
INTERNATIONAL JOURNAL OF CURRENT RESEARCH IN BIOLOGY AND MEDICINE

ISSN: 2455-944X

www.darshanpublishers.com

DOI:10.22192/ijcrbm

Volume 1, Issue 7 - 2016

Review ArticleDOI: <http://dx.doi.org/10.22192/ijcrbm.2016.01.07.003>

A Review of beneficial effects of Siddha medicinal herbs on Snake bite

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Abstract

Siddha system of medicine is one of the oldest traditional systems of medicine, which has been originated from India and is practiced mostly in the southern part of this Country for treating various disease conditions by the herbals and herbo-mineral drugs. Snake envenoming and consequent deaths are of common occurrence in tropical and subtropical regions. Approximately 1,25,000 deaths are witnessed every year and WHO has declared it as a neglected tropical disease in 2009. Snake bite is a life threatening problem causing mortality from ancient period to till date. About 94,000 snake bite deaths are recorded globally and 15000 in India per year. The immunotherapy is the only treatment available, but it has side effects like serum sickness, pyrogen reactions moreover the non-availability and storage problems has rendered the mankind to look in others sources to treat snake bite deaths. The recent experiments work not only proves its efficacy of various herbal drugs on snake bite, but also evidently show their mode of action along with active principle. This study surveys the substances identified in plants reputed to neutralize the effects of snake venoms. So single plant and combination of poly herbal preparation of siddhar's are beneficial for the treatment of snakebite and may find alternative to antiserum.

Keywords: Snake bite, Siddha medicine, Medicinal plants, Anti ophidian property

1. Introduction

The Siddha System of Medicine (Traditional Tamil System of medicine), which has been prevalent in the ancient Tamil land, is the foremost of all other medical systems in the world. Its origin goes back to B.C 10,000 to B.C 4,000 as per the textual and archeological evidences, which indicate the remote antiquity of the Tamil civilization of the erstwhile submerged land kumarikandam¹.

The Siddha system of medicine comprising with it all kind of sciences like Philosophy, Alchemy, Yoga,

Astrology etc.² This Siddha system of medicine provides the health care through Prophylaxis (*Noyillaneri*), Treatment (*Maruthuvam*) and Rejuvenation (*Kayakarpam*). For a physician, it nourishes knowledge about the art of diagnosis (*NoiNadal*), pharmacology (*Gunapadam*) and toxicology (*Nanjumurivunool*). Siddhars are too good in the work of documentation too in manuscripts which is the backbone for generations of Siddha physicians. They taught the above said sciences to their disciples, and also written their works.

Medicinal ingredients in Siddha Vaidya are classified into three main groups *Thavaram* (includes the thousands of whole plants and plant products), *Jangamam* (those derived from animals), and *Thatu* (those derived from earth and organic toxins).

In many developing countries, Traditional medicine plays an important role in meeting the primary health care needs of the population. Some studies have shown that individuals choose Traditional medicine for various reasons, including an increasing dissatisfaction with existing health care services, and a rekindled interest in whole person care and disease prevention which are more often advocated in Traditional medicine. In addition Traditional medicine recognizes the need to focus on quality of life when a cure is not possible³

The branch of Toxicology is the developed one since the Siddhar's period itself, Siddhars said about the toxic effect of drugs and poisonous bites with treatment for the toxic conditions. It shows that the Siddhar's and ancient physicians are well knowledge about the safety aspects in medical practice. Siddha system of medicine is self sufficient to meet the needs of public health. It is high time to work on the quality assurance, safety and efficacy of Siddha formulations to make our system beneficial for population at large. Being a Siddha Toxicology student I am interested to tell here some siddha medicinal herbs act on snake bites are *Leucas aspera*, *Corallocarpus epigaeus*, *Eclipta prostrate*, *Curcuma longa*, *Ophiorrhiza mungos*, *Strychnos nux-vomica*, *Sapindus saponaria*, *Musa paradisiaca*, *Aristolochia bracteolata*, *Aristolochia indica* and *Symplocos racemosa*.

