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Anti-venoms for snake bite: A synthetic and traditional drugs review

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Abstract
The mortality related to snake bites is an extreme public health problem because the estimated death prevalence per year is about 1,25,000 globally. Insufficient health services, bad transportation and consequent delay in synthetic anti-snake venom management are the main motives for excessive mortality. Adverse drug reactions and inadequate storage conditions limit the use of synthetic anti-snake venom. The medicinal flora, available domestically and used widely by traditional healers, consequently need attention. Most of the snake bite cases are typically undermined due to loss of proper consciousness of the mass people. However, present evaluation has been focused at the artificial and traditional herbs and their anti-venom property, which can be a venturing stone in setting up the future treatment against snake bite treatment and management.

Keywords: snake bite drugs; traditional anti-snake venom, synthetic anti-snake venom

1. Introduction
Snake bite constitutes a neglected general medical issue globally [1]. World Health Organization revealed venomous snakes brought on 5.4 million snakes each year around the globe, of them 2.5 million endured with envenoming and around 125,000 died [2]. Snakebite is frequently an under perceived general medical problem in Bangladesh [3]. Topographical area and the tropical condition of Bangladesh permit the developing of various types of snakes. Thus, around 82 unique species including 12 types of ocean snakes are grossly available all over Bangladesh, of them 28 species are venomous [4]. Yearly a roughly 15,372 (10.98/100,000) people were bitten by snakes and of them 1709 (1.22/100,000) passed on consistently [5]. A more recent study directed in 2009 demonstrated higher than past reviews, which was 623.4/100,000 persons per year [6]. In Bangladesh, snake-bite is considered as a typical medical issue among the country populace. However, because of absence of broadly illustrative information, the correct magnitude is as yet obscure [7]. Appropriate emergency treatment and restorative support in type of counter-agent venom may lessen mortality of snake bite to a more noteworthy extent. Apart from possessing side effects, anti-venom development is time consuming, expensive and requires ideal storage condition [8], and hence search for anti-venom, either synthetic or natural, that could complement or substitute for the activity of anti-venoms are of prone significance.

In spite of the fact that majority of the snake species are non-venomous and ordinarily kill their prey with choking instead of venom, venomous snakes (15% out of 3000 known species) [9-11] are accounted for to be found on each continent aside from Antarctica [9]. Envenomation is totally intentional, i.e., every venomous snake are equipped for biting (dry bite) without infusing venom into their victim [12]; practically around 20% of snake bites are dry bites [13]. The measure of venom infused shifts markedly between species - Gaboon snake convey 450-600mg venom for each bite, the most of any snake [14]. Snake venoms are complex substances that, depending upon the species, can contain a variety of poisons. Poison segments can incorporate proteases, nucleases, phosphodiesterases, and different compounds which alters physiological procedures and cell uprightness. The venom toxins are largely classified as neurotoxins, cytotoxins, myotoxins, and cardiotoxins. Venomous snake bites may bring about a variety of side effects, including pain, swelling, tissue necrisis, hypotension, neuromuscular collapse, blood clotting dysfunction, respiratory depression, kidney failure, coma and death [15].

