



## Review Article

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### A REVIEW ON SNAKE VENOM: AN UNREVEALED MEDICINE FOR HUMAN AILMENTS: GREAT SCOPE FOR PHARMACEUTICAL RESEARCH

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#### ABSTRACT

Snake venom is the poisonous secretion (saliva), ejected from the poison apparatus of a poisonous snake, during the act of biting. Venoms of the different species of poisonous snakes are complex mixture of a number of proteins, toxic substances or toxins, peptides, enzymes, and non-protein inclusions in varying proportion. Snake venom is harmless if ingested in liquid or crystal form after drying through mouth and it will be excreted unchanged. It produces toxicity only if contacted with blood. This is very well understood by *Ayurveda*. Therapeutic uses of snake venom in various diseases have been explored by *Acharya Vagbhata* in 48<sup>th</sup> chapter of *Uttartantra* of *Ashtanga Sangraha*, i.e. "*Vishopayogiya Adhyaya*." Forty-seven different Formulations have been mentioned by *Acharya vagbhata* in which snake venom is pertinently used with other Ayurvedic herbal drugs. Since last two decades, various researches explore the therapeutic potential of snake venom in various diseases like diabetes, high blood pressure, stroke, Neurological diseases such as Parkinson's disease and Alzheimer's disease, Cancer (various types), aging, skin diseases, excessive bleeding condition etc. Current review sums up the therapeutic use of snake venom which is mentioned in *Ayurveda* as well as in contemporary science which provide new thoughts in field of pharmaceutical research where the use of snake venom is beautifully understood by our ancient Acharyas.

**Keywords:** Snake venom, Ayurveda, Pharmaceutical research

#### INTRODUCTION

Snake venom is the poisonous secretion (saliva), ejected from the poison apparatus (modified parotid gland) of a poisonous snake, during the act of biting. <sup>1</sup> Venoms of the different species of poisonous snakes are complex mixture of a number of proteins, toxic substances or toxins, peptides, enzymes, and non-protein inclusions in varying proportion. <sup>2</sup> It is a unique physiological product of nature having mixtures of different substances, which are highly specific and have great affinity for different crucial and essential functional organization of cells and tissues. <sup>3</sup>

It is over sixty years since it was first realized that the physiologically active components of snake venoms might have therapeutic potential. <sup>4</sup> But therapeutic use of snake venom in various diseases has been beautifully mentioned by our Ancient *Acharyas*, where they used snake venom as medicine. In *Charak samhita*, cobra venom has been said to be useful in *Dushyodara* and *Jalodara* (Ascities). <sup>5</sup> *Sushruta* and *Vagbhata* also mentioned similar use. In the *Unani* system of medicine, cobra venom has been used as a tonic, aphrodisiac, hepatic stimulant and for revival in collapsed conditions. Venoms of viper, *Crotalus*, cobra and *Lacasis* are also routinely used in homeopathic medicine. Chinese physicians use snake venom products routinely to treat stroke and view them as effective and relatively safe. <sup>6</sup> The dangerous effect of snake venom on humans is well known, but now a day's new revelation has been discovered, claiming that toxins in snake venom could potentially open doors to cutting-edge drugs being able to treat

severe medical conditions, such as diabetes, high blood pressure, stroke, Neurological diseases such as Parkinson's disease and Alzheimer's disease, Cancer (various types), aging, skin diseases, excessive bleeding condition etc. <sup>7</sup>

Snake venom is harmless if ingested in liquid or crystal form after drying through mouth and it will be excreted unchanged. It produces toxicity only if contacted with blood. <sup>8</sup> This is very well understood by our ancient *Acharya*. So that *Acharya Vagbhata* used snake venom in various diseases which has been elaborated in 48<sup>th</sup> chapter of *Uttartantra* of *Ashtanga Sangraha*, i.e. "*Vishopayogiya Adhyaya*." <sup>9</sup> With this background, an attempt has been made to critically review this chapter focusing on how *Acharyas* used snake venom as a medicine in various diseases in scientific manner in the light of contemporary science.

The present study was aimed for compilation of the description of therapeutic uses of snake venom in various diseases mentioned in *Ayurvedic* classics as well as to explore researches and scientific studies regarding uses of snake venom in contemporary science.

Classical literature of *Ayurveda* as well as modern medical science on the subjects of toxicology and therapeutic uses of snake venom from the library of Mahatma Ganddhi Ayurveda college hospital and research centre, salod (H) Wardha were explored for this study. The Internet services of the MGACH &RC, salod (H) Wardha library IT center were also used. The data

Obtained were critically analyzed and presented.

