IOSR Journal of Applied Chemistry (IOSR-JAC)
e-ISSN: 2278-5736.Volume 17, Issue 3 Ser. 1 (March 2024), PP 31-41
www.iosrjournals.org

Plant Extracts and Terpenes with Antivenom Properties

Sylvia A. Opiyo, Peter W. Njoroge
Department of Physical and Biological Sciences, Murang'a University of Technology, Kenya

Abstract
Envenoming and snakebite mortality are a significant public health concern in rural tropical areas in developing countries due to limited access to healthcare. Anti-snake venom (ASV) is the most effective counter-measure for treating snake bites. The antivenon is unavailable to the rural folk due to its high cost and poor health systems. Medicinal plants are a rich source of bioactive compounds with therapeutic activities and have been reported to exhibit antinenom properties. The aim of this study was to provide a review of antivenom plant extracts and terpenes. From the accessed literature information, 345 plants were reported to exhibit antivenom properties against snake venoms. However, the information on identification of the antivenom principles is scanty. Most of the plants investigated belong to the Fabaceae, Euphorbiaceae, Apocynaceae, Asteraceae, Lamiaceae and Rubiaceae plant families. Tepenoids reported to have antivenom properties include β-sitosterol, stigmasterol, lupeol, lupeol acetate, lupenone, 28-hydroxylupenone, betulin, betulinic acid, friedelin, β-amyrin, arjunolic acid, oleanolic acid, 11-deoxoglycyrrhetinic acid, quinovic acid and ursolic acid. The results from this study show that plant extracts posses potent snake venom neutralizing activity and could provide an alternative way to inhibit venom toxins in snakebite. Further research to isolate and characterize the antivenom principles from the medicinal plants, and make antivenin formulations is necessary.

Keywords*: Snake venom; antivenom; plant extract; terpenes*

Date of Submission: 06-03-2024 Date of Acceptance: 16-03-2024

I. Introduction

Envenomation from snakebite is a severe and often ignored public health issue that affects people all around the world, and particularly in impoverished nations [1-3]. High concentrations of toxic proteins found in snake venom cause inflammation, bleeding, necrosis, neurotoxicity, cytotoxicity, cardiotoxicity, and ultimately mortality [4]. Every year, between 1.2 and 5.5 million snakebite incidents occur worldwide resulting in 25,000 to 125,000 fatalities [5]. Due to limited access to healthcare caused by poverty, envenoming and snakebite mortality are a significant public health concern in rural tropical areas in developing countries [6].

Currently, the convensional anti-snake venom (ASV) is the most effective counter-measure for treating snake bites. However, the antivenom is hardly available in rural areas due to its expensive price and unfavorable storage conditions requirement [7]. Additionally, not many hospitals or institutions dedicated to managing snake bites are available in rural areas. Therefore, it is necessary to search for a novel, affordable and readily available remedy for snake envenomation [1, 6].

Medicinal plants play an important role in healthcare since they are a rich source of bioactive compounds with therapeutic activities [8-10]. A large proportion of population in developing countries still depend on hearbal medicine for their basic medical care [11-15]. Plant-produced secondary metabolites have anti-disease characteristics for a variety of illnesses [16-20]. In most cases, traditional remedies are favored because of their accessibility, effectiveness, affordability and lack of adverse effects to the user and environment [11, 21-25]. Furthermore, there is little likelihood of acquiring medication resistance [11]. Currently, different medicinal plants are being investigated through *in-vivo* and *in-vitro* trials to ascertain claims on their therapeutic properties [26-30]. Previous phytochemical analysis of bioactive extracts from plants has lead to discovery of a number of important bioactive drugs including terpenoids, alkaloids, steroids, flavonoids and quinones [31-36]. A number of secondary metabolites from plants that had not previously been known to have pharmacological activities are also being studied as a source of medicinal agents [37-41]. Such bioactive compounds are a major source of lead compounds that are useful in new drug discovery and drug development [42-51].
This study provides a review on plant extracts and terpenes with snake antivenom properties.

