Available online on www.ijcpr.com
International Journal of Current Pharmaceutical Review and Research, 3(2),1-10

ISSN: 0976-822X

Review Article

Medicinal Plants of Chhattisgarh with Anti-Snake Venom Property

Vinod Minu*, Verma Harsh, Thakur Ravikant, Jain Paridhi, Shrivatava Noopur.

Rungta College of Pharmaceutical Sciences & Research Kohka, Bhilai, 490023 Chhattisgarh, India.

ABSTRACT

Snakebite is a major health hazard that leads to high mortality rate especially in India. Since the last century, antivenom immunotherapy is the only specific treatment against snake venom envenomation. However, antiserum does not provide enough protection against venom induced hemorrhage, necrosis, nephrotoxicity and often develops hypersensitivity reactions. Chhattisgarh has a rich tradition of the usage of medicinal plants. Many Chhattisgarh medicinal plants are mentioned in literature, which are used to treat snakebite victims especially in the rural areas. However, only a few species have been scientifically investigated and still less had their active components isolated and characterized both structurally and functionally. This article presents a review of Chhattisgarh plants showing properties against snake venoms which were assayed in research laboratories, correlating them with ethnopharmacological studies.

KEYWORDS- Anti-snake venom, Plant extracts, Snake bite, Chhattisgarh.

INTRODUCTION

Snakebites represent a public health hazard that leads to high morbidity and mortality in the Indian subcontinent[1]. Conservative sources estimates that the number of accidents globally reaches one million, resulting 600,000 evenomations and more than 20,000 deaths annuall[2]. In India alone more than 200,000 cases are reported and an estimated 35,000 to 50,000 people dies each year[3]. Snake venoms are complex mixture of enzymatic and toxic proteins, which include phospholipase A2 (PLA2s), myotoxins,hemorrhagic metalloproteinases and other proteolytic enzymes, coagulant components,cardiotoxins, cytotoxins and neurotoxins[4-6].

Author for Correspondence: E-Mail- minuvinod23@gmail.com

Traditional herbal medicine is readily available in rural areas of Chhattisgarh for the treatment of snakebite. Plants are used either single or in combination, as antidotes for snake envenomation by rural populations in Chhattisgarh and in many parts of the world. Plants are reported to neutralize the action of snake venom, with a plethora of plants claimed to be antidotes for snakebites in folk medicine[7].

Clinical Complications Of Snake Envenomation: Envenoming by snakes is responsible for several clinical complications of severe systemic and local pathology. Bothrops venoms cause local tissue damage, as well as hemorrhage, proteolysis, myonecrosis and edema. Muscle necrosis is an important local effect induced by several snake venoms, sometimes resulting in an irreversible loss of tissue and occasionally requiring amputation of the affected limb. Myonecrosis may be due to an indirect action as a consequence of vessel degeneration and schemia caused by hemorrhagic metalloproteases or by a direct effect of myotoxic PLA2s homologues upon plasma membranes of muscle cells[8]. Envenoming by Naja n. nigricollis leads to local necrosis, haemorrhage, complement depletion and respiratory arrest or paralysis[9-10]. Its venom consists of PLA2s (an anticoagulant enzyme which inhibits the prothrombinase complex by its binding to coagulation factor Xa) and cardiotoxin[11].

In-Vivo Plant Extract Activity Against Snake Venom : Natural inhibitors of snake venoms play a significant role in the ability to neutralize the degradation effects induced by venom toxins. It has been known for many years that animal sera and some plant extracts are competent in neutralizing snake venoms. Most recent work has been carried out with mice for the testing of total crude extracts and is summarized in Table 1.

Pharmacological Action Of Investigated Plants: Azadirachta indica - A compound [AIPLAI (Azadirachta indica PLA_2 inhibitor)] purified from the methanolic leaf extract of A. indica (Neem) inhibits the cobra and Russell's viper venoms (RVVs) phospholipase A_2 enzymes in a dose-dependent manner. Kinetic study reveals that in in vitro condition, AIPLAI inhibits the purified N.kaouthia PLA_2 enzymes in a non-competitive manner[12].

