Review Article

Do Herbal Medicines Have Potential for Managing Snake Bite Envenomation?

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ABSTRACT

Snake envenomation is a global public health problem, with highest incidence in Southeast Asia. Inadequate health services, difficult transportation and consequent delay in antisnake venom administration are the main reasons for high mortality. Adverse drug reactions and inadequate storage conditions limit the use of antisnake venom. The medicinal plants, available locally and used widely by traditional healers, therefore need attention. A wide array of plants and their active principles have been evaluated for pharmacological properties. However, numerous unexplored plants claimed to be antidotes in folklore medicine need to be studied. The present article reviews the current status of various medicinal plants for the management of snake bite.

Key words: Antisnake venom, medicinal plants, pharmacological activity, snake bite

INTRODUCTION

Snake envenomation is an important global health issue. It constitutes an occupational hazard mainly in the field of agriculture. Highest incidence and mortality due to snake bites is reported from South and Southeast Asian countries having extensive agricultural practices and diversity in snake species.[1] Poor health services, difficult transportation, delay in the antisnake venom administration especially in rural areas are the important factors responsible for high mortality.

It is estimated that in India alone, there are more than 2,00,000 venomous bites per year, of which 35,000–50,000 are fatal.[2] The estimates are arbitrary as majority of deaths are unreported. In rural areas, where most of the bites take place, the victims are mostly taken to traditional healers, who neither report them to the authorities nor document the cases, hence paucity of reliable epidemiological data.

There are more than 3000 known species of snakes of which around 300 are poisonous. In India out of 216 species, approximately 53 are poisonous.[2] Bites are primarily due to the venomous species of the families Elapidae and Viperidae. The common poisonous snakes in India mainly include Indian spectacled cobra (*Naja naja*), common krait (*Bungarus caeruleus*), Russell's viper (*Daboia russelii*) and saw-scaled viper (*Echis carinatus*) [Table 1]. Hump-nosed pit vipers (*Hypnale hypnale* and *H. nepa*) have been reported from South India.[3]

The snake venom is a complex mixture of enzymes including the procoagulants, non-enzyme proteins, peptides, carbohydrates, amines, lipids and metal ions. The venom exerts neurotoxic, cytotoxic and hemotoxic effects. The administration of antisnake venom (ASV), the only specific treatment for snake bite, however, is associated with many drawbacks.

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Antisnake venom and its limitations

Antivenom for ophidian bites is a suspension of antibodies, prepared mainly from horses. Animals are hyper-immunized against the venom of a given species (monovalent) or venoms from several different species at the same time (polyvalent). Infusion of ASV may lead to adverse reactions ranging from early reactions (pruritus, urticaria) to potentially fatal anaphylaxis[4] [Table 2]. The reported incidence of these reactions varies from 5 to 80%.[5–7] There are also pyrogen reactions due to endotoxin contamination. Serum sickness may also develop in certain cases.

Availability and issues in stockpiling

The production and supply of antivenom is associated with logistical, marketing, storage and economic difficulties. The development is a costly, time-consuming process requiring ideal storage conditions. The liquid form of ASV has a half life of 2 years. Storage at 0–4°C is necessary, otherwise rapid deterioration sets in rendering it unfit for use. However, the lyophilized form retains potency up to 5 years when stored in any cool, dark place. In India, polyvalent antisnake venom is prepared from horses, which are hyper-immunized against the venom of the four common poisonous snakes (Cobra, Krait, Russell's Viper and Saw-scaled Viper).

Issue of specificity

Absolute specificity is an issue in management with ASV. The geographic and taxonomic diversity in species leads to a significant variation in composition and antigenic reactivity of venom.[8,9] So the use of a particular ASV may get restricted to a geographical area of relevant specificity. Thus, monovalent ASV would be the solution. But in view of the cost and diverse specificity, polyvalent ASV would provide answers to an extent, considering the medically important species. However, because of paucity of reliable literature on distribution and diversity of venomous species, ASV is not available for all species. This is one of the main obstacles of immunotherapy.