II. Antivenom Plant Extracts

Extracts from various plants have been tested for therapeutic activity againsts snake venoms. From the data accessed/used in this study, 345 plant extracts were reported to have antivenom properties against various snake venoms. The most investigated plants belong to the following plant families (the numbers in brackets

indicate the number of plants investigated): Fabaceae (41), Euphorbiaceae (25), Apocynaceae (18), Asteraceae (16), Lamiaceae (14), Rubiaceae (11), Zingiberaceae (9), Anacardiaceae (8), Annonaceae (8), Bignoniaceae (8), Moraceae (8), and Solanaceae (8) (Figure 1). These studies revealed that plant extracts inhibit enzymes in snake venom and act as antidotes [2, 52, 53]. For example, extracts of *Indigofera pulchra* and *Aristolochia albida* gave 33.3% and 44.4% protection to mice treated with minimum lethal dose of venom by neutralizing the anticoagulant, hemolytic, and phospholipase activity of crude venom [54]. *Curcuma aromatica*, *Aristolochia indica*, *Andrograrphis paniculata* and *Curcuma zeodaria* extracts significantly antagonized *Daboia russelli*, *Echis carinatus*, *Ophiophagus hannah* and *Naja kaouthia* venom-induced lethal activity both in *in vitro* and *in vivo* studies [55]. In another study, hydroethanolic root extract of *Solanum xanthocarpum* significantly neutralized the venom enzymes of Naja [56]. A summary of some plant extracts that have been investigated, plant families, part of plant used and snake venom is provided in Table 1. Phytochemical analysis of the bioactive compounds in extracts of the most cited antisnake bite plants revealed the presence of alkaloids, flavonoids, tannins, aponosides and terpenoids [57].

According to previous reports, snakes with major clinical importance are those ftom the families Elapidae (African and Asian cobras, Asian kraits, African mambas, American coral snakes, Australian and New Guinean venomous snakes, and sea snakes) and Viperidae (Old World vipers, American rattlesnakes and pit vipers, and Asian pit vipers) [58]. From the data accessed in this study the most tested venoms were obtained from snakes belonging to the genus *Naja* (frequency = 240) and *Bothrops* (frequency = 145). *Snake venoms from Bitis, Echis, Daboia, Lachesis, Crotalus* and *Bungarus genus* have also been investigated (Figures 2&3).

