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Medicinal Plants for Snake Bite Treatment - Future Focus

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Abstract

Snake bite is a major health hazard that leads to high mortality and great suffering in victims. The remedies are of great interest since they may have recognizable therapeutic or toxic effects and are steeped in cultural beliefs that invariably conflict with formal health care practices. The study of the interaction between plants and people is invaluable in discovering new herbal medicines and plant-derived drugs. The present study was aimed at conserving largely herbal drug knowledge and availing to the scientific world the plant therapies used as antivenom in the society. The long-term goal is to actualize conventional snake bite therapy options with effective, cheap, accessible and less allergic plant compounds.

Key words: Anti venom; Medicinal Plant; Remedies; Snake bite.

Introduction

Snake bites were considered emergency threats for human life. Perhaps, venomous bites show as double teeth marks than ordinary bites. Snake venom is one of the most amazing and unique adoptions of snakes in animal planet. Venoms are mainly toxic modified saliva consisting of a complex mixture of chemicals called enzymes found in snake poisons throughout the world known to man. Broadly there are two types of toxins namely neurotoxins, which attack the central nervous system and haemotoxins which target the circulatory system. Snakes with neurotoxic venom include cobras, mambas, sea snakes, kraits and coral snakes. Snakes with haemotoxic venom include rattlesnakes, copper head and cottonmouths (Blanchard, 2001).

It is a common belief that snakes are venomous. Of the 2,700 known species of snakes, only about 300 are venomous (Internet, 2007). The most common symptoms of poisonous snake bites likely bloody wound discharge, fang marks in the skin and swelling at the site of the bite, severe localized pain, diarrhea, burning, convulsions, fainting, dizziness, weakness, blurred vision, excessive sweating fever, increased thirst, nausea,

vomiting, numbness, tingling and rapid pulse (Internet, 2008). Mainly the venom is made in special glands located on the head of the animal and that are delivered by transferring method from gland to prey (Internet, 2007).

Worldwide about 30,000 to 40,000 people die annually of snake bites. Of these, about 25,000 people die in India, mostly in rural areas, about 10,000 people in United States and rest of in other countries. Under the Wild Life Protection Act, 1972, all snakes are protected (with the venomous once being at the top of the list of the protected species) and there was a ban on the selling of snake skins since 1976. Snake venom is badly needed to produce anti venom required to treat potentially fatal snakebites (Dravidamani *et al.*, 2008).

The plant constituents have identified which are used to neutralize the effects of snake venoms. The way of management of snake bites through herbals are by treating with single herbal drugs or in combination applications, because of it designed to control infection, stop pain, improve symptoms, correct imbalance, adjust immune system and boost energy for better health and quality of life. With reflection to that area, an attempt is being made to collect available information about some medicinal plants advancement against snakebites and to present in the form of a comprehensive article. Recent scientific investigations have confirmed the efficacy of many of these preparations, some of which are remarkably effective. Traditional Indian medicinal drugs viz. *Excoecaria agallocha, Gloriosa superba, Nerium oleander, Sarsaparilla hemidesmus* and many others are effectively used for snake bites but still lot of clinical and pre-clinical research needs for the evidence. The herbs which appear most effective as per the symptoms of snakebites are relatively non-toxic and have substantial documented efficacy, among them some herbs (*Aristolochia* species, *Cissus assamica, Echinacea* species, *Guiera senegalensis, Hemidesmus indicus, Parkia biglobosa, Securidaca longipedunculata, Tamarindus indica, Trianosperma tayuya, Thea sinensis, Withania somnifera)* are enlisted with proper informations for future research (Table 1).

Table-1. Plants used against snake bites.