This was purely a literary study wherein Conceptual study comprises of the review of the available literature in the ancient classical texts emphasizing the therapeutic uses of snake venom. Literature in modern science concerned with this concept, scientific journals, dissertations, research paper etc. were scrutinized and analyzed to conquer this concept which has been mentioned far long time ago by Ayurveda.

## CONCEPTUAL REVIEW

As per the Ayurvedic concepts, snake venom is not only used as therapeutic agent in poisonous cases where antipoisonous drugs are found to be ineffective but also used in various disease conditions. *Acharya vagbhata* mentioned the specific procedure to procure snake venom.

A hooded snake (cobra/viper) should be made to bite many times on a piece of meat fastened to the tip of stick. After deciding that sufficient amount of snake venom get entered into piece of meat, it should be dried up under sunlight in sufficient dry weather. Dried piece of flesh then get powdered and should administer to that poisoning patient who has not been cured by any other anti-poisonous medicines.<sup>10</sup> Even in other diseases when all other methods of treatment fail, snake venom can be administered in the form of dried flesh powder. It can also be used for rejuvenation purpose.<sup>11</sup> It is administered to those person who has been purified by the use of ghee and who has undergone purification therapies, who is partaking only healthy foods, who is pure in mind should be administered snake venom after sunrise and during winter and spring seasons generally, and in summer for emergency conditions only.<sup>12</sup> It should not be administered during rainy season and on cloudy days, not to be administered who are in anger, suffering from diseases of pitta, to the impotent, the king, the twice born (*bramhana*), who is troubled very much from hunger, thirst, exertion, sun, light, long walk, or diseases, the pregnant woman, children, the aged, those who are dry, (emaciated greatly) and those suffering from diseases of vital organs.<sup>13</sup> If one becomes habituated to use of counter poison, even then one should be cautious about forbidden things and avoid the use of pungent, sours, oils, salts, day sleep, sunlight fire, and dry foods especially *Ajirna* (Indigestion).<sup>14</sup> These are special precautions has been mentioned by *Acharya Vagbhata*, while using snake venom as a medicine. Later on, various yogas (formulations) containing in which dried powder of flesh containing snake venom used in various diseases has been described which are as follows. (Table 1)

## Therapeutic use of snake venom in various diseases as per modern approach

### Fibrinogenolytic and fibrinolytic activity of snake venom

It has been proved through various in vitro and in vivo studies that, snake venom has fibrinogenolytic and fibrinolytic activity. This therapeutic action of snake venom can widely use in treatment of stroke, Deep vein thrombosis, cerebral infarction, myocardial infarction, peripheral atrial thrombosis, priapism, sickle cell crisis.<sup>16</sup>

### Antiplatelet activity of snake venom

Many venoms with procoagulant properties find application in the diagnosis of clotting abnormalities, and most of the clotting pathways can be assayed by some venom component, e.g. "reptilase time" (*B. atrox*) assays for thrombin inhibitors<sup>25,17</sup>, "Ecarin" (*E. carinatus*) and "taipan time" (*Oxyuranus scutellatus*) assays for prothrombin, and Russell's viper

(*Daboia russelii*) venom assays for factor X and for monitoring anticoagulant therapy<sup>26,18</sup>

### Cardiotonic and antiarrhythmic activity of snake venom

It has been observed that, Malayan pit viper has blood thinning property and could be effective in stroke patient. From a study of 500 stroke patients, 42% who were given the snake venom drug (Ancord) within 3 hour of stroke. Mayberg & Fulan reported that onset regained significant functioning compared to 34% who got placebo. Role of ancord in patients with heparin induced thrombocytopenia thrombosis has been clearly established. Ancord has also been reported successive in cardiac catheterization coronary bypass grafting. One study proposes that, toxin from Indian king cobra possess antiarrhythmic property at microgram level.<sup>19,20,21</sup>