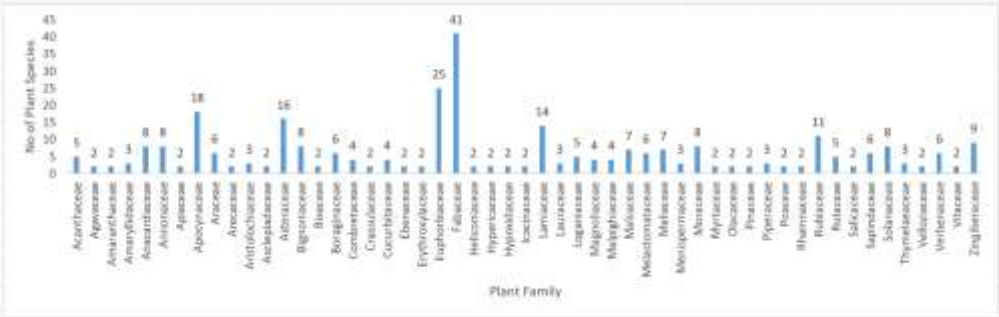

Figure 1. Some plant families studied for snake antivenom activity

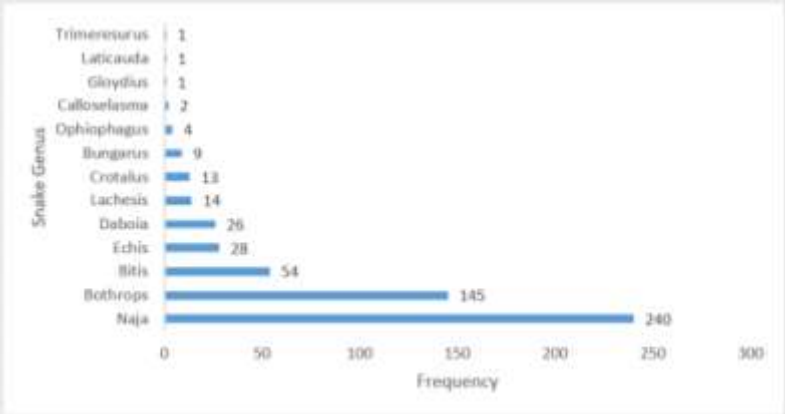

Figure 2: Some most commonly studies snake genus

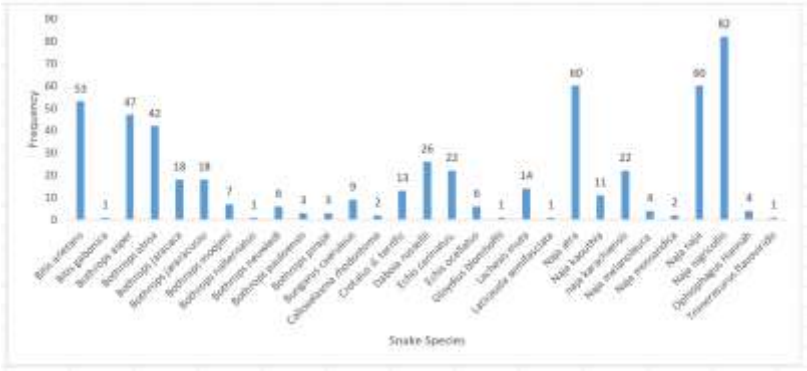

Figure 3. Some snake venomes tested in previous studies

Table 1. Some plants with antivenom activity agaist snake venomes

Plant family	Plant name	Plant part	Snake venom	Ref
Acanthaceae	*Andrographis paniculata*	Root, twigs, flowers, whole plant	*D. russellii, E. carinatus, N. kaouthia, O. hannah, N. nigricollis, N. naja,*	59- 63
	Andrographis stenophylla	Leaf	*N. naja*	64
	Asystasia gangetica	Leaves	*N. melanoleuca*	65
	Jusitica adathoda		*V. russelli*	66
	Justicia pectoralis	Leaf	*B. jararaca*	67
Agavaceae	*Sansevieria liberica*	Rhizome, root	*N. naja nigricollis*	68
	Sansevieria trifasciata	Leaf	ND	69
Amaranthaceae	*Blutaparon portulacoides*	Aerial parts	*B. jararacussu*	70
	Pupalia lappacea	Herbal	*N. nigricollis, B. arietans*	71
Amaryllidaceae	*Allium cepa*	Bulbs	*N. naja karachiensis*	72
	Allium sativum	Bulbs	*N. naja karachiensis*	72
	Crinum jagus	Bulb	*E. ocellates, B. arietance* and *N. nigricollis*	73
Anacardiaceae	*Anacardium excelsum*	Leaf, twig	*B. asper*	74
	Anacardium occidentale	Bark	*V.* russelli	75
	Lannea acida	Cortex	*N. nigricollis, B. arietans*	71
	Mangifera indica	Stem bark	*V. russelli, D. russelli*	76
	Pistacia chinensis	Gall	*Naja n. karachiensis*	72
	Pistacia integerrima	Galls	*N. naja karachiensis*	72
	Sclerocarya birrea	Cortex	*N.. Nigricollis, B. arietans*	71
	Spondias mombin	Cortex, radix	*N. nigricollis, B. arietans*	71
Annonaceae	*Annona senegalensis*	Root bark, Stem bark	*N. nigricollis nigricollis*	77, 78
	Annona squamosal	Leaf	ND	69
	Ephedranthus columbianus	Leaf, twig	*B. asper*	74
	Sapranthus isae	Leaf, twig	*B. asper*	74
	Uvaria chamae	Leave	*N. nigricollis*	79
Apiaceae	*Cuminum cyminum*	Seeds	*N. naja karachiensis*	72
	Hydrocotyle javanica	Twigs, flowers	*N.* nigricollis	60
Apocynaceae	*Acokanthera oppositifolia*	Radix	*N. nigricollis*	80
	Allamanda cath artica	leaf, tem	*B. atrox*	81
	Alstonia venenata	Leaves,stems bark	*N. naja*	82
	Asclepias curassavica	Leaves	*B. asper*	83, 84
	Calotropis gigantea	Fresh plant	*V. russelli*	85, 69
	Calotropis procera	Flowers, latex, exudates, roots	*N. naja karachiensis, N. nigricollis, E. ocellatus* and *B. arietans*	72, 71, 86
	Carissa spinarum	Leaves	Bungarus caeruleus and V. russelli	87
	Cynanchum *paniculatum*	Root	*Deinagkistrodon acutus*	88
	Ervatamia coronaria	Flower	ND	69
	Fernaldia pandurata	Leaf, stem	*B. alternatus, B. jararacussu, B.moojeni, B. pirajai, Crotalus d. terrificus, L. muta*	89, 90
	Mandevilla illustris	Subterranean system	*C. d. terrificus*	91, 92
	Mandevilla velutina	Roots	*B. alternatus, C. d. terrificus*	91
	Strophanthus sarmentosus	Folium	*N. nigricollis*	71
	Strophanthus speciosus	Radix	*N. nigricollis, B. arietans*	71
	Strophantus gratu	Leaf	*N. naja siamensis, E. carinatus*	93, 94
	Strophantus hispidus	Leaf	*N. naja siamensis, E. carinatus*	93, 94
	Tabernaemontana catharinensis	Root bark	*B. jararacussu, C. d. terrificus*	95, 96
	Tylophora indica	Leaf, root	*Naja naja, D. russelii*	97