Andrographis paniculata-Methanol extract of Andrographis paniculata has shown significant inhibition on neurotoxic symptoms caused by the venom (450 µg/ kg b.w) and prolonged the survival time of mice (22 ± 2 g) maximum up to 14.44 ± 0.55 h. This in vivo screened active methanolic extract was further tested for direct inhibitory activity on Naja naja snake venom major enzymes like; acetyl cholinesterase, hyaluronidase, ATPase, protease, and hemolytic activities in vitro[13]. Aristolochia indica- Anti-NNH1 (Naja Naja Hyaluronidase) and aristolochic acid both inhibited the in vitro activity of the purified hyaluronidase, (NNH1)

Table No 1- Investigated Chhattisgarh Plant Extracts Activity Against Snake Venom				
Plant species (family)	**Snake species**	**Part used**	**Extract**	**Reference**
Azadirachta indica (Meliaceae)	*Naja naja*	Leaf	Methanolic	[12]
Andrographis paniculata (Acanthaceae)	*Naja naja, Daboia Russelli*	Whole plant	90% Ethanolic, Methanolic	[13]
Aristolochia indica. (Aristolochiaceae)	*Naja naja*	Root	Etheral, Methanolic	[14]
Emblica officinalis (Euphorbiaceae)	*Vipera russellii and Naja kaouthia*	Roots	Methanolic	[15]
Hemidesmus indicus (Asclepiadaceae)	*Vipera russelli*	Root	Methanolic	[16]
Mimosa pudica (Mimosaceae)	*Naja kaouthia*	Root	Aqueous	[17]
Morus alba (Moraceae)	*Daboia russelii*	Stems and Leaves	_	[18]
Musa paradisiaca (Musaceae)	*Bothrops jararacussu*	Stem	Aqueous	[19]
Tamarindus indica (Leguminosae)	*Viper russelli*	Seed	95% Ethanolic	[20]
Vitex negundo (Verbenaceae)	*Vipera russellii*	Root	Methanolic	[15]
Withania somnifera (Solanaceae)	*Naja naja, Viper russelli*	Root	Aqueous	[21]

and the hyaluronidase activity of whole venom in a dose-dependent manner. Both anti-NNH1 and aristolochic acidabolished the degradation of hyaluronan in human skin tissue sections by NNH1 and by whole venom[14].

Emblica officinalis and Vitex negundo- The methanolic root extracts of *Vitex negundo* Linn. and *Emblica officinalis* Gaertn. were explored for the first time for antisnake venom activity. The plant (*V. negundo* and *E. officinalis*) extracts significantly antagonized the *Vipera*

russellii and *Naja kaouthia* venom induced lethal activity both in in vitro and in vivo studies. *V. russellii* venom induced haemorrhage, coagulant, defibrinogenating and inflammatory activity was significantly neutralized by both plant extracts[15].

Hemidesmus indicus-.The present investigation explored the possible venom neutralizing effect of a pure compound (2-hydroxy-4-methoxy benzoic acid) isolated and purified from the methanolic root extract of Hemidesmus indicus R.Rr. The compound effectively neutralized infammation induced by Vipera russelli venom in male albino mice and reduced cotton pellet-induced granuloma in rats. The compound effectively neutralized viper venom-induced changes in serum phosphatase and transaminase activity in male albino rats[16].

Mimosa pudica- Results from the proteomics assessment showed that 5 proteins– serine protease inhibitor protein, gelsolin, hemopexin, alpha-2-macroglobulin and another unidentified protein – were substantially up-regulated by *Naja kaouthia* venom. These proteins were normalized by co-incubating the venom with MPT (Mimosa pudica tannin) prior to injection into the test mice. This shows that the tannin compounds of Mimosa pudica tannin interacted with *Naja kaouthia* venom proteins to neutralize the up-regulation of the 5 proteins[17].

Morus alba- Morus alba plant leaf extract has been studied against the Indian Vipera/*Daboia russelii* venom induced local and systemic effects. The extract completely abolished the in vitro proteolytic and hyaluronolytic activities of the venom. Edema, hemorrhage and myonecrotic activities were also neutralized efficiently[18].

