Review Article **ISSN: 2394 – 7403**

International Journal of Medicine and Health Profession Research

Journal home page: www.ijmhpr.com

https://doi.org/10.36673/IJMHPR.2021.v08.i01.A02

A CONCISE REVIEW ON ENVENOMATION AND THE RELEVANCE OF ANTIOPHIDIAN PLANTS

Neethu Sara Varghese*[1], P. Dilipkrishnan[1], M. L. Lal Prasanth[1], Shibu Prasanth[1]

[1*]Dm Wims College of Pharmacy, Naseera Nagar, Meppadi Po, Wayanad, Kerala, India.

ABSTRACT

Snakebite is listed as one of the Neglected Tropical diseases by the WHO and it accounts for over 4.5-5.4 million deaths annually. The large death rate is due to the unavailability, lack of specificity and other socio-economic problems. This review was conducted considering the recurrent flood and the resultant rise in snake bites across Kerala and it aims to provide knowledge about snake venom and its effect on a human body, the different treatments available and also to contribute a scientific basis to potent herbal drugs having anti-ophidian activity which can be further employed for the production of a novel antidote against envenomation which would prove to be cost-effective and specific.

KEYWORDS

Snake venoms, Cytotoxins, Anti-venom and Antiophidian plants.

Author for Correspondence:

Neethu Sara Varghese,

Dm Wims College of Pharmacy,

Naseera Nagar, Wayanad, Kerala, India.

Email: neethusaravarghese1@gmail.com

INTRODUCTION

Snakebite is listed as one of the WHO's greatest underestimated public health challenges, particularly in developing countries where socioeconomic and other cultural barriers inhibit appropriate treatment for it, and the people most affected by it, given the lack of data, is estimated to be around 46,900 in India itself, with a mortality rate reported for about 2,8 million deaths annually[1].

As both a hunting device and as a form of protection, snakes attack. In the form of counteragent venom, adequate emergency care and restorative aid will decrease snake bite mortality to a more notable degree. The production of anti-venom is time-consuming, costly and requires adequate storability

in addition to having side effects, so it is likely to look for anti-venom, either synthetic or natural, that could supplement or substitute the action of anti-venom.

Snake venom is a complex compound which, depending on species, can contain a number of poisons. The fragment toxin may be part of proteases, nucleases, phosphodiesterases, and different compounds that modify physiological processes and cell uprightness. Neurotoxins, cytotoxins, myotoxins, and cardiotoxins are many of the known venom toxins. A variety of side effects including discomfort, swelling, tissue necrosis, hypotension, neuromuscular collapse, blood clotting dysfunction, respiratory depression, renal failure, coma, and death, can be caused by venomous snake bites[2,3].

Types

There are approximately 3,400 specimens of snakes known all over the world and they can be broadly classified into five main families, including the Colubridae, Elapidae, Viperidae, Pythonidae, and Boidae, where most of the venomous snakes are distributed in the family of Elapidae and Viperidae. It is understood that snakes envenom either to strike aggressively and whenever defensively attacked. Adapted parotid glands are the venom glands, encased on either side of the head within a muscle capsule below the lips.

Pathophysiology

Snake venom consists of peptides, enzymes, and toxins of hundreds of different kinds. Almost any individual serpent develops a unique venom of its own.

Two primary types of venom are present, i.e., Neurotoxins and cytotoxins/ hemotoxins. Hemotoxins damage the circulatory system. They prevent coagulating agents from properly operating, which leads to abnormal bleeding. In the central nervous system, neurotoxins penetrate. They avoid the muscles functioning, which gives rise to asphyxiation. Neurotoxin-composed venoms are highly lethal as their proteins can block the channels that allow the passage of ions through neuronal membranes. If these forms of communication are disrupted, the systems of the entire body will collapse, resulting in immediate death.

Underneath, numerous cytotoxins and their activity components are described.

Hemotoxins

They can either instigate coagulation or eviscerate erythrocytes, other than death can also cause severe kidney injury, severe respiratory distress disorder, and capillary leak syndrome, such as the venom of pit snakes[4].

Cardiotoxins

They directly affect the cardiovascular system and avert its contraction, causing arrhythmias and heart failures such as the Kraits and Cobras venom[5].

