, India

*Ayurveda* an ancient holistic science has been practiced in our land since time immemorial. *Lord Brahma* propounded this science even before creating the living beings & for the benefit of mankind he divided the science into 8 branches such as *Shalyatantra* (Surgery), *Shalakyatantra* (Opt holmology, Otorhino-

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Laryngiologyetc.),*Kayachikitsatantra*(Innemedicine),*Bhutavidya*(Demonology),*Kaumarabhrtya* (Pediatrics),*Agadatantra*(Toxicology),*Rasayantantra*(Rejuvenation) and *Vajikaranatantra*(Virilification). The branch *Agada tantra* gives a detailed description about the *Visha*(Poison)<sup>1</sup>.

Since the *samhitha kala* the *Vishas* are mainly classified into 2 categories they are *Jangama Visha* (Animal Poison) & the other is *Sthavara Visha*(Plant & Mineral poisons).*Sarpa Visha* comes under the *Jangama Visha* dealing with the poisonous & non-poisonous snakes .In *Kashyap Samhita* (on *Agadatantra*) Sage *Kashyap* expounds to Gautama in metrical form the nature of Serpents, their poisons and cures.In *Rasashastra* the snake poison is not included in *Visha-Upavisha* group, but still it holds a definitive position in treating the emergency conditions, as an important ingredient of certain life-saving drugs. In the recent years the venom has become a base for the development of new drugs,infact it seems like laying as a stepping stone in crafting the new era of drugs.Hence furnishing the details of the *Sarpa Visha* and its recent exploitation in the medical field becomes a necessity.The study is a longitudinal approach which not only potrays the utilization and contribution of the venom in the treatment

of various life threatening diseases but also reveals as to what in this toxin could actually not kill but rather save humans in the coming years. It is a compiled work from literary to clinical implications in the contemporary science as well.For a better understanding the complete details of the *Visha* has been compiled from the Classical literature & the electronic media and further the application of its constituents like the neurotoxins,haemotoxins etc are highlighted.The part of the title ...."Inching to the Longitudinal Extent" itself signifies that how the *Visha* has evolved from the very Macro level to the Micro level and no longer starred as a Killer but serving the mankind as a Saviour.

Note:-Here *KrshnaSarpavisha* which is also known as *Garala visha*, *Darada visha*, *Jangama visha* is referred to Black cobra as the poison of the black cobra has more therapeutic efficacy than any other venomous extract.

### Methodology

The present update study and prospective study has been compiled under the following subheadings:

Method of poison extraction--This will explain the classical and recent ways of extracting the poison from the fangs of the snake.

*Shodhana of sarpavisha*--Being toxic the purification automatically applies to reduce its ill effects and enhance its therapeutic value.

Properties of the *Visha*--This will aid to a better understanding of the application of the *Visha* in Drug development to saving the life of the diseased.

Its overview in *Ayurveda* & Its insight in the present era-- This depicts its status in the gone days ,present time and the coming era.

How it evolves from toxin to drug--from macro to micro level--This will give a detailed description as to what in this toxin will make it a life saviour.

Lastly Discussion and Conclusion will be wrapping the key notes of the study.

### Method of poison extraction

An oyster shell which is smeared with oil is covered with palm leaf & fastened tight. This shell is tied to one end of a sufficiently long stick which is brought near to the cobra. On reacting to this act, the cobra lets out the poison via the fangs, into the shell by biting the palm leaf. The poison which is exudated into the shell is then collected carefully, once the palm leaf covering is removed. This act is repeatedly done to extract more poison.

Other than this the professionals & the snake-charmers catch the cobra tactfully & squeeze the poison from its fangs.

### *Shodhana of sarpavisha*

About 1/4<sup>th</sup> part Mustard oil is squeezed in a *shukti*. 1 part *Sarpavisha* is poured in the same & then *Sarshapa taila* (one forth quantity of *Sarpavisha*) is mixed along. This is placed under the sunlight. Once this dries and turns to yellow crystal-consistency it is carefully collected, preserved & used for medicinal purposes.