2. Materials and Methods

Already scientific researches and various antidote activities have done on herbals in recent years. Now the author, present review on snake venom, anti-venom, common snake types, herbal antidote, phytocompounds and pharmacological activity which will provide of a text of references as well as information on the aspect for minimizing socio-medical problem of snake bite.

2.1. Snake venom

The venom produced by the snake's venom gland apparatus is delivered in to the target tissue from fangs by injection mechanism.^{4,5} The venom contains

complex mixture of enzymatic and non-enzymatic proteins, peptides and small organic compounds such as citrate, nucleoside and acetylcholine.⁶

2.2. Clinical effects of snake venom

The clinical effects of snake bite includes neurotoxicity, cardio toxicity, coagulant (either poor anti), hemostatic (either activating or inhibiting), hemorrhagic, hemolytic and edema forming activities.⁷

2.3. Anti -venom

Datta K Animesh *et al*, Anti -venoms can be classified into monovalent (when they are effective against a given species' venom) or polyvalent (when they are effective against a range of species, or several different species at the same time) types. Generic name Equine (horse derived)/ Ovine (sheep derived) immunoglobuline F(ab')₂ fragments. Pharmacologic therapeutic class, Immunosera and immunoglobulins. Equine immunoglobuline F (ab')₂ anti-venoms, FAV AFRICA polyvalent equine F(ab')₂ anti-venom for Subsahara African snakes *Bitis*, *Echis*, *Naja*, *Dendroaspis*. FAVIREPT polyvalent equine F(ab')₂ anti-venom for middle east snakes *Bitis*, *Echis*, *Naja*, *Cerastes*, *Macrovipera*. VIPERFAV polyvalent equine F(ab')₂ anti-venom for European snakes *Vipera*.⁸

2.4. Side effects of anti-venom

- Anaphylactic reactions such as difficulty in breathing, reddening of skin, swelling of eyes and face, fever.
- Pyrogen reaction probably due to the action of high concentrations of non-immunoglobulin proteins.
- Inflammation of joints, Enlargement of lymph gland⁹.

2.5. Limitations of antisnake venom therapy

Antivenom immunotherapy is the only specific treatment against snake venom envenomation. There are various side effects of antivenom such as anaphylactic shock, pyrogen reaction and serum sickness. Most of these symptoms may be due to the action of high concentrations of non immunoglobulin proteins present in commercially available hyper immune antivenom.¹⁰ Although an intravenous administration of antivenom, prepared from IgG of

venom-immunised horses or sheep, is an effective treatment for systemic envenoming the clinical consensus is that antivenom is of limited effectiveness against the effects of local envenoming that develop

rapidly after a bite.¹¹Such effects include severe pain, oedema, localized haemorrhage, and necrosis. Which often results in permanent scarring and deformity.¹²

2.6. Types of snakes found and their feature¹³

Common krait



Found all across India up to Assam.
The venom of the snake is neurotoxic.

Russel's viper



Found all across Indian sub-continent.
Its venom is hemotoxic.

Saw scaled viper



Found across Indian sub-continent except in west Bengal and north east India.
Its venom is hemotoxic.

Spectacled cobra

Found across Indian sub-continent except north east India.
Its venom is neurotoxic.

2.7. Some medicinal plants used for snake bite in siddha medicine

S.No	Botanical name	Family	Local name (siddha)	Part used
1.	<i>Leucas aspera</i>	Lamiaceae	Thumpai	Whole plant
2.	<i>Corallocarpus epigaeus</i>	Cucurbitaceae	Kollankovai, Akasagerudan	Root
3.	<i>Eclipta prostrata</i>	Asteraceae	Karisalai	Whole plant
4.	<i>Curcuma longa</i>	Zingiberaceae	Manjal	Dried rhizome
5.	<i>Ophiorrhiza mungos</i>	Rubiaceae	Keerippundu, Kiripurandan	Root
6.	<i>Strychnos nux-vomica</i>	Loganiaceae	Yetti	Seed
7.	<i>Sapindus saponaria</i>	Sapindaceae	Puvandi, Soapnut tree	Root
8.	<i>Musa paradisiaca</i>	Musaceae	Vallai	Stem juice
9.	<i>Aristolochia bracteolata</i> <i>Aristolochia indica</i>	Aristolochiaceae	Adutinnapai, Perumarindu	Root
10.	<i>Symplocos racemosa</i>	Symplocaceae	Vellilothiram	Bark