Musa paradisiaca- Interaction of Musa paradisiaca extract (MsE) with snake venom proteins has been examined in this study. Phospholipase A2 (PLA2), myotoxic and hemorrhagic activities, including lethality in mice, induced by crotalidae venoms were significantly inhibited when different amounts of MsE were mixed with these venoms before assays[19].

Tamarindus indica- Tamarind seed extract inhibited the Phospholipase A2 (PLA 2), protease, hyaluronidase, l-amino acid oxidase and 5'-nucleotidase enzyme activities of venom in a dose-dependent manner. These are the major hydrolytic enzymes responsible for the early effects of Evenomation, such as local tissue damage, inflammation and hypotension.

Furthermore, the extract neutralized the degradation of the beta chain of human fibrinogen and indirect haemolysis caused by venom[20].

Withania somnifera- A phospholipase inhibitor *Withania somnifera* glycoprotein (WSG) has been purified from Withania somnifera using gel-filtration and ion-exchange chromatographies. The WSG is an acidic glycoprotein. It

Table no- 2. Plants used against snake bite in chhattisgarh region.

Plant species	**Common name**	**Family**	**Part use**	**Direction**	**Reference**
Achyranthes aspera	Kakralata	Amaranthaceae	Root,leaves	Paste	[23]
Acorus calamus	Bach	Acoraceae	Rhizome	Extract	[24]
Aegle marmelos	Bael	Rutaceae	Bark	Decoction	[25]
Allium cepa	Pyaj	Liliaceae	Root	Paste	[26]
Albizia lebbeck	Sirsa tree	Fabaceae	Flowers	Juice	[25]
Amaranthus spinosum	Jangli Chaulai	Amaranthaceae	Fresh roots	Juice	[25]
Andrographis paniculata	Bhumi neem	Acanthaceae	Whole plant	Extract	[23]
Argemone mexicana	Piwala, Dhotra	Papaveraceae	Leaf ,Seed	Decoction	[26]
Aristolochia indica	Ishar mool	Aristolochiaceae	Whole plant	Extract	[25]
Azadirecta indica	Neem	Meliaceae	Leaf	Extract	[23]
Buchanania lanzan	Char	Anacardiaceae	Fruit,Bark	Extract	[24]
Butea monosperma	Parsa	Leguminocea	Flower,gum, fruit	Extract	[24]
Careya arboreaRoxb.	Kumahi	Myrtaceae	Leaf, fruit	Extract	[24]
Diospyrus melanoxylum	Tendu	Ebenaceae	Root, fruit	Extract	[24]
Eclipta alba	Bringharaj	Compositae	Whole plant	Paste	[26]
Emblica	Awla	Euphorbiaceae	Root	Extract	[26]

officinalis					
Garuza pinnata	Kenkar	Burseraceae	Bark, fruit	Extract	[24]
Gloriosa superba	Kalihari	Liliaceae	Tuber	Paste	[26]
Hemidesmus indicus	Dudhi bel	Periplocace	Whole plant	Decoction	[26]
Leucas aspera(Wild.)	Gumma	Labiateae	Whole Plant	Extract	[24]
Morus alba	Shahtoot	Moraceae	Leaf	Extract	[26]
Mimosa pudica	Chui mui	Mimosaceae	Whole plant	Extract	[26]
Michelia champaca	Champa	Sapotaceae	Seeds	Decoction	[25]
Madhuca indica	Mahuwa	Sapotaceae	Fruit, Root Flower	Extract	[24]
Maringa oleifera	Munga bark	Moringaceae	Bark	Aqueous Extract	[25]
Madhuca longifolia	Mahuwa	Sapotaceae	Fruit, root, Flower	paste	[25]
Nyctanthes arbour-tritis	Harshringar	Oleaceae	Leaf and bark juice	Juice	[25]
Ocimum sanctum	Tulsi	Lamiaceae	Leaf	Juice	[26]
Pergularia daemia	Utran	Asclepiadaceae	leaves	Extract	[27]
Piper nigrum	Black pepper	Piperaceae	Flower	Paste with ghee	[26]
Polygonum glabrum Wild.	Bhilamgori	Polygonaceae	Root	Paste	[28]
Sapium	Lidwi	Euphorbiaceae	Leachate	Bath with	[23]