Phospholipases

These kinds of compounds are responsible for glycerophospholipid hydrolysis and are present in all living organisms[6]. A venom transforms a phospholipid atom into a lysophospholipid that pulls the fats and destroys the particle. Eg; Venom of Cobra

Complications include inflammatory near the location of the bite and acute respiratory failure

Different types of neurotoxins and their mechanism of action is described below:

Fasciculins

These toxins demolish the enzyme acetylcholinesterase, which contributes to the accumulation of acetylcholine in the receptor, thus preventing muscle contractions[7].

Dendrotoxins

These toxins inhibit nerve impulse transmission by blocking ion exchange in the neuronal membrane, leading to nerve paralysis. Present in mamba's venom[8].

α- neurotoxins

These are peptides or curar mimetic neurotoxins that obstruct the flow of acetylcholine by imitating the molecular structure and adhering on the skeletal muscle with the nicotinic receptors resulting in paralysis and numbness[9]. Other complications include paralysis of the respiratory system. Present in King Cobra's venom.

Symptoms of snake bite

Fang marks

Puncture marks seen in the shape of an arc indicates the bite of a non-venomous snake whereas two puncture wounds indicate a bite by a poisonous snake

Pain

Bursting or pulsating pain can occur immediately and spread proximately to the bitten section. The pain can be accompanied by a burning sensation. Draining the lymph nodes quickly becomes painful. Krait and sea snake bites are, often, quite pain free.

Local swelling

In the case of viper attacks, severe local swelling is observed which is evident within a span of 15 minutes and lasts up to three weeks. A severe inflammation is observed within 3 days where the swelling extends to the entire limb and the trunk adjacent to it. Regionally, lymphadenopathy can progress. If the poisoned tissue, such as the digit pulp space or anterior tibial compartment, is situated in a neighbouring fascial compartment, it may undergo ischaemia[3].

Local necrosis

Swelling, blistering and necrosis can occur in viper bites within a few days after the bite. Asian pit vipers and some rattlesnakes bite is distinguished by the necrosis around the bite site. Tender local swelling and blistering can also be caused by bites from Asian cobras. Krait bites is devoid of any local reaction.

Venom ophthalmia can develop in patients who spit on elapids by spitting. Venom ophthalmia can develop by envenomation of spitting elapids like spitting cobra.

Secondary infection: Bacteria found in the snake's oral cavity leads to secondary infection.

Systemic characteristics

Clotting and haemolysis defects

Viperidae poisoning is characteristic of haemostatic abnormalities. Continuous bleeding from fang bruise or other bruise sites, and other new wounds that is partially healed indicates the blood is incoagulable. Cases of epistaxis, haematemesis, cutaneous echymosis, haemoptysis, retroperitoneal, subconjunctival, and intracranial haematoma are often frequently found along with spontaneous systemic bleeding in mucosal sulci[2].

Neurotoxicity

Severe neurotoxicity is found in elapid and sea snake venom. Paralysis is first detectable after an elapid bite but within fifteen minutes ptosis and outer ophthalmoplegia occurs. The facial muscles and organs are damaged and are eventually incapacitated. Owing to airway obstruction or impairment of the intercostal muscles and the diaphragm, pulmonary failure happens. The neurotoxic effects, either acutely in reaction to antivenom or anticholinesterase, are completely reversible, and therefore can automatically fade off in about 1 to 7 days. These neurotoxins do not reach the brain's blood barrier and hence do not hinder awareness[3].

Myotoxicity

The sea snake bite can result in myalgia due to the myotoxins present in their venom. Myotoxins are responsible for myalgia, rhabdomyolysis and myopathy. Within half hour generalised muscle pain, rigidity and tenderness develop due to these toxins.

Cardiotoxicity

Viper and elapid venom are known to cause cardiotoxicity and can result in direct myocardial impairments' such as arrhythmias, bradycardia, hypotension or tachycardia.

Nephrotoxicity

In Viper bites, kidney damage is indicated which is linked to ischaemia.

Shock

A variety of variables contribute to shock. They include anxiety, hypovolemia, myocardial depression, adrenal and pituitary haemorrhage, and increased kininin synthesis.

Management of the bite of a snake

First-aid for snake bite

If a snake bite is suspected,

- Transfer from the location where the bite occurred. Sea snake victims need to be moved to dry land to prevent sinking.
- Avoid traditional first aid techniques, herbal medicines and other forms of first aid that are unproven or unsafe.
- Generally, snake bites are accompanied by inflammation. As it may cause injury, remove

everything tight from around the bitten part of the body. Never use an arterial tourniquet that is tight.