2.7.1 *Leucas aspera*

If a person is bitten by snake become unconsciousness, the flower juice of *Leucas aspera* few drop is put in each nostril. Then give leaf juice internally and external bandage with leaf will cure poisonous bite.^{14,15}

Anti ophidian activity:

The methanolic leaf extract of *Leucas aspera* was explored for the first time for antisnake venom activity. This plant extract was significantly antagonized the spectacled cobra (*Naja naja naja*) venom induced lethal activity in a mouse model. It was compared with commercial antiserum *Naja naja naja* venom induced a significant decrease in

antioxidant superoxide dismutase, glutathione (GSH) peroxidase, catalase, reduced GSH and glutathione-S-transferase activities and increased lipid peroxidase (LPO) activity in different organs such as heart, liver, kidney and lungs.

Inhibition of these enzymes was generally considered as important step in the management of snakebite. Methanolic extract of *Leucas aspera* having Protease inhibitors, Hyaluronidase inhibitors, Phospholipase inhibitors, Hemolytic inhibition evaluated for its major enzymes. From the study it was demonstrated that methanolic extracts of *Leucas aspera*, possess antivenom activity against *Naja naja naja* venom enzymes and supports their traditional use in herbal medicine against snakebites.¹⁶

2.7.2 *Corallocarpus epigaeus*

Corallocarpus epigaeus root powder one teaspoon with equal amount of sugar intake is good for snake bite. During this medication the diet should be free of salt and tamarind.^{14,15}

Chandra et al, *Corallocarpus epigaeus* useful in snake bite. Reddy et al, This stem decoction is used to treat poisonous bite. Audichya et al, Root paste is applied on snake bite. Hemadri et al, Root tuber is given orally for treating snake bite.¹⁷

Anti ophidian activity:

In vivo study in mice at dose level of 500mg/kg administration of methanolic and aqueous extract *Corallocarpus epigaeus* was studied against the lethal effect of Russell's viper venom. Mortality of the mice was reduced progressively and significant protection was also observed at 500mg/kg dose. The percentage survival was observed as 66.66 and 50.0 at dose level for methanolic and aqueous extracts respectively. From this study of *Corallocarpus epigaeus* reveals significant antisnake venom activity in the treatment of Russell's viper snake bite.¹⁸

2.7.3 *Eclipta prostrata*

Eclipta prostrata leaf juice 90 drops with water or butter milk will cure snake bite¹⁴. *Eclipta prostrata* fresh aerial part used to treat snake bite.¹⁹

The leaves of *Eclipta prostrata* are used in treatment of scorpion stings. They are used as an antidote for snake bites in Korea.¹⁹

Butanol and ethanolic extract as well as wedelolactone was isolated from the aerial parts of the plant showed both in vitro and in vivo anti-venom effects.^{20,21,22}

Anti ophidian activity:

Eclipta prostrata three of its constituent (wedelolactone, stigmaterol, and sitosterol, Sn) were investigated. Both in vivo and in vitro studies in rat or mouse were conducted for inhibition of the myotoxic and hemorrhagic activities of crotalid venoms. The myotoxicity of crotalid venoms, purified myotoxins (bothropstoxin, BthTX; bothropasin and crotoxin), and polylysine was quantified in vitro by the release rate of creatine kinase from rat or mouse extensor digitorum muscles and in vivo by the plasma creatine kinase