Species Name	Family	Geographical sources	Parts used
Aristolochia odoratissima	Aristolochiaceae	Mexico, South America	Leaves
Cissus assamica	Vitaceae	India, China, Thailand	Leaves
Echinacea angustifolia and *E. Purpurea*	Asteraceae	Western USA	Roots, Rhizomes
Guiera senegalensis	Combretaceae	West and Central Africa	Leaves
Hemidesmus indicus	Asclepiadaceae	Southern India, Srilanka	Roots

Parkia biglobosa	Leguminosae	Nigeria	Stem Bark
Securidaca longipedunculata	Polypodaceae	Nigeria, Asia	Roots
Tamarindus indica	Papilionaceae	India, Africa, Sudan	Unripe fruits, Ripe pods.
Trianosperma tayuya	Cucurbitaceae	Brazil	Roots
Thea sinensis	Theaceae	India	Leaves
Withania somnifera	Solanaceae	India, Pakistan	Roots

Aristolochia odoratissima and ***Aristolochia fordiana*** (Aristolochiaceae)

Aristolochia is a native to Mexico, Central America, Antilles, Colombia, [Ecuador], Venezuela, Brazil, Peru, Bolivia, and Paraguay. *Aristolochia* species are characterized by the outlandish shape of the flower (Internet, 2008). The leaves are ovate, 3.5 cm long and 2.5 cm wide, petiole 3-6.5 cm long. It has glabrescent vines with presence of pseudostipules. The flowers are axillary, solitary, on leafy branchlets, peduncle and ovary 4.5-10 cm long, ebracteolate, gynostemium are 3.5-5 mm long (Internet, 2008).
Aristophyllide A (Terpenoids), Aristolochic acid, (-)-Cubebin (Lignan) are the main active constituents.

Traditional uses

Flowers are used as dyes. Aristolochic acid is said to cure wounds or snake bites in a spectacular way. Furthermore, it contains a disinfectant, which drains off fluid from the wound.

Research evidences

To test the efficacy of the plant, doses of 60, 40, 30, and 20 ml of *A. odoratissima* aqueous extract obtained from 30 g of leaves in 150 mL of water, were given to 4 groups of 40 mice 96 hours before i.p. injection of *Bothrops atrox* venom. It was observed that animals that received orally the higher doses of plant extract (60 and 40 mL) protected against the highest dose of venom (16 mg/kg) since mortality descended from 100% to 80% (Usubillaga *et al*., 2005).

Oral administration of the water and alcohol extracts from *Cissus assamica* and *Aristolochia fordiana,* and the water extracts from *Desmodium microphyllum, Cynanthum paniculatum* and *Polygonum cillinerve* are very helpful in reducing the acute death caused by ET-1 (Endothelin-1) and S6b (sarafotoxin S6b) (i.v.), while the extracts from *Cissus assamica, Aristolochia fordiana* and *Cynanthum paniculatum* can dilate the vasoconstriction by ET-1 (Endothelin-1) in a dose dependent manner. Pharmacodynamic parameters have shown that the potencies of alcohol extracts from *Cissus assamica* and *Aristolochia fordiana* are greater than

that of *Cynanthum paniculatum*. These data suggest that traditional anti-snake venom herbs have antagonizing effects on ET-1 (Endothelin-1) (Wang *et al.*, 1997).

Cissus assamica (Vitaceae)

Cissus plant was originated from China. It has other species, viz, *C. kerrii* Craib, *C. pteroclada* Hayata, *C. repens* Lam, *C. sicyoides.* The plant is distributed in Chile, Cambodia, India, Thailand and Vietnam. It is a woody plant. The plant has branchlets terete, with longitudinal ridges and sparse. The plant contains versatile hairs. Leaves are simple, stipules oval, herbaceous, nearly glabrous and apex are obtuse (Internet, 2008). The main active principle of this plant is resverotrol (3,4'5-trihydroxytransstilbene).

Research evidences

Cissus assamica (Laws.) is a herbal medicine used to treat snake bite in Guangxi province. Resverotrol (3,4'5-trihydroxytrans stilbene) was isolated from the fraction of ethyl acetate part of ethanolic extract and showed antagonistic effect for endothelin, studied in both *in vivo* and *in vitro*. They also antagonized the lethal effects of ET-1 (Endothelin-1) in mice and inhibited blood pressure elevation induced by ET-1 (Endothelin-1). It is possible to find ET antagonists in Chinese anti-snake venom medicinal herbs (Yang *et al.*, 1998).