- In some cases, the application of pressure at the bite site with a pressure pad may be appropriate. Reassure the individual and completely immobilise him. And carry the individual to the health care facility immediately.
- For local pain (which can be severe), paracetamol may be given.
- Vomiting may occur, so place the individual in the recovery position on their left side.
- Monitor the airway and respiration closely and be ready to resuscitate if necessary.

Barriers to Early Antivenom Access

Some of the key contributors to the postponement of antivenom therapy are

1. The Distance
2. Cultural constraints
3. Absence of transport;
4. Shortage of cold-chain storage in rural health facilities for antivenoms and other medicines.
5. Stock shortages or absence of any inventory at all.
6. Usage regulations that prohibit the administration of antivenom in primary health centres.
7. High antivenom prices

As a result of being transported lying flat on their backs and having their upper airway obstructed by vomit, or paralysis of muscles in the tongue, many people die every year on the way to a health facility. This can be prevented by lying the patient on their left lateral position

Improving the clinical results for snake bite victims requires much more than just access to safe antivenoms. Intravenous access should be achieved at an early stage, hydration status should be determined and corrected if necessary, and vital signs should be monitored closely. It is crucial that an adequate dose of effective antivenom is administered early to patients with signs of envenoming. If no antivenom is accessible, referral to a facility that has resources should be scheduled and carried out immediately. Antivenoms are not only life-saving, but can also save patients from some of the damage inflicted by necrotic and other toxins in snake venom, resulting in quicker recovery, less hospitalisation, and a speedier transition to a full recovery. Some of the effects of snake venom may not be effectively neutralised in patients who do not receive the full potential benefit of antivenom, resulting in prolonged disease, slower recovery and increased risk of disability. Sustained airway and breathing assistance using either manual resuscitators or mechanical ventilators may be needed for those affected by toxins that cause paralysis[6].

Antivenom

The use of anti-venom therapy is still the only snake bite treatment available. Anti-venoms bind to the venom and neutralise it, stopping further trauma, but do not invert the already done damage. They should therefore be given as soon as possible after envenomation, but are of some benefit as long as the venom is present in the body. Albert Calmette invented the first anti-venom against Indian Cobra. Anti-venom is produced and then isolated from the mammalian blood by immunising mammals such as horses, goats, rabbits with specific snake venom, and particular immunoglobins.

The recipient animal will undergo an immune response to the venom, producing antibodies to the bioactive portion of the venom that can then be extracted from the blood of the animal and used to treat envenomation. Snake anti-venoms are categorized as monovalent and polyvalent on the basis of antigens (venoms) used in development[10].

In order to create a neutralising antibody, the donor animal is hyperimmunized with a non-lethal dose of at least one or more concentrations of various venoms. Then the blood from the donor animal is obtained at a given time period, and neutralising antibodies are processed from the blood to create an anti-venom. Antivenoms are purified by several methods, but may still carry other serum proteins that may act as antigens. Some individuals with acute anaphylaxis or delayed serum sickness can react to the antivenom, so antivenom should be used with caution. Severe hypersensitivity reactions

particularly anaphylaxis to antivenin, are also possible[11].

Antivenom therapy

In treating a snakebite situation, the most significant decision is to determine whether or not to prescribe antivenom.

There is proof that the benefits of this procedure significantly outweigh the likelihood of complications in patients with extreme toxicity. Specific indications for the administration of antivenoms are:

- Haemostatic conditions like systemic bleeding, disorders of blood coagulation, or thrombocytopaenia
- The neurotoxicity
- Irregular hypotension / shock / ECG / other cardiovascular condition
- Generalized rhabdomyolysis
- Local swelling that covers more than half the bitten limb, severe blistering or bleeding.
- Supportive laboratory confirmation of systemic envenoming, when clinical signs are not present.

As long as there are systemic symptoms of envenoming, it is never too late to include anti-venom therapy. Antivenom has been found to be effective in patients being defibrinated up to two days after the bite of the sea snake and weeks after the bite of the viper.

- A polyvalent equine antiserum is the anti-venom available in the Armed Forces. This is successful against Cobra, Common Krait, Russell's viper and saw-scaled viper, the four most powerful venomous snakes in India.

Higher dosages are indicated for elapid bites because elapid venom is less antigenic and is more readily absorbed. An initial dose of 100 - 200ml is administered. The dose is the same as for children and adults.