### Antineoplastic activity of snake venom

Various in vitro and in vivo studies prove the anticancer activity of snake venom which has been extracted from various varieties of snakes. Indian krait *Bungurus caeruleus* venom has been evaluated against Ehrlich ascites carcinoma (EAC) in Balb C mice. This venom at various dose levels inhibited tumor cell growth, both in vivo and in vitro. This cytotoxic anticancer activity of venom was also observed by MTT assay and confirmed by <sup>3H</sup> thymidine incorporation.<sup>22</sup> Phospholipase A2 was isolated from *Bothrops newweidii* venom which produced cytotoxic activity on B16 F10 melanoma cell.<sup>23</sup> It is observed that Indian cobra *Naja naja* venom was cytotoxic to Ehrlich ascites tumor cells.<sup>24</sup> Cytotoxic P4 was isolated from *Naja nigricollis* venom, which produced cytotoxic effect on Wehi-B leukemia cell.<sup>25</sup> Various researches is going on to prove the antitumor activity of various constituents of different varieties of snakes on various animal models. Malignant brain and spinal-cord tumors (gliomas) are not curable by surgery as they invade the surrounding brain tissue without clear boundaries, making removal impossible. Disintegrins, like contortrostatin from American copperhead (*Agkistrodon contortrix*) venom, prevent cells from sticking together, and inhibit their interaction with surrounding tissue, resulting in a blockage of cell motility and invasiveness<sup>26</sup>. It has been demonstrated that fibrinogen) plays separate and distinctive roles at different stages of tumor growth and dissemination. At the primary site, fibrin deposition around the tumor could form a protective barrier, but also limit tumor progression. On the other hand, fibrin deposits formed by metastatic tumor cells may help disseminating these tumors.<sup>27</sup>

### Antiparalytic activity of snake venom

Notexin, a snake venom phospholipase is now considered to be effective in the treatment of ptosis, as it attacks motor nerve terminals and muscular cells. It was found that the satellite cells between the muscle cells contain mostly normal mitochondria. When skeletal muscle is damaged by notexin, satellite cells divide to form replacement muscle cells and because cell regeneration is accompanied by mitochondria regeneration, the mitochondria in new muscle cell are in much better shape than in old cells. As the ptosis is a result of muscle weakness in the small easily accessible levator muscle of the eyelid, so notexin therapy is an ideal therapy for such disease entity.<sup>28</sup> Myasthenia gravis (MG) is recognized as an autoimmune disorder in which antibodies to acetylcholine (ACh) receptor lead to impairment of neuromuscular transmission. The use of <sup>125</sup>I labeled snake venom toxin to identify AChR and their antibodies ultimately permitted both the purification and characterization of AChR and an understanding of the pathological mechanism impairing neuromuscular transmission in myasthenia gravis (MG). Anti-AChR antibodies have been demonstrated to be the principle agents in pathogenesis of MG, and their determination allowed definite diagnosis of MG.<sup>29</sup>

#### Antiarthritic activity of snake venom

Snake venom has been used to explain the pathophysiology of several experimental model of arthritis. An animal experiment confirmed that the Indian monocellate cobra (*Naja kaouthia*) venom significantly antagonized the changes in the arthritis bio markers where arthritis was induced by Freund's complete adjuvant. Anti-arthritis activity of cobra venom (doses selected in terms of LD50 values) was confirmed through physical parameters (paw and ankle diameter), urinary markers (hydroxyl proline, glucosamine), biochemical markers (acid & alkaline phosphatase), molecular marker (IL10), liver anti-oxidant parameters (catalase, glutathione, etc.) and histopathological observations.<sup>30</sup> The anti-arthritic and anti-inflammatory activity of NN-32, a cytotoxic protein from Indian spectacle cobra snake (*Naja naja*) venom has been studied in Freund's complete adjuvant (FCA) induced arthritis and carrageenan induced anti-inflammatory model. NN-32 treatment showed significant decrease in physical and urinary parameters, serum enzymes, serum cytokines levels as compared to arthritic control group of rats. NN-32 treatment recovered carrageenan induced inflammation as compared to control group of rats. The findings showed that the cytotoxic protein NN-32 shares anti arthritic and anti-inflammatory activity and thus NN-32 may target complex pathophysiological processes like cancer- arthritis inflammation.<sup>31</sup>

#### Analgesic activity of snake venom

Many types of venom have analgesic properties. Hannalgesin, novel analgesic toxin which was isolated from the venom of king cobra (*Ophiophagus Hannah*). Using the hot-plate test, it is shown that this neurotoxin increased latency time dose-dependently when administered i.p. similar analgesic action was observed when it was administered p.o or i.c.v. The rota-road performance, which is a good index for neurological deficits including sedation, muscle relaxant and impairment of motor activity and coordination, was not significantly affected in the dose range of 16-32 ng/g that caused analgesia.<sup>32</sup> Two venom based medications, cobroxin and nyloxin were marketed for the treatment of pain, arthritis and other disorders but were banned by US food and drug administration in 1970 because of ineffectiveness.<sup>33</sup>