Table 1: Common poisonous snakes in India

Family	*Snake species*	Common Name
Elapidae	*Naja naja*	Indian spectacled cobra
	Bangarus caeruleus	Krait
	Ophiophagus hannah	King Cobra
	Naja kaouthia	Monocellate cobra
	Naja oxiana	Central Asian cobra
Viperidae	*Daboia russelii*	Russell's viper
	Echis carinatus	Saw- scaled viper
	Echis sochureki	Sochureki's saw- scaled viper
	Trimeresurus malabaricus	Malabar pit viper

Table 2: Adverse drug reactions profile of antisnake venom

Type 1 Reactions (early anaphylactic reactions)	Urticaria, rash, itching, dry cough, abdominal colic, fever, nausea, tachycardia, hypotension, bronchospasm, angioedema
Type 2 Reactions (pyrogenic reactions)	Rigor, fever, vasodilatation, hypotension
Late (serum sickness type) reactions	Fever, nausea, vomiting, diarrhea, itching, recurrent urticaria, arthralgia, myalgia,lymphadenopathy, periarticular swellings, mononeuritis multiplex, proteinuria with immune complex nephritis, and rarely encephalopathy rare.

Herbs as an alternative to antisnake venom

The plant kingdom provides an alternative to ASV. Medicinal plants have been used as folk medicine for treatment of snake bites. Reliance on medicinal plants is primarily due to their safety, effectiveness, cultural preferences, inexpensive nature and dependence on neighboring forests.

Globally, traditional healers are practicing herbal medicine to cure snake envenomations; however, the practice is not really recognized by modern medicine. The number of studies evaluating the pharmacologically active principles against snake bites are few.[10,11] Though novel phytotherapeutic agents have been isolated from plants due to vital leads from ethnic groups, yet validation is still an issue. Emphasis should be on proper design of both *in vivo* and *in vitro* studies, so that they relate exactly to the clinical situations.[12]

This review is an attempt to present a comprehensive account of numerous herbals used world over for the treatment of snake bite. A thorough literature survey highlights the fact that plant kingdom has tremendous resources which can be exploited for unidentified novel compounds with antivenin activity or those supplementing the action of antisnake venom.

Herbal plants with antitoxin activity

The indigenous systems of medicine use medicinal plants for the treatment of snake bites. There is a huge repository of plants reported to possess antisnake venom activity.[13,14] Investigation of therapeutic potential of plants used for snake bites shows the presence of different phytochemicals [Table 3].

Screening of plants used in traditional medicine and determination of their active principles and different activities is being undertaken. The active principles isolated have been associated with various pharmacological properties and may provide a substantial contribution to the modern therapeutics of snake bite.

Anti-inflammatory activity

Ethanolic extracts of *Bixa orellana*, *Brownea rosa-de-monte*, *Dracontium croatii*, *Struthanthus orbicularis*, *Gonzalagunia*

Table 3: Phytochemicals isolated from plants used for snakebites

Plant	Active principle
Mouriri pusa, Byrsonima crassa, Davilla elliptica	Myricetin,quercetin,amenthof lavone
Echinacea sps.	Echinacoside,cichoric acid,ket oalkenes,alkylamides,polysacc harides
Areca catechu, Quercus infectoria, Pentaceburminica,Pithecellobium dulce	Polyphenols
Casearia sylvestris	Ellagic acid
Harpalyce brasiliana	Edunol
Hemidesmus indicus	2-hydroxy-4-methoxy benzoic acid, lupeol acetate
Trichosanthes tricuspidata	Trichotetral,cucurbitane glycosides,cucurbitacins (Tricuspidation, 2-O-glucocucurbitacin,protease etc.)
Pluchea indica	β-sitosterol, stigmasterol
Vitis negundo, Emblica officinalis	Triterpenoids, phthalates
Delonix elata, Mollugo cerviana, Merremia tridentata, Gymnema sylvestre	Alkaloids,steroids,saponins,glyco sides, triterpenoids,tannins
Enicostemma axillare, Guiera senegalensis	Tannins
Allium cepa	Sulfurous volatile oils,Quercetin
Cissus assamica	Resverotrol
Eclipta prostrata	Wedelolactone,stigmasterol,sito sterol,D-mannitol
Aristolochia sps.	Aristolochic acid
Cordia verbenacea	Rosmarinic acid
Curcuma longa	Turmerin,Ar-turmerone
Mucuna pruriens, Withania somnifera	Glycoproteins
Ehretia buxifolia	Ehretianone
Strychnos nux-vomica	Amide,caffeic acid
Piper sps.	4-nerolidylcatechol

panamensis, and *Trichomanes elegans* are reported to inhibit edema due to Bothrops asper venom.[15] Decrease of edema formation with aqueous extracts of *Casearia sylvestris Sw.* has been noted in rats injected with lethal doses of Bothropic venoms. Ellagic acid has inhibited edematogenic activity due to total venom and phospholipase A2 (PLA2) from *Bothrops jararacussu*.[16]