The antivenom is diluted to approximately 5ml/kg of body weight with isotonic saline or 5 percent dextrose and is administered over 1-2 hours as a slow intravenous infusion. The 'push' technique is another technique where the unmixed serum is pumped intravenously at a rate of 4ml/minute.

Neurotoxic symptoms can improve around 30 minutes, but they sometimes take many hours. Usually, spontaneous systemic hemorrhage stops in less than half an hour, and blood coagulability is retained within 6 hours of administration of antivenom if a neutralizing dose has been administered. If severe symptoms occur after 1 - 2 hours or if blood coagulability is not restored within 6 hours, antivenom treatment must be resumed.

As the antivenom is an equine serum, hypersensitivity reactions can occur. Checking for sensitivity is inaccurate and of minimal value. Early response to antivenom happens 10 - 180 minutes after initiation of therapy. With higher dosages and intravenous administration, it is more likely. Itching, hives, nausea, vomiting, cough, gastrointestinal colic, fever and tachycardia are the symptoms. Hypotension, bronchospasm, and angioedema can further develop in up to 40 percent of patients with these symptoms. The reaction of the pyrogen can evolve 1 - 2 hours after therapy. Serum sickness reaction is really a late reaction evolving within 5-24 days of administration of antivenom.

Supportive therapy

1. Tetanus prophylaxis
2. In severe poisoning with a prominent reaction, antibiotics are suggested.
3. Surgical biopsy of dead tissue
4. Compartmental Fasciotomy for Syndromes
5. Control of respiratory paralysis

Ventilatory assistance should be considered and introduced at an early level. The "test for Tensilon" should be carried out as follows: Neostigmine methyl sulphate (50 - 100µg/Kg body weight) and atropine 4 hours a day or continuous infusion can be maintained in patients who respond convincingly.

6. Hemostatic disorders typically respond well to treatment with antivenom. Cryoprecipitates, platelet concentrate and fresh frozen plasma may be needed in the event of serious bleeding. Heparin is not needed

Long term effects of snake bite

1. “migraine-like-syndrome” characterized by headache, vertigo, and photosensitivity to sunlight

2. Musculoskeletal disorders such as pain, local swelling, muscle weakness, deformities, contractures, and amputations
3. Visual impairment
4. Acute kidney injury
5. skin blisters at the bite site
6. psychological distress
7. hemiplegia
8. right-side facial nerve palsy
9. paresthesia over bite site
10. generalized shivering and chronic nonhealing ulcer
11. nonspecific somatic symptoms such as abdominal colic, chest tightness, wheezing, receding gums, excessive hair loss, and lassitude with body aches

Alternative therapeutic option

Ayurveda the backbone of therapeutics in Kerala has its own unique style of treating a snake bite. Ayurveda classifies snake bite as follows

Sushrutaacharya described four types of snake bites as[12]

Sarpita - Inflamed deep wound, blackish in color.

Radita - Superficial wound, red or bluish in color. This bite is considered as less poisonous.

Nirvisha - Non-poisonous bite. May be a dry bite. Signs of inflammation cannot be observed.

Sarpangabhihata - Actual bite take place in this type.

Some of the methods used to treat snakebites include topical application of plant leaves-juice-paste, etc; chewing of leaves and plant parts; and drinking plant extracts or decoctions. In India as well as in other parts of the world, medicinal plants are used as antidotes for snakebites, administered either singly or in combination with other antisnake venoms or supportive plants. Thus, in the management of snakebite, the study of herbal antidotes against snake venom is of considerable significance to society

Ayurveda states the use of unique plants against specific snake bites, e.g. root extract of *Abrusprecatorius* is used against krait bite, leaf paste of *Azadirachta indica* with rock salt is used against viper bites. Leaves and bark of *Casearia*sylvestris, (guacotonga) are used as a trendy Ayurvedic drug to treat snake bite in Columbia, India, and so on. *Aristolochiaindica* is used as a decoction for snake bite. Seeds of Psoralea corylifolia are used both in Ayurveda and Siddha. Tea made from the leaves of *Cecropia peltata* is used as a remedy for a wide variety of ailments including snake bite. The roots of the plant *Ophiorrhiza mungo*, *Peristrophebicalyculata*, *Gymnema Sylvestre Gloriosasuperba*, *Cucumis colosynthis*, *Alangiumsalvifolium*, leaves of *Enicostemmaaxillare Calycopteris floribunda*, Calotropis gigantea, *Aristolochia indica* are used in Ayurvedic medicine[12]. *Ecliptaprostrata*L. (Asteraceae) is utilized as an antivenom against snake bite in China and in Brazil. *Schumanniophytonmagnificum*, *Ecliptaprostrata* or *Aristolochiashimadai*, have the ability to restrain phospholipase A2, other proteins (e.g. ATPase) alongside other physiological and biochemical properties, (for example, consequences for uterine tone or the protection of mitochondrial layers)[7].