#### Antibacterial activity

Many venoms have antibacterial properties. It was found that, two antibacterial bioactive L-amino acid oxidase components in King brown (*Pseudechis australis*) venom that were 70 and 17.5 times more effective in vitro than tetracycline, a drug of choice for *Aeromonas* infections.<sup>34</sup> Antibacterial and antiparasitic effects of the venom of the Marajo lancehead (*Bothrops marajoensis*) were shown to be caused by PLA2 and L-amino acid oxidase toxins.<sup>35</sup>

#### Antiviral activity

Antiviral activity of snake venom has been demonstrated through various researches, although no commercialization of any of these compounds has yet taken place. The venom of the tropical rattlesnake (*Crotalus durissus terrificus*) from Brazil contains anti-measles virus effects that may be of potential clinical interest.<sup>36</sup> The purified PLA2 venom neurotoxin "taipoxin" from the coastal taipan (*O. scutellatus*), Nigexine from the African black necked cobra (*Naja nigricolis*) and a basic PLA2 from the Mozambique spitting cobra (*Naja mossambica*) have been shown to have potent antiviral activities against HIV-1 virus.<sup>37</sup>

#### Antihypertensive activity

A number of snake venoms create a transient condition of depressed blood pressure in envenomed patients. Angiotensin-converting enzyme (ACE) inhibitors were developed from a bradykinin-potentiating enzyme isolated from the venom of the Brazilian pitviper (*Bothrops jararaca*) and approved in 1979 by the FDA<sup>38</sup> to treat high-blood pressure and heart disease. They work by blocking the switch between angiotensin-I and angiotensin-II, the latter being a vasoconstrictor. These inhibitors are now prescribed worldwide and have saved the lives of millions.

#### DISCUSSION

Snake venoms have the highest toxicity potential that makes them an attractive option to use in various diseases. Evolution of modern high throughput screening systems has developed to recognize and extract new therapeutic substances from biotoxins such as venoms of several snakes that show promising potential in treating various diseases. Snake venoms are the complex mixture of several biologically active proteins, enzymes, peptides and organic and inorganic compounds. Venom from snakes is an important agent which can be used in the treatment of cancer, arthritis, thrombosis, multiple sclerosis, pain, neuromuscular disorders, blood and cardiovascular disorders, infections and inflammatory diseases.<sup>39</sup>

The use of snake venom as a medicine was known to man since ancient time. Various scattered references have been found in different Ayurvedic texts where snake venom has been used as a medicine. Therapeutic uses of snake venom in various diseases have been explored by *Acharya Vagbhata* in 48<sup>th</sup> chapter of *Uttartantra* of *Ashtanga Sangraha*, i.e. "*Vishopayogiya Adhyaya*." Forty-seven different Formulations have been mentioned by *Acharya vagbhata* in which snake venom is pertinently used with other Ayurvedic herbal drugs.<sup>40</sup>

There are different routes of administration of these formulations have been mentioned which includes oral rout, external application, oral rout followed by external application, *Anjan* (Collyrium), *Nasya* (Nasal Rout), *Karnpuran*, *Gandush*. Different forty-seven formulations have been used in various diseases which includes *Jimajwara* (chronic fever), *Prameha* (Diabetes), *Twak vikar* (Skin disorders) *Vicharchika*, *Dadru*, *Kitibh* (Skin diseases), *shwitra* (Leucoderma), *Pundarika* (pathognomic pundarika (a type of leprosy), *Raktapitta* (Bleeding disorders), *Shwas* (*dyspnoea*) and *Hikka* (*Hiccups*), *Chhardi* (vomiting), *Durnama* (piles), *Gulma* (Abdominal tumor), *Arma* (Pterygium), *Timira* (blindness), *Krimi* (worm infestation), *Pandu* (Anaemia), *Galagraha* (Sore throat), *Graha* (Possession by evil spirits, *Unmad* (Insanity), *Mutrakrichhra* (dysurea), *Udawarta* (upward movement inside the abdomen), *Ashmari* (Renal calculi), *Pittashmari* (bile stones), *Shula* (colicky pain), *Vatanda* (Scrotal enlargement), *Pleeharog* (Enlargement of spleen), *Nashtashukra* (loss of semen), *Putinasa* (Bad smell of the nose), *vachah skhalnata* (stammering), *Vedana-Pakiyukta Vran* (Ulcers with pain and pus), *Kushtha* –Mudhgarbh (Applied on the abdomen eases the obstructed foetus (possessing abnormal Presentations) to pass through the parturient canal), *Timira* (blindness), *Kach* (, *Shuklarma* (pterygium), *shukla*, *pilla* and *kacha* (Diseases of cornea, and sclera, blindness), *Naktandhata* (nourishing the eye in case of chronic night blindness), *Shirshula* (Headache), *Palitya* (Gray hairs), *Arunshika* (Ulcers on Scalp), *Karnshula* (Severe pain in ear), *Mukhrog* (Disorders of Mouth).