Methanolic extract of seeds of *Vitis vinifera L.* has shown promise for the treatment of local effects of viperine bites. The extract neutralized edema-inducing property of venom.[17] *Cordia verbenacea* extract significantly reduced paw edema, induced by *Bothrops jararacussu* snake venom.[18]

Different doses of *Tamarindus indica* seed extract upon preincubation with venom before assays significantly neutralized edema.[19] *Anacardium occidentale* bark extract has also been shown to neutralize edema induced by viper venom.[20]

Lupeol acetate from roots of *Hemidesmus indicus R.Br.* is documented to significantly neutralize edema induced by Russell's Viper, in experimental animals, besides the cardiotoxicity, neurotoxicity and respiratory changes induced by *Naja kaouthia* venom.[21]

Antiophidian properties are reported to be associated with triterpenoid saponins. Glycyrrhizin, isolated from the roots of *Glycyrrhiza glabra*, has been found to be anti-inflammatory.[22] Inhibition of edema due to *Naja naja* venom is reported with turmerin isolated from *Curcuma longa*.[23]

Bidens pilosa is documented to have anti-inflammatory potential.[24] *Strychnos nux-vomica* used by tribals for snake bites is reported to be anti-inflammatory.[25] Extracts of *Andrographis paniculata* and *Aristolochia indica* have shown significant decrease in edema.[26] Partial inhibition of edema has been reported with the aqueous extracts of *Pentaclethra macroloba*.[27]

Anti-hemorrhagic and anticoagulant activity

Prolongation of clotting time of blood plasma was observed with *Brownea rosa-de-monte, Pleopeltis percussa, Bixa orellana* and *Heliconia curtispatha, Trichomanes elegans,* after pre-incubation with venom.[15] Methanolic extracts of *Mouriri pusa Garden, Byrsonima crassa Niedenzu, Davilla elliptica St. Hills* upon evaluation have shown complete neutralization of local hemorrhage. Flavonoids namely myricetin, quercetin, amenthoflavone have been attributed the antihemorrhagic potential. Quercetin is a potent lipoxygenase inhibitor.[28] *Tamarindus indica* seed extract has neutralized the hemorrhage, indirect hemolysis and degradation of Bbeta chain of human fibrinogen, caused by viper venom in experimental animals.[19]

The aqueous extract of leaves of *Schizolobium parahyba* significantly inhibited the coagulant, hemorrhagic and fibrinogenolytic activities induced by *Bothrops pauloensis* and *Crotalus durissus terrificcus* venoms and their isolated toxins after preincubation with venoms and toxins before assays.[29] *In vivo* tests with polyphenols of *Areca catechu L* and *Quercus infectoria Oliv* showed inhibition of the hemorrhagic activity of *Calloselasma rhodostoma Kuhl* venom and dermonecrotic activity of *Naja kauothia* venom.[30]

Prolongation of clotting time of *Echis carinatus* venom-treated blood has been observed with the aqueous extracts of *Mucuna pruriens, Strophanthus hispidus*, and *Strophanthus gratus*.[31]Activation of coagulative activity by *Mucuna pruriens* seed extract is well documented in literature.[32]

Inhibition of fibrinocoagulation activity induced by *Bothrops jararaca* venom is reported with the extracts of *Masypianthes chamaedrys*.[33] Neutralization of hemorrhage and partial inhibition of procoagulant activity of venom and abolition of degradation of Aalpha and Bbeta chains of human fibrinogen has been observed with *Vitis vinifera* seed extract; against viper venom induced local effects.[17]

The organic acid from root extract of *Hemidesmus indicus* significantly antagonized hemorrhagic, coagulant and anticoagulant activities in experimental rodents, induced with viper venom.[34] Lupeol acetate from the plant has neutralized hemorrhage and defibrinogen induced by Russell's Viper.[21] Inhibition of hemorrhage and dermonecrotic activities of venoms *in vivo* is reported with methanolic extracts of leaves of *Camellia sinensis*. The action has been attributed to complexation and chelation of plant phenolic compounds and venom proteins.[35]