insigne				leachate	
Sapindus emargiatus	Reetha	Sapindaceae	Bark	Paste	[26]
Terminalia arjuna	Arjuna	Combretaceae	Bark	Paste	[26]
Tectona grandis	Sagon	Lamiaceae	Roots	Aqueous Extract	[25]
Uraria picta	Prasniparni	Fabaceae	Roots	Decoction	[28]

neutralized the enzyme activity and pharmacological properties such as cytotoxicity, edema, and myotoxicity of a multi-toxic Indian cobra venom phospholipase (NNXIa–PLA). The results suggest that the neutralization of the pharmacological effects of the toxic phospholipase is brought about by inhibition of the enzyme activity by formation of a complex between the WSG and the toxic phospholipase[21].

Traditional Plants Used Against Snakebite In Chhattisgarh Region: The Chhattisgarh state in India is one of the best representatives of the bio-geographic zone that obtains biodiversity rich deciduous forests. About 44% geographical area of Chhattisgarh state is under various types of forests with rich plant diversity, of these many species are of ethnobotanical importance[22]. Numerous plant species are used as folk medicine for treatment of snake-bite are summarized in Table 2. Topical application of plant extracts on bitten area, chewing leaves or barks, drinking extracts, can counteract snake venom activity.

CONCLUSION

Chhattisgarh is an important reservoir of rich flora with diverse ethnic population and their traditionally conserved knowledge. In this review article the information regarding the medicinal plants which are traditionally used in the treatment of snake bite (snake venom) by the people of Chhattisgarh is discussed. The use of plant extracts and isolated chemical compounds as antidotes for snake venom is a common practice in Chhattisgarh rural area where a prompt access to serum therapy is lacking, and is also used as a supplemental alternative to conventional anti venom serotherapy. The anti venom activity of traditionally used plant extracts may be due to the presence of enzymatic inhibitors, chemical inactivators or immunomodulator principles. Further studies on the isolation, structural characterization and action mechanism of these traditionally used plants must be carried out in the future.

REFERENCES

1. Saini RK, Sharma N, Singh S, Pathania NS. Snakebite Poisoning. A Preliminary Report. *J Assoc Physicians India* 1984; 32(2): 195-197.
2. Chippaux JP. Bulletin of the World Health Organization 1998; 76 (5):515-524.
3. Bawaskar HS. Snake venoms and antivenoms: critical supply issues. *Journal Association Physicians India* 2004; (52):11-13.
4. Kini RM. Venom Phospholipase A2 Enzymes, Structure, Function and Mechanism, Chichester: John Wiley & Sons Ltd., Chichester, United Kingdom, 1997, 155–183.
5. Aird SD. Ophidian envenomation strategies and the role of purines. *Toxicon* 2002; (40): 335-393.
6. Soares AM, Fontes MRS, Giglio JR. Phospholipases A_2 myotoxins from *Bothrops* snake venoms: Structure-function relationship. *Curr. Org. Chem*. 2004; (8), 1677–1690.
7. Kirtikar KR, Basu BD, 1975. Indian Medicinal Plants, vols. 1–4. International book Distributors, Dehradun, India. p.2793.
8. Guti´errez JM, Lomonte B. Phospholipases A2 myotoxins from Bothrops snake venoms.In: R.M. Kini, Venom Phospholipase A2 Enzymes: Structure, Function and Mechanism. Wiley & Sons, UK, 1997, 321–352.
9. Warrell DA, Greenwood BM, Davidson NM, Ormerod LD, Prentice C R. Necrosis, haemorrhage and complement depletion following bites by the spitting cobra (Naja nigricollis). *Quart. J.Med* 1976; 45(177): 1-22.
10. Schwersenski J, Beatty DW. South African medical journal Suid Afrikaanse tydskrif vir geneeskunde, 1982; 61(16): 597-598.
11. Kerns RT, Kini RM, Stefansson S, EvanS HJ. Arch. *Biochem. Biophys* 1999; 369(1): 107-113.
12. Mukherjee AK, Doleyand R, Saikia D. Isolation of a snake venom phospholipase A_2 (PLA_2) inhibitor (AIPLAI) from leaves of *Azadirachta indica* (*Neem*): Mechanism of PLA_2 inhibition by AIPLAI in vitro condition. Toxicon 2008 Jun 15; 51(8):1548-53.
13. Kadiyala Gopi et al. The neutralization effect of methanol extract of *Andrographis paniculata* on Indian cobra *Naja naja* snake venom. *Journal of Pharmacy Research* 2011; 4(4):1010-1012.
14. Girish KS, Kemparaju K. Inhibition of *Naja naja* venom hyaluronidase: Role in the management of poisonous bite. *Life Sciences* 2006 Feb 78; (13): 1433-1440.