activity in mice. The *in vitro* myotoxicity of the crotalid venoms and myotoxins was neutralized by simultaneous exposure of the muscles to an aqueous extract of *Eclipta prostrata* or wedelolactone. Stigmaterol and sitosterol were less effective than wedelolactone, but interacted synergistically with it. *Eclipta prostrata* and wedelolactone neutralized the *in vitro* and *in vivo* myotoxicity of both these myotoxins and, in addition, displayed antiproteolytic and anti-PLAZ effects in biochemical experiments. Collectively, these data suggest possible mechanisms for the antimyotoxic effects of *Eclipta prostrata* and wedelolactone against crotalid venoms, and for their inhibition of the hemorrhagic lesions induced by proteases present in *B. jararaca* venom. However, wedelolactone and *Eclipta prostrata* were also effective in neutralizing Bothropstoxin, a myotoxin described as devoid of proteolytic or PLAZ activities. Bothropstoxin retains a high degree of sequence homology with other PLAZ myotoxins and a 'residual' phospholipase activity may not be entirely discarded. From this study *Eclipta prostrata* (Asteraceae) extracts and constituents showed inhibition of the myotoxic and hemorrhagic activities of crotalid venoms.²³

2.7.4 *Curcuma longa*

The dried rhizome is used in poisoning and also in snake bite.²⁴

Smoke produced by sprinkling powdered turmeric over burnt charcoal will relieve scorpion sting when the part affected is exposed to the smoke for few minutes.²⁵

Fresh *Curcuma longa* juice is applied in poisonous bites and leech bites.¹⁴

Curcuma longa is indicated for insect's bites.¹⁶

Due to strong anti-septic properties it has been used as a reputed remedy for all kinds of poisonous affections, ulcers and wounds.²⁶

Anti ophidian activity:

Curcuma longa rhizome derived material has been taken for antiplatelet activity measured by platelet aggregometer and compared with aspirin as antiplatelet agent. The active constituent from the rhizome was isolated as ar-turmerone by various spectral analyses. It has inhibitory concentration 50 percentage value. The ar-turmerone was effective in inhibiting platelet aggregation induced by collagen and arachidonic acid. In comparison, ar-turmerone was significantly more potent than platelet inhibitor aspirin against platelet aggregation induced by collagen. From this study

ar-turmerone was useful compound for inhibiting platelet aggregation induced by collagen and arachidonic acid.²⁷

2.7.5. *Ophiorrhiza mungos*

Root of *Ophiorrhiza mungos* is used in snake bite and dog bite.¹⁴

Roots are sold as a charm against snake bite and scorpion sting, especially in Ceylon where it has a high reputation as a remedy for snake bite although nothing trustfully known about it. It is also used as an antidote against bites of mad dogs.²⁵

Medicinal uses of *Ophiorrhiza mungos* in snake bite.²⁶

Anti ophidian activity:

Ophiorrhiza mungos root extract was used in chick embryo study. The membrane stabilizing properties of root extract was estimated by Human Red Blood Cell (HRBC) lysis method. The disc impregnated with venom, root extract or the combination of both was placed on the yolk sac membrane preferably over the anterior blood vessel of 6th day chick embryo. The neutralization/inhibition of venom-induced lethality or hemorrhage was achieved by incubating venom and extract before being applied to the embryo. The LD50 of Russell's viper venom in 6th day chick embryo was found to be 3µg/µl. 100 percentage recoveries of embryos were observed after 6h of incubation. Higher concentration of root extract showed remarkable results by completely abolishing traces of hemorrhagic lesions induced by viper venom. From this study root extract of *Ophiorrhiza mungos* possess potent anti-snake venom neutralizing compounds, which inhibit the activity of viper venom.²⁸

2.7.6. *Strychnos nux-vomica*

Yeti kottaiuppu used in snake bite. Bark of *Strychnos nux vomica* 65-130 mg along with common salt scorpion bite will cure by chewing this¹⁴.

