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Medicinal plants with anti-Snake Venom property-A review

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Abstrac

The aim of the present study is evaluation of various Medicinal Plants used for Anti Venom activity. Snake bite has been the serious issue in India especially in rural areas of India. India has a lot of efficient medicinal Plants which are active against Snake Venoms and they have been using since years by the Traditional Healers. Lot of Medicinal Plants have been tested against various Snake Venoms and they have shown promising results. This article presents review of Medicinal Plants which are active against various Snake Venoms.

Keywords: Medicinal Plants, Snake bite, Anti Venom, Traditional Healers.

Introduction

Snake bites are being considered as a serious issue in India and rest of the World especially in rural areas of India. Higher death rates in India are due to the four poisonous Snakes namely Indian Cobra (*Naja naja*), Saw scaled viper (*Echis carinatus*), Russells viper (*Daboia russelli*) and common Krait (*Bangarus caeruleus*) ^[1]. Due to lack of hospitals in rural areas people tend choose herbal medications from Traditional Healers. Using Anti Venom is the specific treatment available against Snake bite and was developed by Albert calmette in 1985 against the Indian cobra ^[2]. There are some side effects using Anti Venom and its development is time consuming, expensive and requires ideal storage conditions ^[3]. So alternative approach is the finding effective inhibitors from Plant sources. Herbal Antidote may be an alternative but information on this aspect is still inadequate ^[4]. In Ayurvedic text a number of drugs are mentioned which show Anti venomous effects ^[5]. The present article is a review on Medicinal Plants which have been tested against various Snake Venoms.

Snake venom

The venom produced by the snakes venom gland apparatus is delivered in to the target tissue from fangs by injection mechanism [6, 7]. The venom contains complex mixture of enzymatic and non-enzymatic proteins, peptides and small organic compounds such as citrate, nucleoside and acetylcholine [8].

Clinical Effects of Snake Venom

The clinical effects of snake bite includes neurotoxicity, cardiotoxicity, coagulant (either pro or anti), hemostatic (either activating or inhibiting), hemorrhagic, hemolytic and edema forming activities [9].

Medicinal Plants Used Against Snake Venoms

It belongs to a family Vitaceae. Mahadeswaraswamy Y H et al. studied methalolic extract of grapes (Vitis vinifera L.) against the Indian Daboia/Vipera russelli venom induced local effects. The extract showed complete inhibition of proteolytic and hyaluronidase activities and also neutralized the hemorrhage, edema-inducing and myonecrotic actions of venom. In addition, the extract showed partial inhibition of pro coagulant activity of the venom and completely abolished the degradation of $A\alpha$ and $B\beta$ chains of human fibrinogen [10].

Anacardium occidentale

It belongs to a family Anacardiaceae. Ushanandhini S *et al.* studied the ability of bark extract of Anacardium occidentale to neutralize enzymatic and pharmacological activities induced by the *Vipera russelli* venom. The extract neutralized the enzymes such as phospholipase, protease and hyaluronidase. It also neutralized pharmacological effects such as edema, hemorrhage and myotoxin effects [11]

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Tamarindus indica

It belongs to a family Leguminosae. Ushannandini S *et al.* used dried seed extract of *Tamarindus indica* to inhibit the pharmacological as well as enzymatic effects induced by *V. russelli* venom. The seed extract inhibited the PLA2, protease, hyaluronidase, L-amino acid oxidase and 5' nucleotidase enzyme activities. The extract also neutralized the degradation of the beta chain of the human fibrinogen and indirect hemolysis caused by venom [12].

Acalypha indica

It belongs to a family Euphorbiaceae. Shirwaikar *et al.* used ethanol leaf extract of *Acalypha indica* to inhibit the *Russells viper* venom. The leaf extract inhibited venom induced lethality, hemorrhage, necrotizing and mast cell degranulation in rats and cardiotoxic and neurotoxic effects in isolated frog tissue. The extract also inhibited venom induced-lipid peroxidation in RBC, decreased GSH and catalase levels of rat kidney tissue [13].

Mangifera indica

It belongs to the family Anacardiaceae. Dhananjaya B L et al. evaluated anti-venom potential of aqueous extract of stem bark of Mangifera indica against Daboia russelli venom. The extract inhibited phospholipase, protease, hyaluronidase, 5'-nucleotidase, ATPase and phosphomonoesterase activity. The extract significantly inhibited both metalloproteases and serine proteases activities. Further the extract significantly reduced the myotoxicity of the venom. Though the extract completely inhibited in vitro PLA2 activity but unable to completely inhibit in situ hemolytic and in in vivo edema-inducing activities. In lethality studies, co-injection of the venom pre incubated with extract showed higher protection than the independent injection of venom, followed by the extract in the mice [14].