### Properties

In *Jangama vishas* only snake venom is found used. *Krshnasarpa visha* is *Tridoshaghna*, *Agnideepaka*, *Sannipatahara*. It is *Tikshna* & *Ushna* in *Guna*. It is very fatal; it is *Pittaprapakopaka* & *Dahakari*. Besides these it is useful in loss of consciousness at the time of death, by doing the *Kapha vilayana* because of the *Tikshna* & *Ushna guna* it alleviates dyspnoea & kapha accumulation; it is used during the collapsing state of a heart attack & in conditions where the hands & legs become cold. It is useful in complicated state of *Visuchika*; It stimulates the heart in *Sitanga-Sannipata Jvara* & also in all emergency conditions caused due to *Sannipata*. When all the emergency medicines fail to restore the patient, *Krshnasarpa Visha* is used carefully.

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Although the utility of *Krshnasarpa Visha* is vast in the medical conditions it still has its limitations. It is not applicable in very young, very old, pthisis condition, in coma & syncope, emaciation & hemorrhagic disorders.

The **dosage** of the *Krshnasarpa Visha* is not separately given but the medicines prepared with this are given in the dose of a small mustard size, in which the quantity The table no.1 shows various formulations mentioned in our classics which contains *SarpaVisha*.

of the poison that goes into the system is about 1/5<sup>th</sup> of a milligram<sup>2</sup>.

### **The Visha in Ayurveda**

Few classical preparation contain *Krshnasarpa visha* such as *Maha Tarunarka Rasa*, *Suchikabharana Rasa*, *Visuchidhvamsana Rasa* etc. As per classics, these are administered with *adraka swarasa* as *anupana*.

**Table no.1- Table showing the list of formulations containing Krshnasarpavisha.**

Sl.no	Formulation	Ingredients	Quantity/dose	Indications
1.	<i>Suchikabharana Rasa (Prathama) (R.T.24/549)</i>	<i>Krshnasarpavisha, Parada, Gandhaka, Nagabhasma, Vatsnabha, Pitta of Mayura, Varaha, Matsya, Chaaga</i>	<i>Sarpavisha-2 masha, Sarshapamatra</i>	<i>Sannipata roga, Visuchika.</i>
2.	<i>Suchikabharana Rasa (Dwithiya) (R.T.24/563)</i>	<i>Krshnasarpavisha, Shankh Vatsanabha, Hingula, Panchapitta</i>	<i>Sarpavisha-1 masha Sarshapamatra</i>	<i>Swasakrcha, Sarpa visha</i>
3.	<i>Visuchidhwamsana Rasa (R.T.24/566)</i>	<i>Krshnasarpavisha, Vatsanabha, Hingula, Parada, Gandhaka, Makshika, Tankana, Nagara, Nimbuswarasa</i>	<i>Sarpavisha-1 masha Sarshapamatra</i>	<i>Visuchika, Sheeta padakara</i>
4.	<i>MrtaSanjeevani Rasa (R.T.24/571)</i>	<i>Krshnasarpavisha, Vatsanabha, Hingula, Parada, Gandhaka, Makshika, Tankana, Haratala, Pitta of Mayura, Varaha, Matsya, Chaaga</i>	<i>Sarpavisha-1 masha Sarshapamatra</i>	<i>Tivra shwasa, Pralapa Badhirya, Mookata, Himagaatra (During Mrta Avastaha)</i>
5.	<i>MahaTarunarka Rasa (Basavarajiyam. Chap 1)</i>	<i>Krshnasarpavisha Gandhaka Tankana, Abhrak, Vanga, Raktachandana, Matulungaswarasa</i>	<i>4mg</i>	<i>Sarvajvara</i>
6.	<i>KrshnaSarpa Masi (Su. Chi. 9/17)</i>	<i>KrshnaSarpa bhasm, Vibhitaka Taila</i>	<i>-</i>	<i>This bhasma form of the Visha Cures all kinds of vitiligo</i>

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In *Krshnasarpa Masi* the head, tail and intestines of the *Sarpa* are burnt in a closed *Sharava* and the *Bhasm* is obtained. Besides the above there are few other *Yogas* in *Rasa* which contains the *Visha* and yet are vividly practiced in our nation.