It also acts as an antidote to snake bite administrated hypodermically (1/16 to 1/10th grain) close to the bitten part. A paste of *Strychnos nux-vomica* a seeds is used in rat bites.²⁵

The seeds of *Strychnos nux-vomica* are used in rat bites, venomous reptile bite.²⁶

Anti ophidian activity:

Seed extract of *Strychnos nux-vomica* dose level was 5mg/kg in mice administrated. The neutralization

testing models were selected cardiotoxicity, neurotoxicity. It was observed that seed extract effectively antagonized viper and cobra venom induced actions in different *in vivo* and *in vitro* test models. From this study seed extract effective in viper and cobra venom neutralization in presence of polyvalent snake venom antiserum.²⁹

Ethanollic extract neutralized *Daboria russelii* venom induced lethal haemorrhage, PLA2 enzyme activity in mice while Najakaouthia venom induced *in vivo* cardiotoxicity, neuro toxicity and PLA2 enzyme activity in mice. Anti-snake venom activity was attributed to an active compound isolated from the extract.^{30,31}

2.7.7. *Sapindus saponaria*

Root is grind with vinegar applied in scorpion and poisonous bites.¹⁴

Pulp is given to people bitten by venomous reptiles. Externally applied to bites of reptiles, centipedes, scorpion sting.²⁵

Anti ophidian activity:

The extracts and fractions from callus cultures of *Sapindus saponaria*, significantly inhibited the toxic and pharmacological activities induced by snake venoms and toxins. The lethal, clotting, phospholipase, oedema inducing, hemorrhagic and myotoxic activities were partially inhibited by the different extracts and fractions. *Sapindus saponaria* from the study presented anti ophidian activity and could be used as an adjuvant to serum therapy or for its supplementation.³²

2.7.8. *Musa paradisiaca*

Stem of *Musa paradisiaca* used in poisonous bite.¹⁴

Juice of bark and leaf has been recommended in bites or stings from poisonous animals.¹⁹

Musa paradisiaca stem juice 15ml at a time and then 4hours once. It is anti-dote for snake poison.³³

This stem juice is effective in snake bite especially in hemotoxic bite.³⁴

Anti ophidian activity:

Extract of *Musa paradisiaca* was administrated in mice model was used *in vivo* and *in vitro* against the toxicity of snake venom. It was suggested that these compounds can be responsible for the *in vitro* inhibition of the toxic effects of snake venoms. Neutralizing properties of *Musa paradisiaca* extract

on phospholipase A₂, myotoxic, hemorrhagic and lethal activities of crotalidae venoms. From the study protection against the toxic effects of snake venoms *in vitro*, was very effective when compared with experiment were done *in vivo*.³⁵

2.7.9. *Aristolochia bracteolata* & *Aristolochia indica*

Root powder of *Aristolochia bracteolata* 2-4 gram cures snake bite and other poisons.¹⁴

Root powder of *Aristolochia indica* 1-2 gram is used in poisons. Its leaf powder 2 grams twice a day cure snake bite¹⁴.

Aristolochia indica leaf juice is used in snake bite.¹⁵

The root of *Aristolochia bracteata* can be powdered and 5grams twice a day for three days. During these days diet should be free of salt.³³

The leaf juice of *Aristolochia indica* is good for many types of poisons and insect bite. Dosage will vary according to the type of insect.³³

Aristolochia indica is an antidote to snake bites however that it obtained most repute and by the early Portuguese settler was termed Raiz de cobra, its efficacy in those cases, even in the bite of cobra de capeello. In the Philippine Islands, the bitter nauseous root is the most popular remedy for poisonous bites and stings.¹⁹

Aristolochic acid an alkaloid from *Aristolochia bracteolata* was found to interact with phospholipase A₂ from viperarusselli venom and from human synovial fluid and inhibited the oedema inducing activity of phospholipase A₂ in mice *in vitro*.²³

Aristolochia indica is useful in all types of poisonous bites and stings.³⁶

Aristolochic acid acted as a competitive inhibitor of phospholipase A₂ enzyme in snake venom. It also inhibited the oedema – inducing activity of phospholipase A₂ obtained from human synovial fluid.³⁷

Anti ophidian activity:

The interaction of aristolochic acid, an alkaloid from *Aristolochia* species, with phospholipase A₂ (PLA₂) from *Viperarus selli* venom was followed by circular dichroism measurements. The results showed that the both plant extracts were capable of neutralizing the lethality induced by the venom activity.³⁸

The ethanolic extract of *Aristolochia indica* has protective effect against the red scorpion venom and

shows 50 percentage survival benefits in mice. Further clinical studies are required in humans to potentiate this claim and discover the new treatment strategy for red scorpion envenoming.³⁹

2.7.10. *Symplocos racemosa*

It is used in poisons¹⁴.Bark is used in scorpion sting.²⁵ *Symplocos racemosa* is used in the treatment of snake - bite.⁴⁰

Anti ophidian activity:

Symplocos racemosa was extracted as Phenolic glycosides, benzoyl salireposide, salireposide, symploracemoside and symplomoside (500–25 mm/mL) were evaluated for inhibitory activity against snake venom phosphodiesterase-I. Salireposide, Symploracemoside showed moderate inhibitory activity, symplomoside showed a weak activity, as compared to the strong inhibitory potential of benzoyl salireposide. Benzoyl salireposide and salireposide were also evaluated for their inhibitory activity against human nucleotide pyrophosphatase phosphodiesterase-I. Ahmad et al, Choudhary et al, Gupta and Pehsin, From this study it was displayed that isolated substance of *Symplocos racemosa* *in vitro* inhibitory activity against snake venom phosphodiesterase-I.⁴¹

3. Results

Snakebite is a significant health hazard that leads to high mortality rate worldwide especially in developing countries like India. Antiserum is the only available for snake venom poisoning which has high cost and various side effects. The plant *Leucas aspera* extract significantly antagonized the spectacled cobra (*Naja naja naja*) venom induced lethal activity in a mouse model. *In vivo* antisnake venom studies of the methanolic extract of *Corallocarpus epigaeus* reveals significant antisnake venom activity and could have a promising role in the treatment of Russell's viper snake bite. *Eclipta prostrata* extracts and constituents had Inhibition of the myotoxic and hemorrhagic activities of crotalid venoms. From *Curcuma longa*, the ar-turmerone was useful compound for inhibiting platelet aggregation induced by collagen and arachidonic acid. The root extract of *Ophiorrhiza mungos* inhibit the activity of viper venom. Seed extract of *Strychnos nux-vomica* was observed effectively antagonized viper and cobra venom induced actions in different *in vivo* and *in vitro* test models. *Sapindus saponaria* from the study presented anti-ophidian activity. Neutralizing properties of

Musa paradisiaca extract on phospholipase A₂, myotoxic, hemorrhagic and lethal activities of crotalidae venoms. The alkaloid from *Aristolochia species*, both plant extracts were capable of neutralizing the lethality induced by the venom activity with phospholipase A₂ (PLA₂) from *Viperarus selli* venom. The *Symplocos racemosa* in vitro inhibitory activity against snake venom phosphodiesterase-I

4. Conclusion

Siddha system of medicine has rich collection of herbs for the treatment of various acute and chronic ailments. These plants represent rich source of pharmacologically active compounds that interact with the toxins and neutralizes them. The recent experiments work not only proves its efficacy of various herbal drugs on snake bite, but also evidently show their mode of action along with active principle. So single plant and combination of poly herbal preparation of Siddhar's are beneficial for the treatment of snakebite and may find alternative to antiserum. Further studies of these single herbs and combination of the poly herbal preparation still needed for their chemical contents, toxicity and their mechanism in order to increase the efficacy and beneficial to mankind.

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S.Manonmani, R.Madhavan, P.Shanmugapriya, V.Manjari, S.Murugesan, V. Banumathi. (2016). A Review of beneficial effects of Siddha medicinal herbs on Snake bite. *Int. J. Curr. Res. Biol. Med.* 1(7): 27-35.

DOI:<http://dx.doi.org/10.22192/ijcrbm.2016.01.07.003>