This review covers the area of envenomation ranging from the different types of venom, its action and antivenom in a detailed manner so that the future researchers can employ different approaches for envenomation therapy. It also emphasis the scope of alternative medicine for the development of novel anti-venom and enumerates the plants according to the different parts used for the treatment of snakebites having scientific evidence for their activity. Acanthaceae, Araceae, Fabaceae, and Rubiaceae are the commonly used families. Plants belonging to the families of Apocynaceae, Euphorbiaceae and Lamiaceae are also found to possess antiophidian nature. During the course of the study, it was found that roots, leaves, bark, whole plant, seed, fruit, stem, other parts such as latex and flowers exhibits antiophidian behaviour in a descending order. This review classifies the antiophidian-plants based on the parts used to treat envenomation.

Table No.1: Leaves used for antiophidian activity

S.No	Plants	Family
1	*Abutilon Indicum*	Malvaceae
2	*Acalypa indica*	Euphorbiaceae
3	*Acalypha indica*[7]	Euphorbiaceae
4	*Andrographis lineata*	Acanthaceae
5	*Argemone mexicana*	Papaveraceae
6	*Bridellia ferruginea*[13]	Euphorbiaceae
7	*Cassia alata*	Caesalpiniaceae
8	*Cassia tora*	Caesalpiniaceae
9	*Clinacanthusmutans*	Acanthaceae
10	*Ecliptaprostrata*	Compositae
11	*Guiera senegalensis*[14]	Combretaceae
12	*Leucas cephalotes*	Lamiaceae
13	*Morus alba*	Moreaceae
14	*Nicotiana tabacum*	Solanaceae
15	*Ocimum sanctum*	Lamiaceae
16	*Oldenlandia umbellate*	Rubiaceae
17	*Phyllanthus reticulates*	Euphorbiaceae
18	*Symplocos cochinchinensis*[15]	Simplocaceae
19	*Tylophora longifolia* Leaf Flower	Asclepiadaceae
20	*Vitex negundo*	Verbenaceae

Table No.2: Seeds and fruits used for antiophidian activity

S.No	Plants	Family
1	*Abutilon Indicum*	Malvaceae
2	*Argemone mexicana*	Papaveraceae
3	*Caesalpinia bonduc*	Caesalpiniaceae
4	*Citrus limon*	Rutaceae
5	*Glycine max*	Leguminosae
6	*Helianthus annuus*	Asteraceae
7	*Madhucalongifoila*	Sapotaceae
8	*Mucuna pruriens*[16]	*Fabaceae*
9	*Nerium oleander*	Apocynaceae
10	*Phyllanthus Emblica*[17]	Euphorbiaceae
11	*Piper longum*[18]	Piperaceae
12	*Pluchea indica*	Asteraceae
13	*Strychnosnux vomica*[19]	Loganiaceae
14	*Tamarindus indica*[20]	Leguminosae

Table No.3: Whole plant used for antiophidian activity

S.No	Plants	Family
1	*Achillea millefolium*	Asteraceae
2	*Andrographis paniculata*[21]	Acanthaceae
3	*Cymbopogon citrates*	Poaceae
4	*Eclipta alba*	Compositae
5	*Euphorbia hirta*	Euphorbiaceae
6	*Hibiscus aethiopicus*[21]	Malvaceae
7	*Mimosa pudica*	Mimosaceae
8	*Ocimumbasilicum*	Lamiaceae
9	*Oldenlandiadiffusa*	Rubiaceae
10	*Pouzolzia indica*[22]	Utricaceae
11	*Punica granatum*	Punicaceae
12	*Thymus vulgaris*	Lamiaceae
13	*Tragia involucrate*	Euphorbiaceae