Table 1: Various yogas (Formulations containing snake venom)<sup>15</sup>

Sr. No.	Yoga (formulation containing snake venom)	Indication with rout of administration of formulation
1	Snake venom with <i>Lodhra</i> ( <i>Symplocos racemosa</i> Roxb.), <i>Chandan</i> ( <i>Santalum album</i> Linn.), <i>Vacha</i> ( <i>Acorus calamus</i> Linn.), mixed with sugar, ghee, honey and milk.	Best to cure <i>Jirnjwara</i> (chronic fever) (oral)
2	Snake venom with <i>Nikumbh-Trivrutta</i> ( <i>Operculina turpethum</i> Linn.), <i>Triphala</i> [Powder of <i>Haritaki</i> ( <i>Terminalia chebula</i> ), <i>Bibhitak</i> ( <i>Terminalia belerica</i> ) and <i>Aamalaki</i> ( <i>Emblica Officinalis</i> ) mixed with honey and ghee	Cures <i>Jirnjwar</i> (chronic fever), <i>Prameha</i> (Diabetes), <i>Twak vikar</i> (Skin disorders) (oral)
3	Snake venom mixed with the juice (decoction) of <i>Chitrak</i> ( <i>Plumbago zeylanica</i> Linn.), and <i>Karkatshrungi</i> ( <i>Pistacia integerrima</i> Stewart ex Brandis)	<i>Vishamjwar</i> (intermittent fever) (oral)
4	Snake venom with <i>Yashtimadhu</i> ( <i>Glycyrrhiza glabra</i> Linn.), <i>Rasna</i> ( <i>Pluchea lanceolata</i> C.B.Clarke), <i>Ushira</i> ( <i>Vetiveria zizanioidis</i> Linn), and <i>Utpal kandaka</i> ( <i>Nelumbo nucifera</i> Gaertn) consumed with <i>Tandulodaka</i> (rice-wash)	Best for <i>Raktapitta</i> (Bleeding disorders) (oral)
5	Snake venom, <i>Rasanjana</i> (Extract of <i>Berberis aristata</i> ), <i>Bharangi</i> ( <i>Clerodendrum serratum</i> ), <i>vrushchikali</i> , <i>mahasaha-Mashaparni</i> ( <i>Phaseolus triloba</i> )	Good for <i>vedana and paki Vrana</i> (Ulcers with pain and pus.) (External application)
6	Snake venom, sugar, <i>kshirataru prawal</i> (leaves of <i>Panchvalkala</i> trees) macerated with honey.	By licking it cures <i>Shwas</i> ( <i>dyspnoea</i> ) and <i>Hikka</i> ( <i>Hiccups</i> ). (oral)
7	Snake venom, <i>Yavakshar Ushira</i> ( <i>Vetiveria zizanioidis</i> Linn), <i>Yashtimadhu</i> ( <i>Glycyrrhiza glabra</i> Linn.), <i>Haridra</i> ( <i>Curcuma longa</i> Linn.), <i>kutaj bark</i> ( <i>Holarrhena antidysenterica</i> Linn.) mixed with honey.	Cures <i>Chhardi</i> (vomiting). (oral)
8	One <i>pala</i> (40 gm) each of <i>Haritaki</i> ( <i>Terminalia Chebula</i> Retz), <i>Pippalimula</i> (Root of <i>Pippali</i> of <i>Piper longum</i> Linn), <i>Pippali</i> ( <i>Piper longum</i> Linn.), <i>Gajapippali</i> ( <i>scindapsis officinalis</i> , <i>Chitrak</i> ( <i>Plumbago zeylanica</i> Linn.), <i>Pushkarmula</i> ( <i>Inula racemosa</i> Hook. F.), <i>Shathi</i> ( <i>Hedychium spicatum</i> Buch Ham), <i>Draksha</i> ( <i>Vitis vinifera</i> Linn), <i>Yawani</i> ( <i>Trachyspermum ammi</i> Linn.), <i>Yavakshar</i> (Alkali obtained from <i>Yawa</i> ), <i>Ajamoda</i> ( <i>Carum Roxburghianum</i> (DC) Craib.), <i>Sita</i> (Sugar), <i>Yashtimadhu</i> ( <i>Glycyrrhiza glabra</i> Linn.), <i>Bruhati</i> ( <i>Solanum indicum</i> Linn.), <i>Kantakari</i> ( <i>Solanum surattense</i> Burn.f.), <i>Saindhava</i> (Rock salt) with half <i>Pala</i> (20 mg) of snake venom and ghee taken one <i>prastha</i> (2460 ml) and prepare medicated ghee	This is administered after the food having digested cures <i>Durnama</i> (piles), <i>Meha</i> (Diabetes), <i>Gulma</i> (Abdominal tumor), <i>Arma</i> (Pterygium), <i>Timira</i> (blindness), <i>Krimi</i> (worm infestation), <i>Pandu</i> (Anaemia), <i>Galagraha</i> (Sore throat), <i>Graha</i> (Possession by evil spirits, <i>Unmad</i> (Insanity), <i>Kushtha</i> (Skin diseases) (oral)