Araceae	*Acorus calamus*	Roots		98
	Colocasia esculenta	Tuber	*N. nigricollis*	71
	Dracontium croatii	Rhizome	*B. asper*	99
	Penellia ternate	Rhizome	*B. jaracaca*	100
	Philodendron megaloph yl um	Liana, vine	*B. atrox, B. jararaca*	67, 101
	Phylodendrum tripatitum	Branch, leaf	*V. russelli, B. atrox*	102, 103
Araliaceae	*Polyscias fulva*	Cortex	*N. nigricollis, B. arietans*	71
Arecaceae	*Areca catechu*	Seeds	*Bungarus caeruleus*	52
	Borassus aethiopum	Fruit	*N. mossandica*	104
Aristolochiaceae	*Aristolochia indica*	Root, Leaves, Whole plant	*D. russellii, E. carinatus, N. kaouthia, O. hannah, B. atrox , N. naja*	55, 59, 105
	Aristolochia odoratissima	Leaves	*B. atrox, N. naja and V. russelli*	106, 105
	Aristolochia bracteolata	Leaf, root	*N. naja, D. russelli*	97
Asclepiadaceae	*Hemidesmus indicus*	Roots	*V. russelli, B. atrox, E. carinatus, N. naja, Bungarus caeruleus, D. russelli*	55, 59, 102, 103, 107, 108
Asclepiadaceae	*Pergularia daemia*	Stem Bark	*N. naja*	109
Asteraceae	*Artemisia absinthium*	Aerial parts	*Montivipera xanthina*	110
	Artemisia campstresis		*Macrovipera lebetina*	111
	Bidens pilosa	Leaves, whole part	*Dendroaspis jamesoni and E. ocellatus*	112
	Callilepis laureola	Radix	*N.nigricollis*	71
	Chaptalia nutans	Leaf	*B. asper*	113
	Cynara scolymus	Leaves	*B. jaracaca*	114
	Echinacea purpurea	Roots	*B. asper*	115
	Eclipta prostrata	Roots, aerial parts, herbs	*C. durissus,C. d. terrificus ,Calloselasma rhodostoma, B. jararaca, B. jararacussu, L. muta,* Malayan pit viper	105, 107, 116
	Enhydra fluctuans	Leaf	ND	69
	Mikania glomerata	Leaves, stem, roots	*B. jararaca, L. muta, Crotalus spp*	89, 114, 117, 118
	Mikania laevigata	Leaf	*Philodryas olfersii*	119
	Neurolaena loba a	Leaf, stem	*B. atrox*	81
	Pluchea indica	Root	*E. carinatus, N.naja, Bungarus caeruleus, D. russelii, N. kaouthia*	55, 120
	Pseudelephantopus spicatus	Whole plant	*B. atrox*	81
	Elephantopus scaber	Leaves	*B. jaracaca*	114
	Vernonia condensata	Leaves	*B. jaracaca*	114
Balanitaceae	*Balanites aegyptiaca*	Stem bark	*E. carinatus*	121
	Basella alba	Fruit	*B. atrox*	106, 112
Bignoniaceae	*Fridericia chica*	Leaf	*B. atrox, C. d. ruruima*	122
	Jacaranda decurrens	Leaves, roots,	*B. jararacussu, C. d. terrificus*	123
	Kigelia africana	Cortex, folium	*N. nigricollis, B. arietans*	71
	Newbouldia leavis	Leaves	*N. melanoleuca*	65
	Radermachera xylocarpa	Fruit	ND	69
	Stenolobium stans	Roots	*N. naja karachiensis*	72
	Tabebuia aurea	Stem bark	*B. neuwiedi, V. russelli, B. atrox, B. asper*	81, 99, 103
	Tecoma stans		*N. n. karachiensis*	72
Bixaceae	*Bixa orellena*	Branch, leaf	*V. russelli, B. atrox*	102, 99
	Cochlospermum tinctorium	Radix	*B. arietans*	71
Boraginaceae	*Argusia argentea*	Bark	*T. flavoviridis, G. blomhoffii, B. arietans*	124
	Cordia macleodii	Bark	*N. naja*	125, 126
	Cordia nodosa	Bark	*N. atra, B. asper, B. atro*	127
	Cordia verbenacae	Leaves	*B. jararacussu*	128
	Ehretia buxifolia	Rootbark	*E. carinatus*	129
	Trichodesma indicum	Whole plant	*N. naja karachiensis*	72
Burseraceae	*Boswellia delzielli*	Stem Bark		130
Capparaceae	*Capparis tomentosa*	Radix	*N. nigricollis, B. arietans*	71
Capparidaceae	Crateva magna	Twigs, flowers	*N. nigricollis*	60
Caricaceae	*Carica papaya*	Leaves	ND	131