15. Alam MI, Gomes A. Snake venom neutralization by Indian medicinal plants (*Vitex negundo* and *Emblica officinalis*) root extracts. *Journal of Ethnopharmacology* 2003; (86):75–80.
16. Alam M.I., Gomes A, Viper venom-induced inflammation and Inhibition of free radical formation by pure compound (2-hydroxy-4-methoxy benzoic acid) isolated and purified from Anantamul (*Hemidesmus Indicus* r.br) root extract, Toxicon 1998; 36(1): 207±215.
17. Ambikabothya A, Ibrahima H, Ambub S, Chakravarthib S, Awangc K, Vejayand J. Efficacy evaluations of Mimosa pudica tannin isolate (MPT) for its anti-ophidian Properties. *Journal of Ethnopharmacology* 2011; (137): 257– 262.
18. Chandrashekara KT, Nagaraju S, Nandini SU, Basavaiah, Kemparaju K. Neutralization of local and systemic toxicity of Daboia russelii venom by Morus alba plant leaf extract, *Phytother Res*. 2009 Aug; 23(8): 1082-7.
19. Borges MH, Alves DL, Raglan DS, Piló-Veloso D, Rodrigues VM, Homsi-Brandeburgo MI, De Lima ME. Neutralizing properties of Musa paradisiaca L (Musaceae) juice on phospholipase A2, myotoxic, hemorrhagic and lethal activities of crotalidae venoms. *J Ethnopharmacol* 2005; 03(14): 21-9.
20. Ushanandini S, Nagaraju S, Harish Kumar K, Vedavathi M, Machiah DK, Kemparaju K, Vishwanath BS, Gowda TV, Girish KS. The anti-snake venom properties of Tamarindus indica (leguminosae) seed extract. *Phytother Res* 2006; 09 (27): 851-8.
21. Deepa MT, Veerabasappa Gowda. Purification and characterization of a glycoprotein inhibitor of toxic phospholipase from Withania somnifera. *Archives of Biochemistry and Biophysics* 2002; 408: 42–50.
22. Kala CP. Aboriginal uses and management of ethnobotanical species in deciduous forests of Chhattisgarh state in India. *Journal of Ethnobiology and Ethnomedicine* 2009; 5:20.
23. Jain SP, Singh J. Traditional medicinal practices among the triabal people Raigarh (CHHATTISGARH) India. *Indian journal of natural products and resources* March 2010; 1(1):109-115.
24. Pankaj Oudhia. Traditional medicinal knowledge about common herbs used in treatment of snake bite: The result of recent ethnobotanical surveys in Chhattisgarh, India. Available fro http://www.botanical.com/site/column_poudhia/285_snakebite.html

25. Ankaj Oudhia. Traditional Medicinal Knowledge about Plant Leachate Used For Herbal Bath in Chhattisgarh, India. 189. Lindwi (Sapium insigne). Available from http://www.pankajoudhia.com/TAK2.pdf
26. Makhija IK, Khamar D. Anti-snake venom properties of medicinal plants. *Der Pharmacia Lettre* 2010; 2(5): 399-411.
27. Pankaj Oudhia. Medicinal herbs of Chhattisgarh, India having less known traditional uses. XXXXXIX. Utran (Pergularia daemia, family Asclepiadaceae). Available from http://botanical.com/site/column_poudhia/370_utran.html
28. Kadel C, Jain A K. Folklore claims on snakebite among some tribal communities of Central India. *Indian Journal Traditional Knowledge* April 2008; 7(2):296-299.