9	Poison mixed with <i>Pathya</i> ( <i>Terminalia chebula</i> Retz), <i>Chitrak</i> ( <i>Plumbago zeylanica</i> Linn.), <i>Danti</i> ( <i>Baliospermum montalum</i> Muell-Arg.), <i>Draksha</i> ( <i>Vitis vinifera</i> Linn), <i>Haridra</i> ( <i>Curcuma longa</i> Linn.), <i>Ativisha</i> ( <i>Aconitum heterophyllum</i> Wall.)	Cures <i>Mutrakrichhra</i> (dysurea) (oral)
10	Snake venom with <i>shilajatu</i> ( )	Cures <i>Udawarta</i> (upward movement inside the abdomen), <i>Ashmari</i> (Renal calculi) (oral)
11	<i>Gomutra</i> (cows urine) <i>Yavakshar</i> (Alkali obtained from <i>Yawa</i> ), <i>Saindhava</i> (Rock salt), snake venom, and <i>Pashanbhedaka</i> ( <i>Bereinia ligulata</i> (Wall)Engl.) mixed together.	And consumed breaks up the <i>Pittashmari</i> (bile stones) like thunder bolt. (Oral)
12	<i>Pippali</i> ( <i>Piper longum</i> Linn.) plant together with its root, cow's urine, and snake venom.	Best to relieve <i>Shula</i> (colicky pain). (oral)
13	Snake venom with <i>Drawanti</i> ( <i>Croton Tinglium</i> Linn.), <i>Madhuka</i> ( <i>Glycyrrhiza glabra</i> Linn.), <i>Draksha</i> ( <i>Vitis vinifera</i> Linn), <i>Rasna</i> ( <i>Pluchea lanceolata</i> C.B.Clarke), <i>Shathi</i> ( <i>Hedychium spicatum</i> Buch Ham), <i>Pippali</i> ( <i>Piper longum</i> Linn).	Best to relieve <i>Shula</i> (colicky pain). (oral)
14	<i>Erand taila</i> (castor oil), <i>Triphala</i> , cows urine, <i>Chitrak</i> ( <i>Plumbago zeylanica</i> Linn.), and snake venom added with ghee.	Cures <i>Vatanda</i> (Scrotal enlargement). (Oral)
15	<i>Triphala</i> , <i>swarjika kshar</i> , and snake venom (32)	Cures <i>gulma</i> (Abdominal tumors). (Oral)
16	<i>Shatavha</i> , <i>krimitit</i> , and snake venom consumed with milk	Cures <i>gulma</i> (Abdominal tumors), <i>Pleeharog</i> (Enlargement of spleen) (oral)
17	Snake poison consumed with decoction of <i>Wayasi mula</i> .	Cures <i>kushtha</i> (skin diseases) (oral)
18	<i>Vayasi</i> , bark of <i>rajavruksha</i> , <i>Trayanti</i> , seeds of <i>Bakuchi</i> , <i>kana</i> and <i>visha</i> (poison) made into decoction and consumed	Cures skin diseases. (oral)
19	An application of the seeds of <i>Avlguja</i> and <i>edagaja</i> , two <i>kshar</i> , snake venom, and <i>saindhav</i> macerated with water on the skin. (36)	Cures skin diseases. (External application)
20	Paste of <i>chitrak</i> ( <i>Plumbago zeylanica</i> Linn.), root of <i>arka</i> , <i>hastipippali</i> , <i>bakuchi</i> , and snake venom macerated with cows urine.	Cures skin diseases. (External application)
21	Paste of <i>manoha</i> , milk latex of <i>snuhi</i> , snake venom, <i>chandralekha</i> , <i>edgaja</i> , seeds of <i>karanja</i> , <i>saindhav</i> , <i>vyosha</i> , <i>swrjika kshar</i> , <i>yavakshar</i> , <i>nishadwaya</i> , and <i>Aagardhuma</i> macerated with buttermilk.	Cures skin diseases. (External application)
22	<i>Bhallatak</i> , <i>Agni</i> , <i>Shamyak</i> , and snake venom macerated with cows urine.	<i>Vicharchika</i> , <i>Dadru</i> , <i>Kitibh</i> (skin diseases) (External application)
23	Leaves, bark, and root of <i>shamyak</i> and snake venom macerated with buttermilk	Cures skin diseases. (External application)
24	<i>Bhallatak</i> , <i>dwipi</i> , <i>gunja</i> , and <i>nimbphala</i> macerated with sour juices (38)	Cures <i>shwitra</i> (Leucoderma), <i>Pundarika</i> (pathognomic <i>pundarika</i> (a type of leprosy) (External application)