Eclipta prostrata is used for snake bites in China and Brazil. The aqueous extract of *Eclipta prostrata* and wedelolactone, a potent and selective 5-lipoxygenase inhibitor isolated from the plant, has shown anti-hemorrhagic activity against *Bothrops jararaca*, *Bothrops jararacussu* venoms and myotoxins, bothropstoxin and crotoxin.[36,37] Partial inhibition of hemorrhagic activity has been observed with the butanolic extracts of *Eclipta prostrata* containing demethylwedelolactone as the main constituent.[38]

Glycyrrhizin a thrombin inhibitor, from the roots of *Glycyrrhiza glabra* has shown anti-thrombotic properties *in vivo*. Prevention of venom-induced changes in hemostasis, both *in vivo* and *in vitro*, have also been noted.[22] Neutralization of hemorrhagic, fibrinolytic and proteolytic activities of metalloproteases from Bothrops snake venoms is reported with a triterpenoid saponin isolated from *Pentaclethra macroloba*.[39]

Ar-turmerone from *Curcuma longa* roots has shown neutralization of the lethal effect of *Crotalus durissus terrificus* and hemorrhagic effect of *Bothrops jararaca venoms*.[40] Tannic acid is documented to neutralize hemorrhage due to *Crotalus adamanteus* venom.[41] *Baccharis trimera* has yielded clerodane diterpenoid, possessing anti-hemorrhagic properties against snake venoms.[42] Neutralization of hemorrhage due to viper venom is documented with seed extract of *Strychnos nux-vomica*.[43]

Enzyme inhibitory activity

Enzyme inhibiting and protein binding properties have been associated with chemically active compounds of flavonoids, polyphenols, terpenoids, xanthene etc. The phytochemicals also inhibit PLA2 activities of viper and cobra venom.[44] Phenolics, especially polyphenols, like some tannins bind proteins, acting upon components of venom directly and disabling them to act on receptors. They could also act by competitive blocking of the receptors.[45] Tannic acid has been found to be a potent inhibitor of hyaluronidase.[41]

Inhibition of enzymatic activity is reported with extracts of *Casearia sylvestris* in experimental animals, injected with lethal doses of Bothropic venoms.[16] Significant inhibition of PLA2 activity induced by *Bothrops pauloensis* and *Crotalus durissus terrificcus* venoms is documented with the leaf extract of *Schizolobium parahyba*.[29] Neutralization of *Vipera russelii* venom enzymes namely phospholipase, protease and hyaluronidase is reported with the bark extract of *Anacardium occidentale* in a dose-dependent manner.[20]

Abolition of hyaluronidase and proteolytic activities of viper venom with methanolic extract of seeds of *Vitis vinifera* has been reported.[17] Edunol, a pterocarpan isolated from *Harpalyce brasiliana* was found to be antiproteolytic and an inhibitor of PLA2.[46] Inhibition of azocaseinolytic activity of *Bothrops jararaca* venom has been seen with the extract of *Masypianthes chamaedrys*.[33]

Lupeol acetate from roots of *Hemidesmus indicus* significantly neutralized PLA2 activity induced by Russell's Viper.[21] Antihyaluronidase activity is reported with *Mimosa pudica* against *Naja naja*, *Vipera russelii* and *Echis carinatus* venoms.[47]

Methanolic leaf extract of *Azadirachta indica* has shown significant inhibition of PLA2 enzymes of Cobra and Russell's Viper venoms.[48] *Withania somnifera* has yielded a glycoprotein inhibitor, found to be effective in cobra and viper bite. The compound inhibited the PLA2 activity of *Naja naja*.[49] 4-nerolidylcatechol has been isolated from *Piper* species. Various species of the plant are reported to inhibit activity of PLA2 from venoms of Bothrops species.[50]

Plant extracts of *Andrographis paniculata* and *Aristolochia indica* effectively inhibited the main toxic enzymatic effects of *Echis carinatus*, responsible for a large number of deaths in India. Inhibition of PLA2 and neutralization of procoagulant activity was observed with both the extracts.[26] Aristolochic acid from *Aristolochia radix* is reported to inhibit the enzymatic and pharmacological activities of PLA2 induced by *Vipera russelii* venom.[51,52]

In vitro tests with polyphenols from *Areca catechu L* and *Quercus infectoria Oliv* showed inhibition of PLA2, proteases, hyaluronidase and L-amino acid oxidase of *Naja naja kaouthia* and *Calloselasma rhodostoma* venoms.[30] Edunol, from *Harpalyce brasiliana* is reported to be an inhibitor of PLA2.[46]