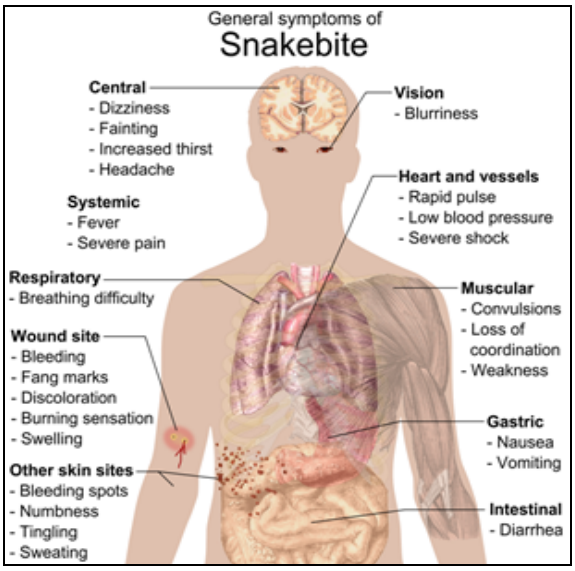

Fig 1: Symptoms of snake bite

The treatment for snake bite varies from snake to snake. The main accessible treatment is the use of anti-venom against snake bite. The first anti-venom (called an anti-ophidic serum) was discovered by Albert Calmette, a French researcher of the Pasteur Institute in 1895, against the Indian Cobra (naja). Anti-venom binds and neutralizes the venom, ceasing further harm, yet don't turns around the harm officially done. A few people may respond to the anti-venom with a prompt hyper sensitivity [16]. Other options of treatment includes the utilization of folk and traditional medicines in snake bites. Medicinal herbs are the regional heritage with worldwide significance. Different plants have been utilized against snake bite, in folk and traditional medicine. In Ayurvedic system of medicine distinctive plants and their composites are reported to pose anti-snake venom activity. However, they likewise have their individual toxicities and most of the folk medicinal plants have no scientific validation. This survey is an endeavour to concentrate on the anti-venom treatment of snake bite, herbal antagonists and herbal constituents active against snake bite and its future.

Synthetic anti-venom review

Anti-venoms are generally produced by utilizing a benefactor animal, for example, a horse or sheep. The donor animal is hyper-immunized with non-lethal dose of at least one or varied amounts of different venoms to produce a neutralizing antibody. Then at a specific time interval the blood from the donor animal is collected and neutralizing antibodies are purified from the blood to produce an anti-venom. On the basis of, antigens (venoms) used in the production process, snake anti-venoms are classified as monovalent and polyvalent. Monovalent anti-venoms are that hyper-immunizing venom which contains neutralizing antibodies against single species of snakes and polyvalent against two or more species of snakes.

Structures of the anti-venom can be classified as whole IgG, or fragments of IgG. Entire antibody products comprise of the whole antibody molecule, frequently immunoglobulin G (IgG), while antibody fragments are determined by processing the entire IgG into Fab (monomeric binding) or F (ab') 2 (dimeric binding). The fragment antigen binding, or Fab, is the particular antigen binding site. An antibody, for example, IgG, can be processed by papain to create three fragments: two Fab parts and one Fc part. An antibody can likewise be digested by pepsin to create two parts: a F (ab') 2 part and a pFc' part. The fragment antigen-binding (Fab fragment) is a region on an antibody that binds to antigens, such as venoms. The molecular size of Fab is roughly 50kDa, making it smaller than F (ab') 2 which is around 110kDa. These size contrasts enormously influence the tissue distribution and rates of elimination [17].

Brown Snake Anti-venom: These are used for nullifying systemic envenomation by members of the Australian brown snake group. It is made from horse IgG. Each ampoule contains 1000 units of neutralising potency. One unit of anti-venom activity should neutralise 0.01mg of dried venom from the species of animal against which the anti-venom has been raised. Average volume per ampoule is 4.5-9mL. The immunising venom used is common brown snake venom [18].

Tiger Snake Anti-venom: These are used for neutralising systemic envenoming by members of the Australian tiger snake group and also copperheads, the rough scaled snake, the broad-headed snake, the pale-headed snake, Stephen's banded snake and many members of the black snake group (but not the mulga or king brown snake or Collett's snake). It is also powerful against many sea snake bites. it is made from horse IgG. Every ampoule incorporates 3000 units of neutralising potential against the target venoms. Average extent per ampoule is nine-12mL. The immunising venom is common tiger snake venom [18].

Black Snake Anti-venom: These are used for neutralising systemic envenoming by members of the Australian black snake institution. It is made from horse IgG. Every ampoule carries 18000 units of neutralising capacity towards the target venoms. Average quantity per ampoule is 30-50mL. The immunising venom is mulga snake venom. The primary species for which this anti-venom is used are the mulga snake, Butler's mulga snake, Collett's snake and the Papuan black snake. It is also effective for bites by other participants of this genus, particularly the red bellied black snake and the blue bellied black snake [18].

Death Adder Anti-venom: Used for neutralising systemic envenoming with the aid of members of the Australian death adder group. It is made from horse IgG. Each ampoule carries 6000 units of neutralising capacity towards the target venoms. Average volume per ampoule is 25-26mL. The immunising venom is from the common death adder [18].

Taipan Anti-venom: These are valued for neutralising systemic envenoming with the aid of members of the Australian taipan snake group. It is made from horse IgG. Every ampoule carries 12,000 units of neutralising ability against the target venoms. Average volume per ampoule is 43-50mL. The immunising venom is from the common taipan [18].

