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A REVIEW ON ANTI-VENOM ACTIVITY OF SOME MEDICINAL PLANTS

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ABSTRACT: In almost every part of the world, where venomous snake occur, numerous plant species are used as folk medicine to treat snake bite. The mortality associated with snake bites is a serious public health problem as the estimated death incidence per year is about 1,25,000 globally. In India, about 35,000 to 50,000 people reportedly die of snake bite; although, unreported cases may be even more in rural areas. Considering the socio-medical problem due to snake bite, a review is being conducted on snake bite (management aspects), snake venom (natural and its utility), anti-venom and herbal antidote to provide adequate information to researchers for better future prospective.

INTRODUCTION Snake bite is one of the major health hazards that leads to high mortality rate especially in India and the common poisonous (Venomous) snakes found in India are cobra (*Naja naja*), krait (*Bungarus caeruleus*), Russell's viper (*Daboia russelli*), and saw scaled viper (*Echis carinatus*)¹. Anti-venom immunotherapy is the only specific treatment against snake venom envenomation. There are various side effects of antivenom sera such as anaphylactic shock, pyrogen reaction and serum sickness².

Snakebite is declared as a "Neglected Tropical Disease" by the World Health Organization. As a result, this may be considered as a matter of global health concern for the people in general and the rural communities of the developing countries in particular.

The reasons for the death of true statistical data on epidemiology of snakebite, particularly from some of these countries are mainly due to the lack of properly co-ordinated epidemiological survey programme. Therefore, the published data on snakebite based on hospital records were biased and did not reflect the true magnitude of the problem. Snakebite data based on diverse methodologies show that global incidence of snakebite is around 5,400,000 bites per year leading to over 2,500,000 envenoming and around 125,000 fatal cases annually³. As a result, snake envenomation warrants urgent medical attention and must be considered as a severe health issue.

India has rich assortment of snake fauna, of which only 242 species have been identified including 57 poisonous or harmful species. The four major species of venomous snakes ubiquitous in India known as "Big four" are considered responsible for life-threatening envenomation around the country. These include- Indian cobra (*Naja naja*), the common krait (*Bungarus caeruleus*), the Russell's viper (*Daboia russelii*) and the saw-scaled viper (*Echis carinatus*).

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Although many other species of venomous snakes, for example, Indian Banded Krait (*Bungarus fasciatus*), *Naja kaouthia*, *N. oxiana*, *N. sagittifera*, *Echis sochureki*, *Hypnale hypnale*, are also responsible for fatal and/or mild envenomation in different parts of India^{4,5}.

Snake Bite: A snake bite is an injury caused by a snake, often resulting in puncture wounds inflicted by the animal's frangs and sometimes resulting in envenomation. Although majority of snake species are non-venomous and typically kill their prey with constriction rather than venom, venomous snakes (15% out of 3000 known species)^{6,7,8} are reported to be found on every continent excepting Antarctica⁶.

MATERIALS & METHODS: Various books incorporating the research articles related to ethno botany and ethno medicine were scrutinized and reviewed in respect to reported antivenom activity of medicinal plants. The details of the books including title, publisher, year of publication and page number were noted^{9 to 19}.

The medicinal plants which are reported for antivenom activity were noted down in a specially designed format in regards to their botanical names, family, form of administration and species along with references. The shortlisted plants were cross checked from the classical text of Ayurveda with regards to their pharmacological properties and actions.

Antivenom treatment of snake envenomation & its limitation: The most common and effective method of treating snake bite victims is through antivenom, a serum made from the venom of the snake²⁰.

In India, polyvalent antivenom is prepared by Central Research Institute, Kasauli, Shimla and the Haffkine Corporation, Parel, Mumbai. The WHO has designed the Liverpool School of Tropical Medicine as the international collaborating centre for antivenom production and/or testing²⁰.

Antivenomes, in most countries are costly and may be in limited supply. Antivenoms for therapeutic use are often preserved as freeze-dried ampoules, but some are available only in liquid form and must be kept refrigerated. The majority of snake antivenoms are administered intravenously. The intramuscular route has been questioned in some situations as they are not uniformly effective. Antivenom should be given as quickly as possible so that the venom's side effects can be managed. Antivenom should be given only if the range of specificity is stated which includes the species known or through to have been responsible for the bite.

Liquid antivenom that turned opaque should not be used because precipitation of protein indicates loss of activity which is directly proportional to increased risk of reactions. In India, other centres which are involved in manufacturing of antivenom are Bharat Serum and Vaccines Ltd.; Mumbai, Serum Institute, Pune, King Institute, Chennai, Vins Bio-products Ltd.; and Biological "E" Ltd., Hyderabad, etc. Antivenom serum (AVS) manufacturers recommend skin sensitivity testing to predict adverse AVS reactions. But, the usefulness of skin testing is doubtful, as skin testing carries the risk of inducing an acute reaction and delays the initiation of AVS administration²¹.