Tamarindus indica has shown potent venom neutralizing properties. Main hydrolytic enzymes responsible for

the early effects of envenomation by Russell's Viper (inflammation, local tissue damage, and hypotension) have been inhibited by the seed extract, in a dose-dependent manner.[19]

Methanolic extract of fresh leaves of *Camellia sinensis* showed inhibition of PLA2, hyaluronidase, L-amino acid oxidase in venoms of *Naja naja kaouthia* and *Calloselasma rhodostoma*, by *in vitro* neutralization.[35] Pentacyclic triterpenes, betulin and betulinic acid extracted from *Betula alba* have demonstrated activity against PLA2.[53]

A triterpenoid saponin from *Gymnema sylvestre*, potassium salt of gymnemic acid has inhibited ATPase induced by *Naja naja* venom.[54] Neutralization of PLA2 activity has been documented with seed extract of *Strychnos nux-vomica*.[43] *Eclipta alba* is documented to inhibit PLA2 activity.[55]

Antibacterial and antiparasitic activity

Mikania laevigata and *Mikania glomerata*, having antiophidian, antibacterial and antiparasitic activity, have been used in Brazil for the treatment of snake bites.[56] A broad spectrum of antibacterial activity has been associated with root extract of *Aristolochia bracteata* in snake bites.[57] Extracts of *Delonix elata* and *Mollugo cerviana* and *Merremia tridentata* have shown significant antibacterial activity. Medicinal properties may be attributed to bioactive compounds like alkaloids, glycosides, tannins found in these plants. They have been used for various ailments including snake bites.[58]

Antimyotoxic activity

Ellagic acid from *Casearia sylvestris* aqueous extract has shown inhibition of myotoxic activity in rats when tested against effects, from both total venom and PLA2 from genus Bothrops.[16] Neutralization of myotoxic effects of *Vipera russelii* venom is reported with the bark extract of *Anacardium occidentale*.[20] Significant inhibition of myotoxicity induced by *Bothrops pauloensis* and *Crotalus durissus terrificcus* venoms and their isolated toxins by aqueous extract of leaves of *Schizolobium parahyba* has been documented.[29]

Methanolic extract of seeds of *Vitis vinifera* has shown neutralization of myonecrotic properties of viper venom.[17] Edunol from Harpalyce brasiliana was found to be antimyotoxic.[46] Myotoxicity induced by *Bothrops jararacussu* snake venom and its main PLA2 homologues is reported to be inhibited with *Cordia verbenacea* extract.[18]

Significant neutralization of myotoxic effects due to Russell's Viper have been observed with extracts of *Tamarindus indica*.[19] The aqueous extract and wedelolactone, from *Eclipta prostrata*, has shown antimyotoxic activity against *Bothrops jararaca*, and *Bothrops jararacussu* venoms and two isolated myotoxins bothropstoxin and crotoxin.[36,37] The extracts of genetically modified *E.alba* inhibited myotoxicity induced by PLA2 from the venoms of *Crotalus durissus terrificus* and *Bothrops jararacussu*.[55]

Dried root extracts of *Mimosa pudica* have inhibited the myotoxicity due to *Naja kaouthia* venom.[59] *Curcuma longa* has shown inhibition of myotoxicity due to *Naja naja* venom.[23] Partial inhibition of myotoxic activity has been reported with the *Pentaclethra macroloba*.[27]

Antivenin activity

There is huge repository of medicinal plants used for treating snake bites [Table 4]. Many plants have been conserved and used as antidotes for snake envenomations.[60] Increase in survival rates of rats has been observed with *Casearia sylvestris* extract.[16]. Different species of *Echinacea* are used in North America for treating snake bites.[61] The plant contains echinacoside, cichoric acid, ketoalkenes, alkyl amides and polysaccharides.[62] Anisodamine, an alkaloid isolated from *Anisodus tanguticus* with the chemical structure and pharmacological action similar to atropine and scopolamine, has been proposed to be an effective drug for snake bites.[63]

Mucuna pruriens seeds are reported to neutralize toxicity due to *Echis carinatus*. A glycoprotein with functional oligosaccharide chains isolated from the plant is said to be responsible for the neutralization of venom-induced actions.[64] The seeds of the plant have been used as oral prophylactics for snake bite in Nigeria. Experimental studies on rats pretreated with extract and challenged with different snake venoms were done to investigate the effectiveness of anti-Mucuna pruriens antibody, to neutralize the toxicity of snake venoms *in vitro*. It was observed that pretreatment provided effective protection against lethality of venoms of *Naja sputatrix* and moderate protection against *Calloselasma rhodostma*, showing involvement of immunological neutralization.[65]