Echinacea angustifolia and ***Echinacea purpurea*** (Asteraceae)

It is known as Echinacea, purple coneflower, coneflower and American coneflower. It is native of the prairies of the Western USA. There are nine species of Echinacea. The three species most commonly found in herb products are *Echinacea angustifolia, E. purpurea* and *E. pallida.* Echinacea is a perennial herb, up to a meter in height, with simple rough stems, hollow near the base and thickening slightly close to the flower head. The leaves are elongated, slightly elliptical with entire margins and covered with coarse hairs and protuberances. The flowers are purple in colour. The tapering root is grayish-brown flecked with white.

The main phytoconstituents are volatile oil (including humulene and caryophylene), glycoside (echinacoside), polysaccharides, polyacetylenes, isobutylalkamines, echinaceine, phenolics, inulin, betain, resins and sesquiterpene.

Therapeutic uses

The extracts exhibited immunostimulant properties and are mainly used in the prophylaxis and therapy of colds, flu and septic complaints (Hostettmann, 2003). The Indian plants are used it as an antiseptic, an analgesic, and to treat poisonous insect bites, toothaches, sore throat, wounds and communicable diseases such as mumps, smallpox, and measles. *Echinacea* had been used by American Indians as a remedy for snakebites. An infusion of the plant was used to treat snake bites. *Echinacea* is believed to inhibit hyaluronidase, a component of snake venom (Holisticonline.com, 2008). The root stalk and rhizomes are used to treat snake bites.

Research evidence

Echinacoside is a caffeoyl conjugate of *Echinacea* with known anti-hyaluronidase properties. The wound healing effects of Echinacea on vocal fold wound healing and functional voice outcomes have been investigated in pigs (Rousseau et al., 2006).

Guiera senegalensis (Combretaceae)

It is a shrub of the savannah region of West and Central Africa. The leaves are 3-5 cm long and 1.5-3 cm broad, are opposite or subopposite, oblong-elliptic, rounded or slightly cord- date at base, mucronate at apex. They are softly tomatoes on both surfaces, with scattered black glands beneath (Hutchinson and Dalziel, 1954). Main phytoconstituents are mucilage, tannins, flavonoids, alkaloids and amino acids.

Traditional Uses

In Ghana, e.g., leaves are used against dysentery, diarrhoea, gastro-intestinal pains and disorders, rheumatism and fever (Abbiw, 1990).

Research evidences

The extract of the leaves of *Guiera senegalensis* was found to detoxify (*in vitro*) venom from two common northern Nigerian snake species, *Echis carinatus* and *Naja nigricollis*, in separate experiments. There was a remarkable reduction in the mortality of albino mice after intra-peritoneal (i.p.) administration of reconstituted venom incubated with the extract, when compared to those challenged with the venom only. The survival of the animals exposed to the venom incubated with the different concentrations of the extract was used as the *in vitro* detoxification parameter (Abubakar *et al*., 2000).

Hemidesmus indicus (Asclepiadaceae)

Indian Sarsaparilla (*Hemidesmus indicus*) is a species of plant that is found in South Asia belongs to the family Asclepiadaceae. In Ayurveda it is known as *ananthamoola*. It is also called the False Sarsaparilla. It is found from the upper Gangetic plain eastwards to Assam and throughout central, western and southern India. The Moluccas and Sri Lanka are the other places of its distribution (*Hemidesmus Indicus*, Internet, 2008).

Flower contains hyperoside, isoquercitin and rutin. Leaves having tannins 2.5 %. Roots are reported to contain sitoserol. A new ester identified as lupeol octacosanoate in addition to the known compounds viz., lupeol, α-amyrin, ß-amyrin, lupeol acetate, (-) amyrin acetate, and hexatriacontane.