Polyvalent Snake Anti-venom: Used for neutralising systemic envenoming by all dangerous Australian snakes. It is obtained from horse IgG. Every ampoule contains 1,000 units of neutralising capacity against brown snake venom, 3,000 units towards tiger snake venom, 18,000 units against mulga snake venom, 6,000 units against death adder venom and 12,000 units towards taipan venom. It is consequently equivalent in neutralising power, to giving the affected person 1 ampoule of each of the 5 "monovalent" snake antivenoms. Average volume per ampoule is high, as expected, approximately 46-50mL [18].

Sea Snake Anti-venom: These are used for neutralising systemic envenoming by all species of sea snakes. It is obtained from horse IgG. Each ampoule contains 1000 units of neutralising capacity against the target venoms. Average

quantity per ampoule is 15-35mL. The immunising species are the beaked sea snake, *Enhydrina schistosa* and the Australian tiger snake, *Notechis scutatus*. The antivenom has been shown to be powerful, to various levels, in neutralising a wide variety of sea snake venoms, along with olive sea snake *Aipysurus laevis*, Stoke's sea snake *Astrotia stokesii*, olive headed sea snake *Disteira* (Hydrophis) major, banded sea snake Hydrophis cyanocinctus, elegant sea snake Hydrophis elegans, Daudin's sea snake *Hydrophis nigrocinctus*, narrow banded sea snake Hydrophis spiralis, Gunther's sea snake *Hydrophis stricticollis*, spine-bellied sea snake *Lapemis hardwickii*, banded sea krait *Laticauda semifasciata* and needle-headed sea snake *Microcephalophis gracilis* [18].

Vipera tab: Each vial containing 100 mg of antigen binding fragments (Fab) in 4mL of 20mM sodium acetate buffer, pH 4.0. Fab fragments were derived from antibodies raised in sheep immunised with the venom of *Vipera berus*, the European adder [19].

Crotalidae Polyvalent Immune Fab (Ovine): It is a sterile, nonpyrogenic, purified, lyophilized preparation of ovine Fab (monovalent) immunoglobulin fragments acquired from the blood of healthful sheep flocks immunized with one of the following North American snake venoms: *Crotalus atrox* (Western Diamondback rattlesnake), *Crotalus adamanteus* (eastern Diamondback rattlesnake), *Crotalus scutulatus* (Mojave rattlesnake), and *Agkistrodon piscivorus* (Cottonmouth or Water Moccasin). To attain the final antivenin product, the four specific monospecific antivenins are combined. Every monospecific antivenin is prepared by means of fractionating the immunoglobulin from the ovine serum, digesting it with papain, and separating the venom specific Fab fragments on ion exchange and affinity chromatography columns [20].

European Viper Venom Antiserum: It is manufactured in the Institute of immunology in Croatia and acts against following species-

Name of animal	Taxonomy	Type of antibody	Reference
Macrovipera lebetina	Species	Para specific	[21]
Vipera ammodytes	Species	Specific	[21, 22]
Vipera aspis	Species	Para specific	[21, 22]
Vipera berus	Species	Specific	[21, 22]
Vipera ursinii	Species	Para specific	[21, 22]
Vipera xanthina	Species	Para specific	[22]

Polyvalent Anti-vipers Venom: It is manufactured in the VACSERA of Egypt and acts against following species of snakes-

Name of animal	Taxonomy	Type of antibody	Reference
Cerastes cerastes	Species	undetermined whether specific or para specific	[23, 24]
Echis pyramidum	Species	undetermined whether specific or para specific	[23, 24]
Vipera palestinae	Species	undetermined whether specific or para specific	[23]

Anti-venom selection: selection of the ideal anti-venom is a very critical step. Venom detection kits (available only in Australia – include a rapid stepped enzyme immunoassay wherein wells are lined with antibodies to the numerous snake venoms through a swab from the bite website, blood or urine) help to select the sort of anti-venom. When venom type detection isn't feasible polyvalent anti-venoms are used [25].

Limitations of anti-venom: 1. Cause diverse side effects. 2. Can't undo damage already caused by venom, so anti-venom treatment need to be started out as soon as feasible. 3. Usually administered intravenously however the route may not be uniformly effective. 4. Production is time consuming and high-priced. 5. Limited supply. 6. Liquid anti-venom can also lose its activity due to protein precipitation, if not stored properly. 7. Have to be preserved always as freeze-dried sample [25].