Significant neutralizing capacity against *Macrovipera lebetina* venom has been observed with the dichloromethane extract of *Artemisia campestris*.[66] Antiophidian activity of *Masypianthes chamaedrys* is reported in literature.[33] 12-methoxy-4-methylvoachalotine isolated from *Tabernaemontana catharinensis* has inhibited the lethal activity of crotoxin, the main toxin of *Crotalus durissus terrificus*.[67]

2-hydroxy-4-methoxy benzoic acid isolated form *Hemidesmus indicus* has shown antisnake venom activity in experimental models. It increased the lethal action neutralization of venom by polyvalent antiserum, suggesting the use of herbal antagonists for snake bites. It

Table 4: Plants used for treating snakebites

	Plant	Common name English/Hindi	Family
Whole plant	*Andrographis paniculata*	*King of bitters/Chiretta*	*Avanthaceae*
	Eclipta alba	*Trailing eclipta/Bhringaraj*	*Asteraceae*
	Gymnema sylvester	Gymnema*/Kavali*	*Asclepiadaceae*
	Leucas aspera	*Pansi-pansi/Dronapushpi*	*Lamiaceae*
	Mimosa pudica	*Touch-me-not/Lajjavanthi*	*Leguminoceae*
	Pouzolzia indica	*Pouzolz'sbush/Vishakarappan*	*Urticaceae*
	Punica granatum	*Pomegranate/Anar*	*Punicaceae*
Aerial parts	*Viscum articulatatum*	*Leafless Mistletoe/Pudu*	*Loranthaceae*
	Bombax ceba	*Red silk cotton tree/Shalmali*	*Bombacaceae*
Stem	*Ensete edule*	*Banana tree/Kelaa*	*Musaceae*
	Moringa oleifera	*Drum stick tree/Sahjan*	*Moringaceae*
Stem bark	*Alstonia scholaris*	*Dita bark/Satvin*	*Apocyanaceae*
	Bunchanania lanzan	*Chironji tree/Chironji*	*Anacardiaceae*
	Derris scandens	*Jewel vine/Gonj*	*Fabaceae*
	Holarrhena pubescens	*Easter tree/Kadva indrajao*	*Apocyanaceae*
Bark	*Butea monosperma*	*Butea gum tree/Markundi*	*Rubiaceae*
	Pavetta breviflora	*Indian Pavetta/Kankara*	*Rubiaceae*
Leaf	*Abutilon indicum*	*Country mallow/Kanghi*	*Malvaceae*
	Acalypha indica	*Indian nettle/Kuppi*	*Euphorbiaceae*
	Acacia Arabica	*Babul/Keekar*	*Miomosaceae*
	Anona senegalensis	*Wild custard apple/Ramphal*	*Annonaceae*
	Allium cepa	*Onion/Pyaaz*	*Iridaceae*
	Asparagus racemosus	*Wild asparagus/Satmuli*	*Liliaceae*
	Boerhavia diffusa	*Spreading hogwood/Snanthikari*	*Nyctaginaceae*
	Bombax ceba	*Silk cotton tree/Semai*	*Bombacaceae*
	Bryophyllum pinnatum	*Sprout leaf plant/ Zakhm-haiyat*	*Crassulaceae*
	Clitoria ternatea	*Butterfly pea/Aparajita*	*Leguminaceae*
	Erythrina indica	*Coral tree/Pangar*	*Papilionaceae*
	Evolvulus alsinoides	*Dwarfmorning glory/Shankhpushpi*	*Convoluvlaceae*
	Lobelia nicotianifolia	Lobelia*/Dhaval*	*Compunalaceae*
	Moringa oleifera	*Drumstick/Sahijan*	*Moringaceae*
	Tinospora cordifolia	*Heart leaved tinospora/Gudachi*	*Minispermaceae*
Root	*Achyranthus aspera*	*Prickly Chaff-flower/Chirchita*	*Acanthaceae*
	Amaranthus spinosus	*Prickly Amaranth/Kanta Chaulai*	*Amaranthaceae*
	Argemone mexicana	*Prickly poppy/Satyanashi*	*Papaveraceae*
	Cassia tora	*Wild senna/Charota*	*Leguminaceae*
	Cayratia trifolia	*Fox-grape/Amalbel*	*Vitaceae*
	Cissampelos pareira	*Velvet leaf/Patha*	*Menispermaceae*
	Commelina bengalensis	*Bengal day flower/ Kanchara*	*Commelinaceae*
	Emblica officinalis	*Indian gooseberry/Amla*	*Euphorbiaceae*
	Hemidesmus indicus	*Indian sarsaparilla/Anantamuli*	*Asclepiiiclaceae*
	Ophiorrhiza mungos	*Mangoose /Sarhati*	*Rubiaceae*
	Rawfolia serpentina	*Indian snakeroot/Sarpgandha*	*Apocyanaceae*
	Strychnos nux-vomica	*Nux vomica/Kuchla*	*Loganiaceae*
	Tephrosia purpurea	*Wild Indigo/Sarphonk*	*Fabaceae*
	Tabernaemontana divaricata	*East Indian rosebay/Tagar*	*Apocyanaceae*
	Withania somnifera	*Winter cherry/Asgandh*	*Solanaceae*
	Wattakaka volubilis	*Green wax flower/Haran dodi*	*Asclepiadaceae*
Rhizome	*Acorus calamus*	*Sweet flag/Bach*	*Acoraceae*
Tuber	*Allium cepa*	*Onion/Pyaaz*	*Iridaceae*
	Arisaemia tortuosum	*Whipcord cobra lily /Bagh Jandhra*	*Aracaceae*
	Sauromatum venosum	*Voodoo lily/Samp ki bhooti*	*Araceae*
Flower	*Azadirachta indica*	*Margosa tree/Neem*	*Meliaceae*
Seeds	*Vitex negundo*	*Five leaved chaste/Shivari*	*Verbenaceae*
	Nerium oleander	*Oleander/Kaner*	*Apocyanaceae*
Plant latex	*Calotropis gigantea*	*Blue madar/Aka*	*Asclepiadaceae*