*Yogas* like *Aghore Nrisingha* containing *Tamrabhasm*, *Louhabhasm*, *Vangabhasm*, *Swarnamakshika*, *Parada*, *Gandhaka*, *Manas hila*, *Trikatu* and *Krshnasarpavisha* has been used by Dr. Sen in chronic malarial fever as mentioned in *Indian Materia Medica*. It is particularly used in the cases where the liver shows tendency to *Cirrhosis*. In fact Malarial cases which do not yield to the combination of *cinchona febrifuge* and *arsenic* are said to yield to this prescription. *Kalanala Rasa* containing *Trikatu*, *Louhabhasm*, *Tamrabhasm*, *Gandhaka*, *Haratala* etc. is practiced in

continued fever complicated with coma, delirium, cardiac and respiratory weakness etc. *Ardhanarishwara Rasa* containing *Parada*, *Gandhaka*, *aconite root* etc. is widely used as a snuff. Many people believe in its efficacy. Dr. Sen in the *Indian Materia Medica* says that there are many other formulae containing different proportions of Snake venom. The Venom is said to be inert if administered by the mouth. It is inert as regards producing fatal results, for it is thrown out with the stools, because it is a stimulant to the liver and glands of the alimentary tract. He says that there are hundreds of cases where the Venom treatment has produced highly satisfactory results. Even *Acharya Sushrutha* in the *Chikitsa of Udara* mentions the use of the venom with the coconut water<sup>3</sup>.

**Table no.2--Table showing few studies done on Snake venom in India<sup>4,5,6,7</sup>.**

Sl.no	Few Research work carried on Snake venom in India
1	Therapeutic uses of Snake venom components used in Blood clotting test by Payel & Debashish Bhattacharya, Bio-Informatics dept, CSIR, Kolkata.
2	Snake venom for Drug resistant human immunodeficiency virus, by Dr. Uma, Dr. Subramaniam, Dr. Meenakshisundaram (Mar-Apr 2009)
3	Snake Venom - An Anti Arthritis Natural Product Laboratory of Toxinology & Experimental Pharmacodynamics, Department of Physiology, University of Calcutta. (2010)
4	Therapeutic potential of snake venom in cancer therapy by Dr. Vyas, Dr. Bhatt (Feb 2013)

Besides the above studies reference in the book *India Materia Medica* vol-2 clearly flaunts the description

of exploiting the venom in variable diseases. It is said to afford a means of diagnosing *Cancer-formaculidis test*

which depends upon the activation by the venom of the haemolytic action of serum in the deviation of complement test and is applicable if and only if the serum of persons suffer from malignancy. Also recommended in inoperable Ca on the basis of experiments carried out by Calamette and his disciples. In Botulism & in Plague the venom injections proved to be very valuable. In the treatment of epilepsy, the venom is given in the doses of 1/200 gr. by hypodermic injections and if symptoms do not disappear another dose of 1/25 gr. is recommended. It is recently being used in Western medicine in the treatment of epilepsy, haemophilia, chorea, blackwater fever etc. though there is absence of rational basis for its use in the treatment for which it is given by injection by the practitioners of the Western medicine. Dr. Shafa-ul-imraz in the book *Indian Materia Medica* has stated that the blood of *Krsnasarpavisha* is the best application over the leucodermal patches<sup>8</sup>.

### **An Insight to the Venom in the present era**

Venom based medicines aren't new. Besides the Sanskrit literature it has its history way back dated to the 67 B.C. in Rome. Cobra venom, applied for centuries in traditional Chinese and Indian medicine, was introduced to the West in the 1830s as a homeopathic pain remedy. John Henry

Clarke's *Materia Medica*, published around 1900, describes the venom as alleviating many ills, even those caused by venom. "We should always endeavor to use the same drug to cure as produced the symptoms," the author wrote. Clinical applications of carefully diluted cobra venom included "Angina pectoris, asthma, dysmenia, hay-fever, headacshe, infections of oesophagus, spasmodic stricture of Ovaries, infections of throat." But be careful, it was noted: "The curative dose [is] just within the limit of the pathogenic dose"<sup>9</sup>.