Celastraceae	Maytensus senegalensis	Root	*N. naja*	132
Cleomaceae	*Cleome* gynandra	Leaves	*N.naja*	133, 134
Clusiaceae	*Clusia fluminensis*	Leaves, stems, flowers, fruits	*B. jararaca, B. jararaca and B. jararacussu*	135, 136
Colchicaceae	*Gloriosa superba*	Twigs, flowers, radix	*N. nigricollis, B. arietans*	71, 60
Combretaceae	*Combretum leprosum*	Root	*B. jararaca, B. jararacussu*	137
	Combretum molle	Folium	*N. nigricollis, B. arietans*	71
	Guiera senegalensis	Radix	*N. nigricollis, B. arietans, E. carinatus*	71, 138
	Terminalia arjuna	Bark	*N. naja karachiensis*	72
Connaraceae	*Connarus favosus*	Bark	*B. atrox, B. jararaca*	67, 101
Convolvulaceae	*Ipomoea rubens*	Seed	*N. nigricollis*	71
Crassulaceae	*Bryophyllum pinnatum*	Leaf	*B. jararaca*	139
	Kalanchoe laciniata	Leaf	*B. jararaca*	67
Cucurbitaceae	*Citrullus colocynthis*	Whole plant, fruit	*N. naja karachiensis, N. nigricollis*	72, 140
	Luffa cylindrica	Leaf	*N. naja*	141
	Momordica charantia	Fruits	*N. naja karachiensis*	72
	Wilbrandia ebracteata	Roots	*B. jaracaca*	114
Cyperaceae	*Scleria pterota*	Leaves	*B. jararacussu, B.moojeni, B.nalternatus,*	142
Dicranaceae	*Dicranum frigidum*	Whole plant	*B. asper*	74
Dilleniaceae	*Davilla elliptica*	Leaf	*B. jararaca*	143
Dryopteridaceae	*Dryopteris cochleata*	rhizome	ND	69
Ebenaceae	*Diospyros kaki*	Fruits	*Laticauda semifasciata*	144, 145
	Diospyros mespiliformis	Cortex	*N. nigricollis, B. arietans*	71
Erythroxylaceae	*Erythroxylum ovalifolium*	Stem	*L. muta*	146, 147
	Erythroxylum subsessile	Stem	*L. muta*	146, 147
Euphorbiaceae	*Abrus precatorius*	Radix	*N. nigricollis*	71
	Acalypha Fruticosa	Leaves	*E. species*	148
	Acalypha indica	Leaves	*Viper russelli*	149
	Alchornea laxiflora	Cortex	*N. nigricollis, B. arietans*	71
	Argyrolobium stipulaceum	Radix	*N. nigricollis*	71
	Bridelia ferruginea	Leaves	*N. nigricollis*	150
	Burkea africana	Cortex	*N. nigricollis, B. arietans*	71
	Clutia cordata	Radix	*N. nigricollis*	71
	Croton draco	Stems	*B. asper*	83
	Croton urucurana	Stem bark	*B. jararaca*	151
	Emblica officinalis	Roots	*V. russelli, E. carinatus, N. naja, Bungarus caeruleus, N. kaouthia*	55, 152
	Euphorbia hirta	Whole plant	*N. naja,*	89, 153, 154
	Hevea nitida	Leaf, twig	*B. asper*	74
	Jatropha curcas	Stem, leaf, root, latex	*N. naja, N. nigricollis*	155
	Jatropha elliptica	Root, stem	*L. muta*	89
	Jatropha foetida	Stem, leaf, root	*N. naja*	155
	Jatropha gossypifolia	Stem, leaf, root	*N. naja*	155
	Jatropha curcas	Leaf, root, stem	*N. naja*	155
	Jatropha gossypiifolia	Leaf, root, stem	*B. erythromelas, B. jararaca. N. naja*	155-157
	Jatropha mollissima	Leaf	*B. erythromelas, B. jararaca*	158
	Manihot foetida	Leaf, stem	*N. naja*	155
	Phyllanthus emblica	Root	*D.. russelii*	152, 159
	Phyllanthus klotzschianus	Leaves	*B. jaracaca*	114
	Securinega virosa	Leaves	*N.* nigricollis	160
	Stylosanthes erecta	Folium	*N. nigricollis, B. arietans*	71
Fabaceae	*Abarema cochliacarpos*	Stem bark	*B.. leucurus*	161
	Albizia lebbeck	Root/bark, seed	*N. kauothia, N. naja karachiensis, E.* carinatus	162, 163
	Apuleia leiocarpa	Roots	*B. jaracaca*	114
	Bauhinia forficata	Aerial parts	*B. and crotalus*	164
	Bauhinia rufescens	Seed	*N. nigricollis, E. ocellatus, B. arietans*	86
	Bauhinia thonningii	Cortex, radix	*N. nigricollis, B. arietans*	71
	Bauhinia variegate	Roots	*N. naja karachiensis*	72
	Bobgunnia madagascariensis	Folium, radix	*B. arietans, N. nigricollis*	71
	Brongniartia	Root	*B. atros*	165