25-I	Vakra, kushtha, rasa (sarjarasa), dwipi, sprukka, patra, elwaluka, macerated in decoction of khadira mixed with visha and allowed to stay for 3 days and administered to the patient of leucoderma, with thorns the blebs of leucoderma should be pricked with the thorns and paste mentioned in kushtha chikitsa chapter is applied on them	Cures leucoderma. (oral followed by External application)
25-II	The paste of karavira, root of arka, bakuchi, poison, dwipi, the two Pippali, and Arushkar macerated with goats urine	Cures leucoderma. (oral followed by External application)
26	Oil of sesame or katu taila (mustard oil) cooked with decoction and paste of laksha, Surahva, varahikanda, asphota, saptaha, girikarnika, roots of arka, and ashwamara, nagpushpa, nata, haridra, daruharidra danti, visha, ativisha, pippali, and maricha, and used for ointment	Best to be used in leucoderma. it is sure to bring back the normal colour to the skin. (External application-Abhyangarth)
27	An application prepared with the paste of vira, langlika, danti, visha, and pashanbhedaka	Applied on the abdomen eases the obstructed foetus (possessing abnormal Presentations) to pass through the parturient canal. (External application)
28	Fresh juice of bijapurak, vacha, juice of bramhi, visha, and ghee cooked together and taken orally	Bestows children even in barren woman. (Oral)
29	A drink of milk medicated with draksha, kapikacchu, vacha, added with visha is to be administered in persons who	Suffers from loss of semen (Nashtashukra). (Oral)
30	Visha mixed with sugar and honey is to be applied as collyrium	Cures timira (blindness). (Anjana- collyrium)
31	Poison macerated with goats milk and subjected to the fumes of ghee latter applied as collyrium.	Cures timira (blindness) (Anjana-Collyrium)
32	Juice of Dhatriphala, poison along with shankh are soaked several times and prepared as collyrium and applied	Cures even severe stages of timira (blindness) (Anjana-collyrium)
33	Collyrium prepared with poison by name Indrayudha (a plant) macerated with breast milk and applied	Cures the disease Kacha (Partial blindness). (Anjana-Collyrium)
34	Collyrium prepared with poison macerated with juice of bijapurak added with sugar and applied to eyes also	cures kacha. (Anjana-Collyrium)
35	Poison together magadhika, and haridra and daruharidra made as collyrium	Cures kacha. (Anjana-Collyrium)
36	Poison along with krushna soaked in cows urine and applied as collyrium	cures shuklarma (Pterygium) (Anjana-Collyrium)
37	Rasakriya prepared from the drugs samudraphena, sphaltika, kuruvinda, sudha, anjana, and kumaprushtha, taken each equal in quantity and all together making one part, half part of manashila, half quantity of it maricha, and half quantity to maricha is saindhava and ayoraja (bhasma) taken half the quantity of saindhava and added visha equal to the quantity of ayoraja (iron filling) and powdered nicely, macerating it by honey this is used as collyrium.	Cures diseases of cornea, and sclera, blindness (shukla, pilla and kacha respectively). (Anjana-Collyrium)
38	In the disease pilla firstly lekhana (scraping) should be done to the eyes later instilled with juice of surasa macerated along with rasonkanda, maricha, visha, sarshapa, and saindhav later ghee is applied and ghee should be consumed.	Cures Pilla grouped of diseases. (Anjana-Collyrium)
39	Consuming ghee cooked with madhuka sara, madhuka, snake venom, milk and water	Best for nourishing the eye in case of chronic night blindness. (Nasya- Nasal drops)
40	Nasal drops prepared from Pratyakpushpi, sita, and snake venom	Cures headache. (Nasal drops)
41	Ghee mixed with yashtavha, sugar and poison.	Cures headache. (Nasal drops)
42	Shunthi, pathya, snake venom, patha and dravanti instilled as nasal drops	Cures bad smell (Putinasa) of the nose. (Oral)
43	Katutail and snake venom administered as nasal medication	Cures gray hairs, and ulcers on the scalp (Arunshika). (Nasal drops)
44	Shukta (Vinegar) mixed with swarjika kshar, saindhav and snake venom should be filled in the ear	To cure the severe pain in the ear. (Karnapuram)
45	Gandush (holding of the fluid in the mouth) done with the oil prepared with prapaundarika, manjishtha, snake venom, and saindhav	Cures all disorders of mouth.
46	A/c Kashyapa, devadaru, snake venom, cow's urine and kantakari.	Cures vachah skhalnata (stammering). (Oral)