In the West science of transforming venom into cures took off in the 1960s, when an English clinician named Hugh Alistair Reid suggested that the venom of the Malayan pit viper might be used against deep-vein thrombosis. He'd discovered that one of the snake's toxins, a protein called *ancrod*, saps a fibrous protein from the blood, preventing clotting. Arvin, a clot-busting drug derived from pit viper venom, reached clinics in Europe in 1968. Today Arvin has been replaced by other viper venom anticoagulants.

The Brazilian pit viper's venom led to the development in the 1970s of a class of drugs called ACE inhibitors, now widely used against hypertension. Eventually a synthetic version of the Venom made it to human trial, and in 1975 the first oral drug

for hypertension, *captopril*, was approved for use. The ACE inhibitor class of drugs pioneered by *captopril* now treats tens of millions worldwide, with multibillion-dollar sales.

In 1992 an endocrinologist named John Eng at the Bronx/James J. Peters VA Medical Center in New York identified a component in Gila venom that controls blood sugar and even reduces appetite. *Exenatide*, a drug derived from the venom in their saliva, works like a natural hormone, stimulating cells to deal with sugar overload but remaining inactive when sugar levels are normal. It even helps diabetics produce their own insulin and lose weight.

### **Toxin to drug--Aping from Macro to Micro level:**

Snake venoms are made up of hundreds of different types of peptides, enzymes, and toxins. There are two main types of venom—haemotoxins and neurotoxins. Hemotoxins target the circulatory system. They prevent clotting compounds from functioning correctly, which causes uncontrollable bleeding. Neurotoxins target the central nervous system. They stop muscles from working, which leads to suffocation. On the other hand the medicines derived from hemotoxins are used to treat heart attacks and blood

disorders. These medicines are used as a treatment for minor heart attacks and/or severe chest pain. These medicines work by helping to dissolve (and/or prevent the formation of) blood clots. Testing is currently underway for the treatment of stroke with a venom protein taken from the Malayan pit viper. So far, medical trials indicate that small dosages of the venom help to dissolve stroke-related blood clots and prevent new clots from forming. Medicines derived from neurotoxins are used to treat brain injuries, strokes, and diseases such as Alzheimer's and Parkinson's.

Spangler(1925) took the degree of eosinophilia produced as a guide to dosage and frequency of administration of the proteins. Usually the highest rise in the percentage of eosinophils following venom protein injection in the doses of 1/400 to 1/50 gr. occurs by the 2nd or 3rd day. by the 5th to 7th day eosinophils would have dropped to 4% or less. By continuing the injections, the rise of eosinophils gradually becomes less, and finally does not exceed normal limits and the patient is non-specifically desensitized.

Experimental work done by Chopra(Chopras "I.D. of I" pp439-445) and his Co-workers has shown that the Venom is not absorbed in the GI tract. It is therefore difficult to see how the Venom



given by the mouth can produce by the practitioners of indigenous medicine. Besides its irritant effect on the Gut, it does not appear to produce any other marked action. From the experimental data obtained that it has no much effect over the myocardium or on the accelerator nerves of the heart but it undoubtedly produces a small amount of its stimulant action on the Vasomotor centre in the medulla when given intravenously. This effect is not produced when the drug is given by the mouth<sup>10</sup>.

As regards to the action of the Venom on the blood it not only affects the respiratory property of blood, but likewise its coagulability and at the same time causes the disintegration of RBC or acts on the RBC as their solvent.

Researchers at the Universidad Central del Cariba in Puerto Rico are studying venom proteins from the African mamba snake, one of the most poisonous snakes in the world. The scientists are most interested in learning how the venom proteins are able to latch on so tightly to both nerve cell receptors and receptors found on the surface of the brain.