Therapeutic Use

The plant is used for demulcent, nutritional disorders, syphilis, chronic rheumatism, gravel and other urinary diseases diuretic, syphilis, gonorrhea, blood purifier and skin affections. It is administered in the form of powder, infusion or decoction as syrup. The roots are used as addition in main treatment of snake bite and scorpion sting (*Hemidesmus indicus*: Hemidesmus, Internet, 2002).

Research evidences

2-Hydroxy-4-methoxy benzoic acid, isolated and purified from the Indian medicinal plant *H. indicus* possessed anti-snake venom activity. Rabbits immunized with *Vipera russellii* venom in the presence and absence of the compound along with Freund's complete adjuvant, produced a precipitating band in immunogel diffusion and immunogel electrophoresis. The venom neutralizing capacity of this antiserum showed positive adjuvant effects as evident by the higher neutralization capacity (lethal and hemorrhage) when compared with the antiserum raised with venom alone (Alam and Gomes, 1998).

An organic acid, isolated and purified from the root extract of an Indian medicinal plant sarsaparilla *Hemidesmus indicus* R. Br, possessed viper venom inhibitory activity. HI-RVIF significantly antagonized viper venom-induced lethal, haemorrhagic, coagulant and anticoagulant activity in experimental rodents (Alam *et al*., 1994).

Parkia biglobosa (Leguminosae)

It is known as African Locust Bean Tree. These trees are not normally cultivated but can be seen in population of two or more in the Savannah region of Nigeria. African locust bean is a perennial deciduous tree with a height ranging from 7 to 20 m. Bark dark grey brown, thick, fissured. The leaves are alternate and dark green. The bark contained a long-chain ester of trans-ferulic acid together with an unseparable mixture of long-chain cis-ferulates, lupeol, 4-O-methyl-epi-gallocatechin, epi-gallocatechin, epi-catechin 3-O-gallate, and epi-gallocatechin 3-O-gallate (Alabi et al., 2005). Seed contains high proteins (34.02%), lipid (16.86%), carbohydrate (20.70%) and sugar (25.66%) (Tringali *et al.*, 2000).

Therapeutic uses

Stem bark of *P. biglobosa* is prescribed in the treatment of many infectious diseases, violent stomachaches, diarrhoea, pneumonia, bronchitis, severe cough, tracheitis, wounds, dental caries, conjunctivitis, amibiasis, otitis, dermatosis and sexually transmitted diseases.

Research evidences

A water-methanol extract of *P. biglobosa* stem bark significantly ($p<0.001$) protected the chick biventer cervicis (cbc) muscle preparation from *N. nigricollis* venom-induced inhibition of neurally evoked twitches when it was added to the bath 3-5 min before or after the venom. The extract also reduced the loss of responses to acetylcholine (Ach), carbachol and KCl, which are normally blocked by *N. nigricollis* venom, and significantly reduced the contractures of the preparation induced by venom. *P. biglobosa* extract (75, 150 and 300 µg/ml) significantly ($p<0.05$) protect murine muscle cells in culture against the cytotoxic effects of *N. nigricollis* and *E. ocellatus* venoms (Asuzu and Harvey, 2003).

Securidaca longipedunculata (Polygalaceae)

It is known as Violet tree (Eng.w); krinkhout (Afr.); Mpesu (tshiVenda); Mmaba (Tswana). It occurs in various parts of Western, Northern and Eastern Nigeria, and in Malaysia, Guinea, Cuba and several Asian countries. It is a semi-deciduous shrub or small tree that grows to 12 m tall, with an often flattened or slightly fluted bole. The plants are spiny and much branched, with an open, rather straggly looking crown.

It contains beta-D-(3,4-disinapoyl) fructofuranosyl-alpha-D-(6-sinapoyl) glucopyranoside, flavonoids, xanthones and beta-D-(3-sinapoyl) fructofuranosyl- alpha-D-(6-sinapoyl) glucopyranoside.