Table 2: Number of yogas according to routes of administration in various diseases

Sr. No.	No of Yoga	Route of administration	Disease condition
1	21	oral	Jirnajwara (chronic fever), Prameha (Diabetes), Twak vikar (Skin disorders), Raktapitta (Bleeding disorders), Shwas (dyspnoea) and Hikka (Hiccups), Chhardi (vomiting), Durnama (piles), Gulma (Abdominal tumor), Arma (Pterygium), Timira (blindness), Krimi (worm infestation), Pandu (Anaemia), Galagraha (Sore throat), Graha (Possession by evil spirits, Unmad (Insanity), Mutrakrichhra (dysurea), Udawarta (upward movement inside the abdomen), Ashmari (Renal calculi), Pittashmari (bile stones), Shula (colicky pain), Vatanda (Scrotal enlargement), Pleeharog (Enlargement of spleen), Nashtashukra (loss of semen), Putinasa (Bad smell of the nose), vachah skhalnata (stammering)
2	09	External Application	Vedana-Pakiyukta Vran (Ulcers with pain and pus), Kushtha –Vicharchika, Dadru, Kitibh (Skin diseases), shwitra (Leucoderma), Pundarika (pathognomic pundarika (a type of leprosy), Mudhgarbh (Applied on the abdomen eases the obstructed foetus (possessing abnormal Presentations) to pass through the parturient canal)
3	02	Oral followed by External application)	shwitra (Leucoderma)

4	09	<b>Anjana (collyrium)</b>	<i>Timira</i> (blindness), <i>Kach Shuklarma</i> (pterygium), <i>shukla, pilla</i> and <i>kacha</i> (Diseases of cornea, and sclera, blindness)
5	04	<b>Nasya (Nasal drops)</b>	<i>Naktandhata</i> (nourishing the eye in case of chronic night blindness), <i>Shirshula</i> (Headache), <i>Palitya</i> (Gray hairs), <i>Arunshika</i> (Ulcers on Scalp),
6	01	<b>Karnapuram</b>	<i>Karnshula</i> (Severe pain in ear)
07	01	<b>Gandush</b>	<i>Mukhrog</i> (Disorders of Mouth)

It has been reviewed through many research articles that, snake venom toxins contributed significantly to the treatment of many medical conditions. There are many published studies proposes that, venom constituents of different species of snakes have different therapeutic actions such as Fibrinogenolytic and fibrinolytic activity describing and elucidating its used in various diseases which includes deep vein thrombosis, myocardial infarction, pulmonary embolus, and many others. A number of snake venoms have Cardiotonic and anti-arrhythmic activity. There is great deal of research currently being done into the anticancer properties of venoms which show anti-tumor activity. Anti-paralytic activity of snake venom can be used in the treatment of Ptosis and Myasthenia gravis. Various researches demonstrated that, snake venom has potent anti-inflammatory, analgesic and anti-arthritis action which can be used in inflammatory joint diseases such as rheumatoid, rheumatic arthritis. Many varieties of snake venom have antibacterial and antiviral activity which can be used as a potent antibiotic agent in various infectious diseases which are caused by bacteria and viruses.

In this way, various published studies describing and elucidating the medicinal use of snake venom in various diseases. These researches are only a few examples of the many areas in which snake venom is being investigated as a treatment method. Ayurveda described the use of snake venom as a therapeutic agent in various diseases since ancient time. It is need of time to develop various research modules to study the efficacy of various Ayurvedic formulations in which snake venom has been used skillfully. Therapeutic use of snake venom in various diseases in different form reflects in depth research of Ayurveda towards snake venom toxins.

## CONCLUSION

Since last five decades, various researchers are looking towards snake venom as therapeutic agent. Ayurveda has described the use of snake venom as therapeutic agent in different diseases since so many years. Various modern researches defiantly proved the use of snake venom. Further researches will carried out to establish the efficacy of Ayurvedic formulations in which snake venom has been used for various diseases.

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