Traditional/folk anti-snake venom review

The plant kingdom gives other options for anti-snake venom. Restorative plants have been utilized as folk medicine for treatment of snake bite. Dependence on restorative plants is fundamentally because of their safety, viability, cultural preferences, inexpensive nature and reliance on neighboring woods [26]. Comprehensively, local healers are rehearsing natural solution to cure snake envenomations; nonetheless, the practice is not by any means perceived by current medication. The quantity of studies assessing the pharmacologically active standards against snake bite are few [27, 28]. In spite of the fact that novel phytotherapeutic agents have been isolated from plants because of fundamental leads from ethnic societies, yet approval is as yet an issue. Accentuation ought to be on legitimate outline of both in vivo and in vitro considers, with the goal that they relate precisely to the clinical circumstances [29]. For the most part aqueous, methanol or ethanol extract is prepared out of the plant parts. Topical utilization of the plant or its sap onto the bitten zone, biting leaves or barks or drinking plant concentrates or decoctions or infusing the concentrates are a few strategies established to nullify snake venom action.

Ayurveda states the use of unique plants against specific snake bites, e.g. root extract of *Abrus precatorius* is used against krait bite, leaf paste of *Azadirachta indica* with rock salt is used against viper bites. Leaves and bark of *Casearia sylvestris*, (guacotonga) are used as a trendy Ayurvedic drug to treat snake bite in Columbia, India, and so on. *Aristolochia indica* is used as a decoction for snake bite. Seeds of Psoralea corylifolia are used both in Ayurveda and Siddha against snake bite. *Origanum dictamnus* juice is consumed in wine to treat snake bite. Tea made from the leaves of *Cecropia peltata* is used as a remedy for a wide variety of ailments including snake bite. The roots of the plant *Ophiorrhiza mungo*, *Peristrophe bicalyculata*, *Gymnema sylvestre Gloriosa superba*, *Cucumis colosynthis*, *Alangium salvifolium*, leaves of *Enicostemma axillare Calycopteris floribunda*, Calotropis gigantea, *Aristolochia indica* are used in Ayurvedic medicine [30]. *Eclipta prostrata* L. (Asteraceae) is utilized as an anti-venom against snake bite in China and in Brazil. *Schumanniophyton magnificum*, *Eclipta prostrata* or *Aristolochia shimadai*, have the ability to restrain phospholipase A2, other proteins (e.g. ATPase) alongside other physiological and biochemical properties, (for example, consequences for uterine tone or the protection of mitochondrial layers). Antihaemorrhagic impact of persimmon tannin from *Diospyros kaki* is additionally notable. The survival time was drawn out after pretreatment

with concentrates of *Diodia scandens* and *Andrographis paniculata* [31]. Rhizomes of Curcuma Sp. inactivated postsynaptic neurotoxin of the Thai cobra (*Naja naja siamensis*) in mice [32]. *Bothrops atrox* venom induced haemorrhage was totally neutralized by the concentrates of the stem barks of *Brownea rosademonte*, *Tabebuia rosea*, the entire plants of *Pleopeltis percussa, Trichomanes elegans*, rhizomes of *Heliconia curtispatha*, leaves and branches of *Bixa orellena*, *Phylodendrum tripartitum, Struthanthus orbicularis, Gozalagunia panamensis*, the ready product of Citrus limon leaves, branches and stems of *Ficus nymphaeifolia* [33]. Incomplete assurance of discharge was likewise appeared by *Aristolochia grandiflora*, *Columnea kalbreyeriana*, *Sida acuta*, *Selaginella* sp., *Pseudelephantopus spicatus*, rhizomes of *Renealmia alpinia*, stem of *Strychnos xynguensis*, leaves, branches and stem of *Hyptis capitata*, *Ipomoea cairica*, *Neurolaena lobata*, *Ocimum micranthum*, *Piper pulchrum*, *Siparuna thecaphora*, *Castilla elastica*, *Allamanda cathartica*, the macerated fruits of *Capsicum frutescens*, unripe fruits of *Crescentia cujete*, leaves and branches of *Piper arboretum* and *Passiflora quadrangularis* [33].

Numerous plant species are used as folk medicine for treatment of snake-bite are summarized in Table 1. Topical Application of plant extracts on bitten area, chewing leaves or barks, drinking or injecting extracts, can counteract snake venom activity.