Therapeutic uses

The roots and bark are used for treating chest complaints, headache, inflammation, abortion, ritual suicide, tuberculosis, gonorrhea, infertility problems, venereal diseases, constipation, snake bite and coughs. The roots are used to treat snake bites (Ndou, 2006).

Research evidences

The anti-snake venom properties of *S. longipedunculata* root extract have been evaluated in rats by monitoring the levels of the liver enzymes, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), creatinine kinase (CPK), lactate dehydrogenase (LDH), and amylase. The extract produced a significant ($P < 0.05$) dose-dependent alteration in the serum enzymes and urea analyzed. The alterations in these parameters may be responsible for pharmacological activity of the plant extract (Wannang *et al*., 2005).

Tamarindus indica (Papilionaceae)

It is known as Tamarind, Tamarindo, Tamarin and Sampalok. The Tamarind is the only species of the genus *Tamarindus*. The tamarind is native to tropical Africa and grows wild throughout the Sudan, India and other tropical countries. The bright green, pinnate foliage is dense and feathery in appearance, making an attractive shade tree with an open branch structure. Fruits are 3 - 8 inch long, brown, irregularly curved pods are borne in abundance along the new branches.

The main constituents are fruit acids (20%) and sugar (up to 35%). Furthermore, small amounts of terpenes (limonene, geraniol), phenylpropanoids (safrole, cinnamic acid, ethyl cinnamate), methyl salicylate, pyrazine and alkylthiazoles are also reported.

Therapeutic uses

The pods are fed to livestock, and the pulp within the pods is used to make beverages, curries, chutneys and sauces. The juice is used to pickle fish in India. The fruit is said to improve digestion, relieve gas, soothe sore throats, and act as a mild laxative. Unripe fruits and the pulp of ripe pods are used to treat snake bites.

Research evidences

Tamarind seed extract inhibited the PLA_2 (Phospholipase A_2), protease, hyaluronidase, l-amino acid oxidase and 5'-nucleotidase enzyme activities of venom in a dose-dependent manner. The extract neutralized the degradation of the beta chain of human fibrinogen and indirect hemolysis caused by venom. Edema, hemorrhage and myotoxic effects including lethality, induced by venom were neutralized significantly when different doses of the extract were preincubated with venom before the assays (Ushanandini *et al*., 2006).

Trianosperma tayuya (Cucurbitaceae)

It is known as Tayuya, Taiuia, Taioia, Abobrinha-do-mato, Cabeca-de-Negro and Tomba. Tayuya is a woody vine found throughout Brazil and in many parts of the Amazon rainforest. They contain long tuberous roots. Tayuya is known by several botanical names including *Cayaponia tayuya*, *Trianosperma tayuya*, *Trianosperma ficifolia*, *Bryonia tayuya* and *Cayaponia ficcifolia*, however, all of these scientific names refer to the same plant (Tayuya from Internet, 2007).

Main constituents are 29-nor-cucurbitacin glucosides, alkaloids, amentoflavone, cayaponosides, cucurbitacins, cucurbitane triterpenoids, datiscetin, eriodictyol, flavonoides, isoorientin, leucocyanidol, orientin, malic acid, resins, robinetin, saponins and sterols.

Therapeutic uses

It having versatile uses, viz, diuretic to treat diarrhea, epilepsy, for metabolism regulation, backache, sciatic pain, headaches, gout, neuralgia, constipation, anemia, cholera, dyspepsia, stomach problems, fatigue and debility, skin disorders, arthritis and rheumatism, syphilis and also includes snake bite and rheumatism. The roots are used to treat snake bites.

Research evidences

Some species have been selected and tested for analgesic activity (number of contortions) and anti-inflammatory activity (Evans blue dye diffusion--1% solution) according to Whittle's technique (intraperitoneal administration of 0.1 N-acetic acid 0.1 ml/10 g) in mice. Previous oral administration of a 10% infusion (dry plant) or 20% (fresh plant) corresponding to 1 or 2 g/kg of *Apuleia leiocarpa, Casearia sylvestris, Brunfelsia uniflora, Chiococca brachiata, Cynara scolymus, Dorstenia brasiliensis, Elephantopus scaber, Marsypianthes chamaedrys, Mikania glomerata and Trianosperma tayuya* demonstrated analgesic and/ or anti-inflammatory activities of varied intensity (Ruppelt *et al*., 1991).