also reduced venom-induced free radical generation and showed antiserum action potentiation.[68,69] Leaf extract of *Guiera senegalensis* detoxified venom of *Echis carinatus* and *Naja nigricollis in vitro*. Albino mice given reconstituted venom incubated with the extract, intraperitoneally, showed reduction in mortality when compared with those given venom alone.[70] Root bark of *Ehretia buxifolia* is shown to possess antisnake activity. Ehretianone, a quinonoid xanthene is the active compound isolated from the plant.[44] Lipid peroxidation induced by viper venom in experimental animals is reported to be inhibited with *Strychnos nux-vomica* seed extract. The plant effectively neutralized viper venom lethality.[43] It contains caffeic acid and monomeric caffeic acid, an antidote for snake bites.

Allium cepa containing sulfurous volatile oils is used in South America for snake bites.[71] Protective effects of resverotrol (3, 4', 5-trihydroxy trans stilbene) from *Cissus assamica* is well documented.[72] Stem bark extract of *Parkia biglobosa* has shown neutralization of venoms of *Naja nigricollis* and *Echis ocellatus* in experimental models.[73] Snake venom neutralization has been associated with leaf extract of *Acalypha indica*.[74]

Inhibitory activity is reported with salireposide and benzoylsalireposide, phenolic glycosides from *Symplocos racemosa*.[75] Bredemeyeroside D and B, triterpenoid saponins isolated from *Bredemeyera floribunda* have exhibited antisnake venom activity.[76,77] *Cordia ecalyculata* and *Echinodorus grandiflorus* are reportedly used in Brazil for various conditions including snake bites.[78] Pentacyclic triterpenes or glycosides shown to possess antisnake venom activity have been found in *Alstonia scholaris, Aegle marmelos, Centipeda minima, Aloe vera, Elephentopus scaber* etc.[79] Antivenin activity has been reported with extracts of *Crinum jagus* and *Hibiscus aethiopicus* Linn.[80,81]

Indian herbs with potential antivenin activity

Many Indian herbs have been used for the treatment of snake bites.[82–84] An ethno botanical survey of folk plants used in snake bites in southern parts of Tamil Nadu reports the use of 72 medicinal plants in snake bites. Plant extracts of *Aristolochia indica* (terpenoids), *Hemidesmus indica* (phenols), *Gloriosa superba* (esters), *Strychnos nux-vomica*, *Rauwolfia serpentina* (alkaloids), *Eclipta prostrata* (wedelolactone), *Achyranthes aspera* (glycosides) and *Andrographis paniculata* (terpenoids) have shown potent venom neutralizing effect. The plant extracts and partially purified fractions were administered orally to rats, envenomed with rattle snake venom. Significant protection against venom-induced changes in serum SOD and LPx levels were seen, after administration of purified fractions.[85]