Table No.4: Stems used for antiophidian activity

S.No	Plants	Family
1	*Acacia leucophloea*	Mimosaceae
2	*Achyranthes aspera*	Amaranthaceae
3	*Boswellia delzielli*[23]	Burseraceae
4	*Dalbergia melanoxylon*	Fabaceae
5	Erythrina excelsa	Fabaceae
6	*Magnifera indica*[24]	Anacardiaceae
7	*Moringa oleifera*	Moringaceae
8	*Musa paradisiaca*	Musaceae
9	*Parkia biglandulosa*[25]	Mimosaceae
10	*Sapindusemarginatus*	Sapindaceae
11	*Strychnosnux-vomica*	Loganiaceae
12	*Terminalia arjuna*	Combretaceae

Table No.5: roots and rhizomes used for antiophidian activity

S.No	Plants	Family
1	*Abrusprecatorius*	Leguminosae
2	*Acorus calamus*	Araceae
3	*Aegle marmelos*	Rutaceae
4	*Aervalanata*	Amaranthaceae
5	*Alangiumsalvifolium*	Alangiaceae
6	*Allium cepa*	Liliaceae
7	*Aristolochia indica*	Aristolochiaceae
8	*Calotropis gigantean*	Asclepiadaceae
9	*Crinum jagus*[26]	Amyrillidaceae
10	*Curcuma longa*[27]	Zingiberaceae
11	*Curcuma longa*	Zingiberaceae
12	*Cyperus rotundus*	Cyperaceae
13	*Dichrostachys cinerea*[28]	Mimosaceae
14	*Ehretiabuxifolia*	Ehretiaceae
15	*Feronicalimonia*	Rutaceae

16	*Gloriosa superba*	Liliaceae
17	*Gymnemasylvestre*	Asclepiadaceae
18	*Hemidesmus indicus*[29]	Apocynaceae
19	*Hemidesmus indicus*	Asclepiadaceae
20	*Ophiorrhizamungos*	Rubiaceae
21	*Parinari curatellifolia*[30]	Chrysobalanaceae
22	*Pluchea indica*[31]	Asteraceae
23	*Rauvolfia serpentina*	Apocynaceae
24	*Securidaca longipedunculat*[32]	Polygalceae
25	*Semicarpus anacardium*	Anacardiaceae
26	*Teprhosia purpurea*	Leguminosae
27	*Trichodema zeylanicum*	Boraginaceae

Table No.6: Flowers used for antiophidian activity

S.No	Plants	Family
1	*Andrographis lineata*	Acanthacea
2	*Azadirachta indica*	Meliaceae
3	*Calendula officinalis*	Asteraceae
4	*Momordica charantia*	Cucurbitaceae
5	*Phyllanthus niruri*	Euphorbiaceae
6	*Piper nigrum*	Piperaceae
7	*Pluchea indica*	Asteraceae
8	*Sapindus saponaria*[12]	Sapindaceae
9	*Solanum torvum*	Solanaceae
10	*Tylophora longifolia*	Asclepiadaceae

CONCLUSION

Snakebite and its effective treatment are one of the most neglected challenges that the world faces especially in the developing and underdeveloped countries where the statistical death reports, though incomplete, comes around 2.8 million annually. It is listed to be one of the Neglected Tropical Diseases by the WHO in 2009. On the scenario of recurrent flooding across Kerala, the worst issue after receding of water was the invasion of snakes and the proportional increase in the snake-bite reports. The effective treatment for the envenomation is hindered by lack of specificity, unavailability, economic and other socio-cultural barriers. Hence most of them resort to the locally available folk treatments which lack any scientific validation. This review covers types and effects of snake venom, treatment and use of anti-venom. It also the highlights the scope of anti-ophidian plants to resolve the scarcity of an effective antiserum and to provide a scientific platform for the plethora of anti-ophidian plants which can pave way for the discovery of a potent anti-venom which is both cost-effective and specific in nature.

ACKNOWLEDGEMENT

The authors wish to express their sincere gratitude to Dm Wims College of Pharmacy, Naseera Nagar, Meppadi Po, Wayanad, Kerala, India for providing necessary facilities to carry out this review work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

BIBLIOGRAPHY

1. Kasturiratne A, Wickremasinghe A R, De Silva N, Gunawardena N K, Pathmeswaran A, Premaratna R. The global burden of snakebite: A literature analysis and modelling based on regional estimates of envenoming and deaths, *PLoS Med,* 5(11), 2008, 218-220.