Table 1: Folk medicine plant sources for snake bite [34]

Plant species	Family	Parts used
Abrus precatorius	Leguminosae	Roots
Abutilon indicum	Malvaceae	Leaf, Fruits
Acacia leucophloea	Mimosaceae	Bark
Acalypa indica	Euphorbiaceae	Leaf
Achillea millefolium	Asteraceae	Whole plant
Achyranthes aspera	Amaranthaceae	Leaf, Stem
Acorus calamus	Araceae	Rhizome
Aegle marmelos	Rutaceae	Root bark
Aerva lanata	Amaranthaceae	Rhizome
Alangium salvifolium	Alangiaceae	Root bark
Allium cepa	Liliaceae	Skin bulb
Andrographis	Acanthaceae	Whole plant
paniculata		
Andrographis lineata	Acanthaceae	Leaf Flower
Argemone mexicana	Papaveraceae	Leaf Seed
Aristolochia indica	Aristolochiaceae	Root
Azadirachta indica	Meliaceae	Flower
Caesalpinia bonduc	Caesalpiniaceae	Seeds
Calendula officinalis	Asteraceae	Flower
Calotropis gigantean	Asclepiadaceae	Root
Cassia alata	Caesalpiniaceae	Leaf
Cassia tora	Caesalpiniaceae	Leaf
Citrus limon	Rutaceae	Ripe skin
Clinacanthus mutans	Acanthaceae	Leaf
Curcuma longa	Zingiberaceae	Rhizome
Cymbopogon citrates	Poaceae	Whole plant
Cyperus rotundus	Cyperaceae	Rhizome
Dalbergia melanoxylon	Fabaceae	Stem bark
Eclipta alba	Compositae	Whole plant
Eclipta prostrata	Compositae	Leaf
Ehretia buxifolia	Ehretiaceae	Root
Euphorbia hirta	Euphorbiaceae	Whole plant
Erythrina excelsa	Fabaceae	bark
Feronica limonia	Rutaceae	Root
Gloriosa superba	Liliaceae	Tuber
Gymnema sylvestre	Asclepiadaceae	Root
Glycine max	Leguminosae	Seeds
Helianthus annuus	Asteraceae	Seed
Hemidesmus indicus	Asclepiadaceae	Root
Tragia involucrate	Euphorbiaceae	Whole plant
Morus alba	Moreaceae	Leaf
Leucas cephalotes	Lamiaceae	Leaf
Madhuca longifoila	Sapotaceae	Nut
Mimosa pudica	Mimosaceae	Whole plant
Momordica charantia	Cucurbitaceae	Flower
Moringa oleifera	Moringaceae	Bark Root
Musa paradisiaca	Musaceae	Skin bark
Nicotiana tabacum	Solanaceae	Leaves
Nerium oleander	Apocynaceae	Seeds
Ocimum basilicum	Lamiaceae	Whole plant
Ocimum sanctum	Lamiaceae	Leaf

Oldenlandia diffusa	Rubiaceae	Whole plant
Oldenlandia umbellate	Rubiaceae	Leaf Root
Ophiorrhiza mungos	Rubiaceae	Root
Phyllanthus emblica	Euphorbiaceae	Fruit
Phyllanthus niruri	Euphorbiaceae	Flower
Phyllanthus reticulates	Euphorbiaceae	Leaf
Piper nigrum	Piperaceae	Flower
Pluchea indica	Asteraceae	Seed, flower
Punica granatum	Punicaceae	Whole plant
Rauvolfia serpentina	Apocynaceae	Root
Sapindus emarginatus	Sapindaceae	Bark
Semicarpus anacardium	Anacardiaceae	Root
Solanum torvum	Solanaceae	Flower
Strychnos nux-vomica	Loganiaceae	Stem bark
Teprhosia purpurea	Leguminosae	Root
Thymus vulgaris	Lamiaceae	Whole plant
Terminalia arjuna	Combretaceae	Bark
Trichodema zeylanicum	Boraginaceae	Root
Tylophora longifolia	Asclepiadaceae	Leaf Flower
Vitex negundo	Verbenaceae	Leaf
Wedelia calendulae	Asteraceae	Leaf

A few flora show in vivo activities. Screening of plants used in traditional medication and determination of their active principles and specific activities is being undertaken. The active principles isolated have been related to numerous pharmacological properties and can offer a tremendous contribution to the present day therapeutics of snake bite.