Bridelia fergunia

It belongs to a family Euphorbiaceae. Sanni Momoh *et al.* used ethanol dried leaf extract of *Bridelia fergunia* against the *Naja nigricollis* venom. The effect of extract on some selected enzymes activity in the serum/liver of albino rats induced with the snake venom was studied and the histopathology. The result showed the *Bridelia fergunia* leaf extract has little antisnake venom activity [15].

Pluchea indica

It belongs to the family Asteraceae. Gomes A *et al.* isolated major compound β sitosterol and minor compound stigmasterol from root extract of *Pluchea indica* by silica gel column chromatography. The root compounds were found to neutralize the viper induced lethal, hemorrhagic, defribigenation, edema and PLA₂ activity and cobra venom induced lethality, cardiotoxicity and PLA₂ activity were also antagonized the two compounds [16].

Clerodendrum viscosum

It belongs to a family Verbenaceae. This plant traditionally used in India for the treatment of snake bite was evaluated by in vitro and in vivo studies. While *in vitro* studies were performed using human blood, *invivo* studies were carried by using mice administered i.p doses of extract, 5 min before the administration of *Naja naja* snake venom. The results of the in vitro studies showed that the extract probably interacts with blood but does not stabilize membrane protein. In the in vivo studies the extract showed significant anti-snake venom

activity, which may be attributed to possible interaction with the acetylcholine receptor sites. Hence it justifies the traditional use of *Clerodendrum viscosum* as anti-snake venom [17]

Parkia bigblosa

It belongs to a family Mimosaceae. Methanol extract of stem bark of parkia bigblosa used to reduce the effects of two snake venoms (Naja nigricollis, and Echis ocellatus) in several experimental models. 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) protected C2C12 murine muscle cells in culture against the cytotoxic effects of N. nigricollis and E. ocellatus venoms. The extract protected egg embryos exposed to lethal concentrations of E. ocellatus venom for more than 12 h and completely blocked the haemorrhagic activity of the venom at concentrations of 5 and 10 microg/1.5 microl. P. biglobosa extract (400 mg/kg) did not protect mice injected i.p. with 5 and 2.5 mg/kg of E. ocellatus and N. nigricollis venoms, respectively. It, however, protected 40% of the mice from death caused by E. ocellatus venom after the extract and venom were pre-incubated for 30 min before injecting the mixture [18].

Croton urucurana

It belongs to a family Euphorbiaceae. Aqueous extracts of extracts *Croton urucurana* analyzed for anti-*Bothrops jararaca* venom activity. The plant extracts antagonized the hemorrhagic activity of the venom and proanthocyanidins were involved in this activity. This study demonstrates that the rich extracts of proanthocyanidins are powerful inhibitors of bothropic venom metalloproteinase [19].

Crinum jagus

It belongs to a family Amaryllidaceae. The metalonic extract of the bulb of *crinum jagus* plant was investigated in vitro and in vivo against three species *Echis ocellates*, *Bitis arietance* and *Naja nigricollis*. Oral administration of extract (1000 mg/kg) protected 50% of mice, whereas 30 min pre incubated mixture of venom and extract gave 100% protection against lethel effects of *Echis ocellatus* venom (10 mg/kg). *crinum jagus* extract (500 mg/kg) gave 50% protection against *B.arientans* venom (9.5 mg/kg) in mice while pre-incubation of a mixture of same dose of venom and extract (500 mg/kg) gave only 33.3% protection. The pre-incubation of 500mg/kg of *C.jagus* extract with *N.nigricollis* venom (6 mg/ kg) protected 50% of the treated mice [20].

Argusia argentea

It belongs to a family Boraginaceae. Aung HT *et al.* proved that the methanolic extract of *Argusia argentea* inhibited the hemorrhage induced by crude venom of Trimeresurus flavoviridis. Aung HT *et al.* found the Rosamarinic acid as an active principle in extract by using silica gel column chromatography and HPLC [21].