2. Gutierrez J M, Bruno L, Guillermo L, Alexandra R, Fernando C, Yamileth A. Trends in snakebite envenomation therapy: Scientific, technological and public health considerations, *Cur Phar Des,* 13(28), 2007, 2935-2950.
3. Gold B S, Richard C D, Robert A B. Bites of venomous snakes, *The New England Journal of Medicine,* 347(5), 2002, 347-356.
4. Julien S, Jeroen K, Robert A H, Nicholas R. Haemotoxic snake venoms: Their functional activity, impact on snakebite victims and pharmaceutical promise, *Bri Jour Haematology,* 177(6), 2017, 947-959.
5. Fletcher J E, Jiang M S. Possible mechanisms of action of cobra snake venom cardiotoxins and bee venom melittin, *Toxicon,* 31(6), 1993, 669-695.
6. John H and Tracey S D. Secreted phospholipases A2 of snake venoms: Effects on the peripheral neuromuscular system with comments on the role of phospholipases A2 in disorders of the CNS and their uses in industry, *Toxins,* 5(12), 2013, 2533-2571.
7. Sughosh V, Upasania V G, Beldarb A U, Tatiyab M S, Upasanic S J, Divyata S P. Ethnomedicinal plants used for snakebite in India: A brief overview, *Integrative Medicine Research,* 6(2), 2017, 114-130.
8. Harel M, Kleywegt G J, Ravelli B G, Silman I, Sussman J L. Crystal structure of an acetylcholinesterase-fasciculin complex: Interaction of a three-fingered toxin from snake venom with its target, *Structure,* 3(12), 1995, 1355-1366.
9. Harvey A L, Robertson B. Dendrotoxins: structure-activity relationships and effects on potassium ion channels, *Current Medicinal Chemistry,* 11(23), 2004, 3065-3072.
10. Carmel M B, Wayne C H. A Classic toxin review: Alpha neurotoxins, *Toxicon,* 66, 2013, 47-58.
11. Bhoite R R, Bhoite G R, Bagdure D N, Bawaskar H S. Anaphylaxis to scorpion antivenin and its management following envenomation by Indian red scorpion, Mesobuthustamulus, *In Journal of Critical Care Medicine,* 19(9), 2015, 547-549.
12. Amagon K. Anti-snake venom activity of flavonoids from the root barks extract of *Parinaricuratellifolia* in mice, *Inter Journal of Pharma Res,* 4(2), 2012, 55-58.
13. Shirwaikar A, Rajendran K, Ramgopal B, Dinesh C K. Neutralization potential of *Viper russellirusselli* (Russell's viper) venom by ethanol leaf extract of *Acalypha indica*, *Jour of Ethnopharm,* 94(2-3), 2004, 267-273.
14. Momoh S. Anti-venom activity of ethanolic extract of *Brideliaferruginea* leaves against *najanigricollis* venom, *The Journal of Medical Research,* 1(5), 2012, 69-73.
15. Abubakar M S, Sule M I, Pateh U U, Abdurahman E M, Haruna A K, Jahun B M. *In vitro* snake venom detoxifying action of the leaf extract of *Guiera senegalensis*, *Journal of Ethnopharmacology,* 69(3), 2000, 253-257.
16. Tan N H, Fung S Y, Sim S M. The protective effect of *Mucuna pruriens* seeds against snake venom poisoning, *Journal of Ethno Pharmacology,* 123(2), 2009, 356-358.
17. Habib-Ur-Rehman, Khawaja Ansar Yasin, Muhammad Aziz Choudhary, Naeem Khaliq, Atta-Ur-Rahman, Muhammad Iqbal Choudhary and Shahid Malik. Studies on the chemical constituents of Phyllanthus emblica, *Nat Pro Res,* 21(9), 2007, 775-781.
18. Shenoy P A, Nipate S S. Anti-snake venom activities of ethanolic extract of fruits of *Piper longum* L. (Piperaceae) against Russell's viper venom: Characterization of piperine as active principle, *Jour of Ethn,* 147(2), 2013, 373-382.
19. Chatterjee I, Chakravarty A K, Gomes A. Antisnake venom activity of ethanolic seed extract of Strychnosnux vomica Linn, *Indian Jourof Exper Bio,* 42(5), 2004, 468-475.
20. Sailakshmi T, Ramachdra C. Studies on phytochemical evaluation of Tamarindus indica extracts as anti-snake venom agents, *International Journal of Integrative Sciences, Innovation and Technology,* 1(5), 2012, 44-49.
21. Hasson S S, Al-Jabri A A, Sallam T A, Al-Balushi M S, Mothana R A A. Antisnake

Venom Activity of *Hibiscus aethiopicus* L. against *Echisocellatus and Naja N. Nigricollis*, *Journal of Toxicology,* 2010, Article ID: 837864, 2010, 8.