Ethanolic extracts of Bixa orellana, Brownea rosa-de-monte, Dracontium croatii, *Struthanthus orbicularis*, *Gonzalagunia panamensis*, and *Trichomanes elegans* are suggested to inhibit edema due to *Bothrops asper* venom [35]. Lowering of edema formation with aqueous extracts of *Casearia sylvestris* Sw. has been mentioned in rats injected with lethal doses of Bothropic venoms. Ellagic acid has inhibited edematogenic effect due to overall venom and phospholipase A2 (PLA2) from *Bothrops jararacussu* [36].

Methanolic extract of seeds of *Vitis vinifera L*. has shown promise for the treatment of specific site effects of viperine bites. The concentrate neutralized edema-inducing property of venom [37]. *Cordia verbenacea* extract notably reduced paw edema, induced by *Bothrops jararacussu* snake venom [38].

Different doses of *Tamarindus indica* seed extract upon pre-incubation with venom before assays largely reduced edema [39]. *Anacardium occidentale* bark concentrate has also been shown to reduce edema initiated by viper venom [40].

Lupeol acetate from roots of *Hemidesmus indicus R.Br*. is scientifically proved to significantly neutralize edema induced by Russell's viper, in experimental animals, besides the cardiotoxicity, neurotoxicity and respiratory changes caused by *Naja kaouthia* venom [41].

Antiophidian characteristics are noted to be associated with triterpenoid saponins. Glycyrrhizin, isolated from the roots of *Glycyrrhiza glabra*, proved to be anti-inflammatory [42]. Inhibition of edema due to *Naja naja* venom is documented with turmerin isolated from *Curcuma longa* [43].

Elongation of clotting time of blood plasma was experienced with *Brownea rosa-de-monte*, *Pleopeltis percussa*, *Bixa orellana* and *Heliconia curtispatha, Trichomanes elegans*, after pre-incubation with venom [35]. Methanolic extracts of *Mouriri pusa Garden, Byrsonima crassa Niedenzu, Davilla elliptica St. Hills* upon experimentation have shown complete neutralization of local hemorrhage. Flavonoids namely myricetin, quercetin, amenthoflavone have been proving their antihemorrhagic potential. Quercetin is a potent lipoxygenase inhibitor [44]. *Tamarindus indica* seed extract has stopped the hemorrhage, indirect hemolysis and degradation of beta chain of human fibrinogen, caused by viper venom in experimental animals [39].

The aqueous extract of leaves of *Schizolobium parahyba* notably inhibited the coagulant, hemorrhagic and fibrinogenolytic properties of *Bothrops pauloensis* and *Crotalus durissus terrificcus* venoms and their isolated toxins after pre-incubation with venoms and toxins before assays [45]. *In vivo* tests with polyphenols of *Areca catechu* L and *Quercus infectoria Oliv* showed inhibition of the hemorrhagic potential of *Calloselasma rhodostoma Kuhl* venom and dermonecrotic activity of *Naja kauothia* venom [46].

Prolongation of clotting time of Echis carinatus venom-treated blood has been determined with the aqueous extracts of Mucuna pruriens, Strophanthus hispidus, and Strophanthus gratus [47]. Activation of coagulative activity with the aid of Mucuna pruriens seed extract is properly documented in literature [48]. Inhibition of fibrinocoagulation activity precipitated by Bothrops jararaca venom is stated with the extracts of Masypianthes chamaedrys [49].

Enzyme inhibiting and protein binding characteristics had been associated with chemically active compounds of flavonoids, polyphenols, terpenoids, xanthene and so on. The phytochemicals additionally inhibit PLA2 activities of viper and cobra venom [50]. Phenolics, specifically polyphenols, like a few tannins bind proteins, acting upon components of venom without delay and disabling them to act on receptors. They may also act by competitive blocking of the receptors [51]. Tannic acid has been observed to be a potent inhibitor of hyaluronidase [52].

Inhibition of enzymatic activity is pronounced with extracts of *Casearia sylvestris* in experimental animals, injected with deadly doses of Bothropic venoms [36]. Substantial inhibition of PLA2 activity prompted with the aid of *Bothrops pauloensis* and *Crotalus durissus* terrificcus venoms is documented with the leaf extract of *Schizolobium parahyba* [45]. Neutralization of *Vipera russelii* venom enzymes specifically phospholipase, protease and hyaluronidase is reported with the bark extract of *Anacardium occidentale* in a dose-based way [40].