Eclipta prostrate

It belongs to the family Asteraceae. The butanolic extract at 2.5mg per mouse was able to completely neutralize the lethal activity of 2LD₅₀ malayan pit viper venom, but increasing the dose diminished the effect. The extract at 1.5-4.5 mg per mouse, was able to neutralize thelethality of venom at around 50-58%. Both extracts partially inhibited the hemorrhagic activity but displayed very low anti-ohospholipase activity A2 activity but did not inhibit the proteolytic activity of malayan pit viper venom [22].

Morus alba

Morus alba plant leaf extract studied against Indian Vipera/Daboia russelli venom. The exctract completely abolished the in vitro proteolytic and hyaluronolytic activities of the venom. Edema, hemorrhage and myonecrotic activities were also neutralized efficiently and partially inhibited the pro-coagulant activity and completely abolished the degradation of Aα chain of human fibrinogen [23].

Vitex nigundo and Emblica officinalis

Alam MI et al. used methanolic extract of Vitex nigundo and Emblica officinalis for the first time for the anti-snake venom activity. The extract neutralized the lethal activity of Vipera russelli and Naja kaouthia venom in vitro and in vivo condition. V.russelli venom induced-hemorrhage, coagulant, defibringenating and inflammatory activity was completely antagonozed by both plant extracts [24].

Strychnus nux vomica

The Ethanol seed extract of Strychnus nux vomica effectively neutralized the Daboia russelli venom induced lethal, hemorrhage, defibrinigenating, PLA2 enzyme activity and Naja kaouthia venom induced lethal, cardiotoxic, neurotoxic and PLA2 enzyme activity. The seed extract potentiated

polyvalent snake venom antiserum action was significantly potentiated by the active compound [25].

Andrographis panniculata

Shade dried stem and leaf parts of the Andrographis paniculata were extracted with different solvents on the basis of polarity nature such as petroleum ether (polarity 0), ethyl acetate (4.4), methanol (5.1) and water (9.0). All the four extracts were tested for their anti-venom activity through in vivo experiments. Among those methanol extract of Andrographis paniculata has shown significant inhibition on neurotoxic symptoms caused by the venom (450 µg/kg b.w) and prolonged survival time of mice (22±2 g) maximum up to 14.44±0.55h compared to other extracts. This in vivo screened active methanol extract was further tested for direct inhibitory on Naja naja snake venom major enzymes like; acetyl cholinesterase, hyaluronodase, ATPase, protease hemolytic activities in vitro. In these experiments, the venom was preincubated with different concentrations of Androraphis paniculata methanol extract 37 °C for 1 hour before adding to the reaction mixture in vitro. The results confirmed that, methanol extract of Andrographis paniculata possess potent snake venom inhibitors [26].

Balanites aegyptiaca

It belongs to the family Balanitaceae. The stem bark of Balanites aegyptiaca was sequentially extacted with hexane, toluene, chloroform, acetone and methanol at room temperature. The effectiveness of acetone and methanol extracts was tested against the Echis carinatus venom. Both the extracts were found to be effective at 75 mg/ml and 100 mg/mlconcentrations. Phytochemical screening of acetone and methanol extracts revealed the presence of saponins, tannis and voatile oils [27].

S. No	Plant	Family	Part used
1	Dichorostachys cinerea	Mimosaceae	Root
2	Poujolzia indica	Utricaceae	Aerial parts
3	Securidaca longipedunculata	Polygalceae	Root
4	Mucuna pruriens	Fabaceae	Seed

Reference 28 29 30 31 Parinari curatellifolia Chrysobalanaceae Root bark 32 Sapindus saponaria Sapindaceae Callus 33 34 Zingiberaceae Rhizome Curcuma longa 8 35 Hemidesmus indicus Apocynaceae Root 9 36 Piper longum Piperaceae Fruits 37 10 Parkia diglandulosa Minosaceae Stem bark 38 11 Guiera senegalensis Combretaceae Leaves 12 Dipteryx alata Fabaceae Bark 39 13 Cordia verbenacea Boraginaceae 40 14 Boswellia dalzielli 41 Burceraceae Stem bark

Table 1: shows the Plants having Anti-Snake Venom activity

Conclusion

Now a days the focus has been shifted to the Medicinal plants for the effective drugs against snake bites. It is the responsibility of the scientific community to do much greater work for the effective herbal medications. Traditional healers have been using herbal medications since years to treat snake bites and several other diseases. Lot of information from the traditional healers still to be known and has to be gathered and necessarily formulated [42]. The Pharmaceutical companies should come forward to find a plant based drugs which could inhibit snake venom efficiently.

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