Thea sinensis/ Camellia sinensis (Theaceae)

Tea is a beverage made from the processed leaf of a plant. White tea, green tea, oolong and black tea are all harvested from this species, but are processed differently to attain different levels of oxidation. This plant is a tropical evergreen tree that will grow to about fifty feet high. It has glossy leathery elliptic-to-lance-shaped dark green leaves and in the winter produces fragrant whitish flowers. The flowers are followed by woody capsules each of which contain three seeds.

Caffeine, theobromine and theophylline are the main constituents of it.

Therapeutic uses

Caffeine relieves migraines. Black tea kills dental plaque also used as digestive tonic, vomit inductor, cough suppressant, anti-oxidant, natural dye and emollient.

Research evidences

Antivenin activity of melanin extracted from black tea (MEBT) was reported for the first time. The antagonistic effect of MEBT was evaluated for Agkistrodon contortrix laticinctus (broadbanded copperhead), Agkistrodon halys blomhoffii (Japanese mamushi), and Crotalus atrox (western diamondback rattlesnake) snake venoms administered i.p. to ICR mice. The greatest antivenin effect of MEBT was found against Japanese mamushi snake venom. An immediate injection of MEBT substantially reduced the toxic effect of venom and extended time at the 50% level of survival up to 52.3 ± 2.3 hour (Hung *et al*., 2004).

Withania somnifera (Solanaceae)

It is known as ashwagandha, Indian ginseng, and winter cherry. It is a native of India, Pakistan and Sri Lanka.
Alkaloids and withanolides are the main constituents.

Therapeutic use

The plant has been used as an aphrodisiac, liver tonic, anti-inflammatory agent, astringent, and more recently to treat bronchitis, asthma, ulcers, emaciation, insomnia, and senile dementia. Clinical trials and animal research support the use of ashwaganda for anxiety, cognitive and neurological disorders, inflammation, and Parkinson's disease. The roots are used to treat snake bites.

Research evidences

A hyaluronidase inhibitor glycoprotein (WSG) was purified from *W. somnifera.* The glycoprotein inhibited the hyaluronidase activity of cobra (*Naja naja*) and viper (*Daboia russelii*) venoms, which was demonstrated by zymogram assay and staining of the skin tissues for differential activity. WSG completely inhibited the activity of the enzymes at a concentration of 1:1 w/w of venom to WSG (Machiah et al., 2006).

The glycoprotein inhibited the phospholipase A(2) activity of NN-XIa-PLA(2,) isolated from the cobra venom, completely at a mole-to-mole ratio of 1:2 (NN-XIa-PLA(2): WSG) but failed to neutralize the toxicity of the molecule. However, it reduced the toxicity as well as prolonged the death time of the experimental mice approximately 10 times when compared to venom alone. The interaction of the WSG with the PLA(2) is confirmed by fluorescence quenching and gel-permeation chromatography. Application of the plant extract on snakebite wound confirms the medicinal value associated with the plant (Machiah and Gowda, 2006).

Conclusion

Few plants were collected from the natural sources which are effective for snake bites over thousand of years and documented in this review with few information. This is my humble attempt to make a comprehensive report to all scientists whose contributions have led to an existence of such a huge ocean of knowledge on this topic. In spite of having enormous data on the subject, certain aspects of it still need a further probe. There are many areas where few things are unclearly defined, that are needs substantial amount of clinical research work with respect to herbals against snake bites. As per literature survey, it can be conclude that combine applications of plants extracts shows it's more physiological effect than sole extracts for the remedy of snake bite. So, the variation of antivenom medicinal plants in this herbal world effectively illustrates the importance of herbal medicine.

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