Researchers in France have determined two molecules isolated from black mamba venom (referred to as mambalgin-1 and

mambalgin-2) are as effective as morphine in the elimination of pain<sup>11&12</sup>.

Therefore, Snake Venom containing more than 20 different compounds, a complex mixture of proteins & polypeptides, enzymes, and various other substances have very specific effects on various biological functions including blood coagulation, blood pressure regulation, transmission of the nervous or muscular impulse and should be developed for use as pharmacological or diagnostic tools or even useful drugs.

In fact, there are already two drugs on the market that are based on snake venom proteins and are used to prevent heart attacks. One drug called *eptifibatide*, is a modified rattlesnake venom protein. The other is called *tirofiban* and is based on a venom protein from the African saw-scaled viper. Both drugs have been used since 1998 to treat people having minor heart attacks or those with chest pain indicating they are likely to suffer a heart attack.

Stefan Hailey of the University of Delaware and his colleagues in a paper published recently by *Toxicon*, report how a protein called *eristostatin*, which can be extracted from the venom of the Asian sand viper, helps people's immune systems fight malignant melanoma. Dr

Hailey and his colleagues used a technique called atomic-force microscopy to study the interactions between melanoma cancer cells and *eristostatin*. This technique allows the force required to pull the two apart to be measured precisely, to see whether there is a genuine attraction—which he found that there is.

*Crotoxin*, a protein from the South American rattlesnake, though not yet approved for use, may one day be employed to treat cancers. *Crotoxin* seems particularly attracted to cancer cells. One portion of the molecule recognizes a protein on the cell's membrane, and links

to it. The other portion damages the membrane, triggering a mechanism called apoptosis which causes the cell to kill itself. Celtic Biotech, based in Dublin, is running a series of tests using this molecule on cancer patients at the Georges Pompidou European Hospital in Paris.

In our country the clinical efficacy of the *Visha* has been proven from time to time and presently the therapeutic efficacy of Snake venom has been evaluated with reference to its *Anti Arthritic effect, Drug resistant human immunodeficiency potential, Anti-Cancer perspective, in Blood clotting test* etc.

### DISCUSSION

A greatly feared toxin, Snake Venom, happens to be of a very potential therapeutic value due to its components. Ayurveda Classics very clearly mentions the innumerable yogas for the practice of this toxin in saving the unhealthy and diseased.

Not only covering the pages in the Literary area but also clinical utilization by the practitioners to the account of the importance of this *Visha*, which is fading away in the present should be restored.

The recent decade of the drug development investing pricelessly in obtaining

valuable drug from the venom shows the hunger and the potential of this poison which not only protects but also restores life.

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, 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.

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As already mentioned in the classics its various applicative modalities and its recent exploitation it becomes very necessary for the updation of its implications and if in case any further interventions are required for the advancement of the same.

As *Acharya Charaka in Sutrasthana* 1/126 clearly states that “even a sharp poison becomes the best drug by proper administration....” now it is high time to pull the socks and hitch our wagon to the stars.

### CONCLUSION

In various parts of the world works are being carried out to develop drugs from the constituents of this toxin. Being already explained in the Ayurvedic classics about its significance in restoring health, it is high time to evaluate the same. Scientists have long recognized that the way toxins work makes them useful targets for drug development. But the fact that they're harmful poses a problem. This means that drug developers have had to modify toxins to retain their potency and make them safe for drug use. 'So rather than developing synthetic compounds into drugs, our finding suggests one could screen these harmless proteins against whatever target one is interested in. This means using natural products.'

It's time to explore our traditional medicine against chronic diseases, not only for health benefits but also for the preservation and documentation of our ancestral scientific knowledge and culture to make the world a better living place. Venom, then, is proving to be a trove of useful molecules. At a time when drug companies are struggling to develop new products, a novel source of raw materials that have been road-tested by natural selection, and merely need to be subverted from their original purposes rather than created afresh, must be welcome. It is not turning base metals into gold, as Paracelsus and his kind once attempted. But as a transformation of matter, it is surely a far more valuable trick.

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