22. Kadiyala G. The neutralization effect of methanol extract of *Andrographis paniculata* on Indian cobra Najanaja snake venom, *Jour of Phar Res,* 4(4), 2011, 1010-1012.
23. Ushanandini S, Nagaraju S, Harish K K, Vedavathi M, Machiah D K, Kemparaju K, Vishwanath B S, Gowda T V, Girish K S. The anti-snake venom properties of *Tamarindusindica* (leguminosae) seed extract, *Phyto Res,* 20(10), 2006, 851-858.
24. Hasson S S, Mothana R A, Sallam T A, Al-Balushi M S, Rahman M T and Al-Jabri A A. Serine protease variants encoded by *Echis ocellatus* venom gland cDNA: Cloning and sequencing analysis, *Jour of Biomed and Biotech,* 2010, Article ID: 134232, 2010, 1-12.
25. Ahmad A. Anti-snake venom activity of different extracts of *Pouzolzia Indica* against Russell viper venom, *International Journal of Chem Tech Research,* 2(1), 2010, 744-751.
26. Goje L J, Aisami A, Maigari F U, Ghamba P E, Shuaibu I, Goji A D T. The anti-snake venom effects of the aqueous extracts of *Boswellia delzielli* stem bark on the parameters of the hepatic functions and energy metabolism of *Najanigricollis* (spitting cobra) envenomed albino rats, *Res Jour of Chemical and Envir Sci,* 1(4), 2013, 61-68.
27. Dhananjaya B L, Zameer F, Girish K S, Cletus J M D'Souza. Anti-venom potential of aqueous extract of stem bark of *Mangiferaindica* L. against *Daboiarussellii* (Russell's viper) venom, *Ind Journal of Biocheand Biophy,* 48(3), 2011, 175-183.
28. Asuzu I U, Harvey A L. The antisnake venom activities of *Parkia biglandulosa* (Mimosaceae) stem bark extract, *Toxicon,* 42(7), 2003, 763-768.
29. Ode J O, Asuzu I U. The anti-snake venom activities of the methanolic extract of the bulb of *Crinum jagus* (Amaryllidaceae), *Toxicon,* 48(3), 2006, 331-342.
30. Ferreiera L A F, Olga B H, Amelia A S A, Glaucio R F V, Marcia M C C, Gerhard G H. Antivenom and biological effects of ar-turmerone isolated from *Curcuma longa* (Zingiberaceae), *Toxicon,* 30(10), 1992, 1211-1218.
31. Mishal H B. Screening of anti-snake venom activity of *Dichrostachys cinerea* W and A, *Journal of Natural Remedies,* 2(1), 2002, 92-95.
32. Alam A, Auddy B, Gomes A. Isolation, purification and partial characterization of viper venom inhibiting factor from the root extract of the Indian medicinal plant sarsaparilla (*Hemidesmus indicus R.Br.) Toxicon,* 32(12), 1994, 1551-1557.
33. Gomes A, Saha A, Ipshita C, Chakravarty A K. Viper and cobra venom neutralization by β-sitosterol and stigmasterol isolated from the root extract of *Pluchea indica* Less, (Asteraceae), *Phytomedicine,* 14(9), 2007, 637-643.
34. Wannang N N. Evaluation of anti-snake venom activity of the aqueous root extract of *Securidacalongipedunculata* in rats, *Journal of Pharmacy Bioresources,* 2(2), 2005, 80-83.
35. Da-silva M L, Silvana M, Renata S F, Paulo S P, Ana H J. Anti-snake venom activities of extracts and fractions from callus cultures of *Sapindussaponaria*, *Pharmaceutical Biology,* 50(3), 2012, 366-375.
36. Fatima L and Fatah C. Pathophysiological and pharmacological effects of snake venom components: Molecular targets, *Journal of Clinical Toxicology,* 4(2), 2014, 190.

Please cite this article in press as: Neethu Sara Varghese *et al.* A concise review on envenomation and the relevance of antiophidian plants, *International Journal of Medicine and Health Profession Research,* 8(1), 2021, 14-24.