Abolition of hyaluronidase and proteolytic activities of viper venom with methanolic extract of seeds of *Vitis vinifera* has been suggested [37]. Edunol, a pterocarpan separated from *Harpalyce brasiliana* was determined to be antiproteolytic

and an inhibitor of PLA2 [53]. Inhibition of azocaseinolytic activity of *Bothrops jararaca* venom has been seen with the extract of *Masypianthes chamaedrys* [49].

Lupeol acetate from roots of *Hemidesmus indicus* drastically neutralized PLA2 activity triggered by means of Russell's viper [41]. Antihyaluronidase activity is suggested with *Mimosa pudica* against *Naja naja*, *Vipera russelii* and *Echis carinatus* venoms [54].

Methanolic leaf extract of *Azadirachta indica* has proven massive inhibition of PLA2 enzymes of Cobra and Russell's viper venoms [55]. *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* [56]. 4-nerolidylcatechol has been isolated from Piper species. Various species of the plant are said to inhibit activity of PLA2 from venoms of *Bothrops* species [57].

Plant extracts of *Andrographis paniculata* and *Aristolochia indica* notably restricted the main toxic enzymatic effects of *Echis carinatus*. Inhibition of PLA2 and neutralization of procoagulant activity was observed with both the extracts [58]. Aristolochic acid from *Aristolochia radix* is suggested to inhibit the enzymatic and pharmacological properties of PLA2 induced by *Vipera russelii* venom [59, 60].

Keeping in view the numerous obstacles of anti-snake venoms, natural therapeutics for snake envenomations appear to be a viable opportunity. But, there are only a few species of plants, believed to be powerful for snake bites in conventional remedy whose pharmacological assessment has been undertaken up to now. Most current work has been achieved with mice for the testing of overall crude extracts. The venom dose is critical issue, on which the herbal components ought to display their neutralizing effects. There are numerous mechanisms by which snake venom neutralization occur which include protein precipitation, enzyme activation, chelation, adjuvant action, antioxidant, protein folding and many more.

Tests for detection of snake venoms, toxins and venom antibodies Identification of the biting species of a snake by means of the victims is generally tough and clinical manifestations alone aren't dependable because of overlapping signs and symptoms. Detection of snake venom and venom antibodies in body fluids plays a critical role in the management of snake envenomation. Bioassays, immune diffiusion, immune electrophoresis, immune fluoresence, haemagglutination, radioimmunoassay (RIA), enzyme-linked immunosorbent assay (ELISA) etc. have been developed for venom detection, and ELISA is used for venom antibody detection [61] ELISA seems to be the suitable approach for each venom and venom antibody detections [62, 63, 64]. Species diagnosis is made difficult by the many venomous species present within a few geographical place and additionally by the presence of cross-reacting venom antigens. Loss of particular immune reagents, low level sensitivity, prolonged incubation steps and the need for expensive device have hampered the massive use of routine diagnostic methods consisting of RIA and ELISA all through the early 1980s. However, considerable development has been made over the last ten years to develop species-precise ELISA for the detection of venoms/toxins in numerous parts of the world, particularly in developing countries in which the snake bite is a chief medical and social concern. Hybridoma generation and affinity chromatography had been adequately utilized to increase species-precise immune reagents for diagnostic purposes.

Conclusion

Synthetic anti snake venoms are crucial for treating the snake bites as they are with ease available in the markets and is being continuously produced in the companies. And for this snakes or animal source is of top notch importance. However there's no synthetic medication or in different phrases one single venoms obtained from a snake cannot act as an anti-venom for all different snake bites. So we must increase our research to locate an anti-snake venom which may additionally act as versatile anti-snake venom and on this motive we cannot gainsay the role plant kingdom or in other words the conventional plant medicines. Complete phytochemical investigation of extracts and analysis of active principles to be used as mighty therapeutic agents along with well-designed studies evaluating the pharmacologically active standards are essential. Herbs owning anti-venom serum activity need to be properly recognized (plant components/compound) and cultivated, and understanding must be disseminated well so that at least first aid treatments can be supplied to lessen mortality of snake bite. It is our responsibility to discover, domesticate and culture those herbs for the alleviation of human suffering and death against snake bite.

Conflict of interest

The authors declares that there is no conflict of interest regarding the publication of this article.

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