TABLE 1: HERBAL ANTIDOTE

BOTINICAL NAME	FAMILY	EXTRACT	SPECIES
<i>Acalypha indica</i>	Euphorbiaceae	Ethanollic leaf extract	<i>Vipera russelli</i> ²²
<i>Aristolochia indica</i>	Acanthaceae	Methanolic plant extract	<i>V. russelli</i> ²³ , <i>E. carinatus</i> ²⁴
<i>Mucuna pruriens</i>	Fabaceae	Aqueous seed extract	Cobra ^{25,26,27} , Viper ²⁸ , <i>E. carinatus</i> ²⁹ , <i>Naja sputatrix</i> ³⁰ , <i>Bangarus caeruleus</i> ³¹
<i>Mimosa pudica</i>	Mimosaceae	Aqueous extract of dried root	<i>N. naja</i> ³² , <i>B. caeruleus</i> ³² , <i>N. naja kaouthia</i> ³³ , <i>Ophiophagus hannah</i> ³³
<i>Azadirachta indica</i>	Meliaceae	Methanolic leaf extract	Cobra & Russell's viper ³⁴
<i>Clerodendron viscosum</i>	Verbenaceae	Alcoholic root extract	<i>N. naja</i> ³⁵
<i>Emblica Officinalis</i>	Euphorbiaceae	Root extract	Cobra & viper ³⁶
<i>Curcuma zedoaria</i>	Zingiberaceae	Aqueous extract	<i>N. naja siamensis</i> ³⁷
<i>Parkia biglobosa</i>	Mimosaceae	Stem bark extract	<i>Naja nigricollis</i> ³⁸ , <i>Echis ocellatus</i> ³⁸
<i>Balanites aegyptiaca</i>	Balanitaceae	Acetone & methanolic extract of	<i>E. carinatus</i> ³⁹

stem bark			
<i>Mangifera indica</i>	Anacardiaceae	Ethanollic extract of seed kernel	Thai cobra ⁴⁰ , Malayan pit viper ⁴⁰ , <i>C. rhodostoma</i> ⁴¹ , <i>N. naja</i> ⁴¹
<i>Eclipta prostrate</i>	Asteraceae	Butanollic extract	Malayan pit viper ⁴² , <i>Gloydus brevicaudus</i> ⁴³ , <i>G. shedaoensis</i> ⁴³
<i>Crinum jagus</i>	Amaryllidaceae	Methanollic extract of bulb	<i>Echis ocellatus</i> ⁴⁴ , <i>Naja nigricollis</i> ⁴⁴ , <i>Bitis arietans</i> ⁴⁴
<i>Anacardium occidentale</i>	Anacardiaceae	Methanollic extract of bark	<i>V. russelli</i> ⁴⁵
<i>Tamarindus indica</i>	Leguminosae	Seed extract	<i>V. russelli</i> ⁴⁶

Other plant species were found to possess different herbal compounds (acids, alkaloids, steroids, enzymes, peptides, pigments, glycoproteins and glycosides, phenols, pterocarpanes, tannins, terenoids, quinonoid xanthenes and other compounds) which are effective against snake envenomation⁴⁷ by neutralizing different enzymes and toxins (procoagulant enzymes, haemorrhagins, cytolytic or necrotic toxins, phospholipases A2, B, C, D, hydrolases, phosphatases, proteases, esterases, acetylcholine esterase, transaminase, hyaluronidase, phosphodiesterase, nucleotidase, ATPase and nucleosidases) in venoms.

Side effects of Anti-venom: Side effects of anti-venom therapy are anaphylactic reaction (difficulty in breathing and swallowing; hives; itching, especially of feet or hands, reddening of skin, especially around ears, swelling of eyes, face, or inside of nose, unusual tiredness or weakness, sudden and severe), serum sickness (enlargement of the lymph glands, fever, generalized rash and itching; inflammation of joints), pyrogen reaction-probably due to the action of high concentrations of non-immunoglobulin proteins present in commercially available hyper-immune anti-venom⁴⁸.

CONCLUSION: The veracity of the herbal assertions holds a good promise for the development of novel anti-snake venom drug in future. The combination of herbal compounds with anti-venom serum may also be a good prospective as well as effective in neutralizing snake-venom. Most importantly herb(s) possessing anti-venom serum activity should be properly identified (plant parts/compound) and cultivated, and knowledge must be disseminated properly so that at least first aid treatment can be provided to reduce mortality of snake bite.

Till date proper herbal formulations and its efficacy in relation to remedial measure against snake bite are yet not known properly, and research should be triggered in this direction.

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