Trichosanthes tricuspidata is used in Bastar district of Chhattisgarh for snake bites. The plant mainly contains pharmacologically important phytochemicals trichotetral, cucurbitane glycosides and cucurbitacins.[86] Root bark of *Ehretia buxifolia* is shown to possess antisnake activity.[44] *Enicostemma axillare* containing tannins is applied locally in snake bites.[58] Inhibition of lethality, myotoxicity and toxic enzymes of *Naja kaouthia* venom has been reported with aqueous and alcoholic root extracts of *Mimosa pudica*.[59]

Plants used for snake bites in Assam include *Amaranthus spinosus* (roots/stem), *Amaranthus viridis* (stem, leaves), *Argemone mexicana*, *Bryophyllum pinnatum* (leaves), *Commelina bengalensis* (roots), *Pouzolzia indica*, *Cassia tora* (roots).[87] In the Malwa region of Madhya Pradesh, *Eclipta alba* (whole plant), *Moringa oleifera* (root, bark), *Rauwolfia serpentina* (spiral roots) and *Tephrosia purpurea* (root) have been used in snake bites, with latter two having excellent potential.[88]

Documentation of an ethno botanical survey and traditional medicines used by snake charmers in Haryana highlighted the use of 19 different medicinal plants for snake bites.[89] An ethno medicinal survey in Karnataka reports that mainly root extracts of some medicinal plants were used either alone or as a formulation for snake envenomations.[90]

The Zingiberaceae family comprising of rhizomatous medicinal plants is characterized by the presence of volatile oils and oleoresins. Various species of *Curcuma*, used extensively in Indian households, find use in a wide range of disorders. *Curcuma aromatica* and *Curcuma longa* have been used as an antidote in snake bites.[91] Amongst the various other Indian medicinal plants used and recommended for treatment of snake bites, *Vitex negundo, Emblica officinalis* significantly neutralized the *Vipera russelii* and *Naja kaouthia* venom-induced effects both *in vitro* and *in vivo* studies. Triterpenoids from the root extract of *Emblica officinalis* and *Vitex negundo* are believed to significantly neutralize antisnake activity of *Vipera russelii* and *Naja kauothia*.[92]

β–sitosterol and stigmasterol from the root extract of *Pluchea indica* along with antiserum have been proposed to help in neutralization of venom-induced effects.[93] Steroids form complexes with venom, held together by "Vander Waals" and hydrophobic forces.

Viper venom induced lipid peroxidation is reported to be inhibited in experimental animals by *Strychnos nux-vomica* seed extract.[43] *Costus speciosus* roots which contain diosgenin and starch in the rhizome have been used for snake bites.[91] *Ipomoea digitata* contains triterpenoids, phenolic compound and flavonoids and is used in snake bites. The root extract of the plant has shown antioxidant activity.[94] Ethnic people have conserved plants like *Acorus calamus, Buchanania lanzan* (stem bark), *Moringa oleifera* (stem, leaves), *Achyranthes aspera*, *and Gynandropsis*

gynandra, *Bombax ceiba*, whose rhizome paste is an antidote for snake bite and scorpion sting.

CONCLUSION

Keeping in view the various limitations of ASV, herbal therapeutics for snake envenomations seem to be a viable alternative. However, there are only a few species of plants, believed to be effective for snake bites in traditional medicine whose pharmacological evaluation has been undertaken so far. In view of a plethora of active compounds in the plant kingdom, an in-depth scientific investigation is warranted to evaluate their antisnake venom potential, to derive therapeutically effective natural products for snake bites.

Integration of traditional healers who rely mainly on medicinal plants is necessary. Exploration of their materia medica for better alternatives for venom antidotes is essential. The benefit of phytotherapy is controversial because pharmacological and toxicological activities are not well studied and documented.

Complete phytochemical investigation of extracts and analysis of active principles to be used as potent therapeutic agents along with well-designed studies evaluating the pharmacologically active principles are necessary. Further, standardization of the basic active compound along with toxicity and safety studies is mandatory. In view of the conflict of healthcare practitioners with traditional medicine, validation of various reports may be carried out by corroborating their results, and thus selecting plants with potential. Scientific validation of the conventional therapies should be the long-term goal in order to test the veracity of the claims.

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