	podalyrioides			
	Brownea ariza	Bark, leaf	*B. asper*	166
	Brownea rosa-de-monte	Leaf, stem bark	*V. russelli, B. atrox, B. asper*	81, 99, 102
	Butea monosperma	Stem bark	*D. russelii*	167
	Cassia hirsuta	Root	*N. naja*	168
	Cassia occidentalis	Leaves, roots	*B. moojeni*	169
	Cassia fistula	Seed	*B. jararaca*	67
	Clitoria ternatea	Leaf	ND	69
	Detarium microcarpum	Leaves	*E. carniatus*	170
	Dichrostachys cinerea	Folium	*N. nigricollis, B. arietans*	71
	Dipteryx alata	Bark	*B. jararacussu, B. alternatus, B. asper, B. atrox,*	171
	Entada africana	Radix	*N. nigricollis, B. arietans*	71
	Galactia glaucescens	Leaves	*C. d. terrificus*	172
	Glycyrrhiza glabra	Roots	*B. jararaca*	173
	Harpalyce brasiliana	Roots	*B. jaracaca, N. naja*	174-176
	Indigofera capitata	Leaves	*N. nigricollis*	177
	Indigofera pulchra	Leaves	*N. nigricollis*	54
	Mimosa pudica	Root, herbs	*N. naja, N. Kaouthia, V. russelli, E. carinatus, Bungarus caeruleus, D. russelii,* Malayan pit viper	178-181
	Mucuna pruriens	Seed, leaf	*N. naja siamensis, N. naja, Naja hannah, Bungers caeruleus E. carinatus,*	93, 182-184
	Parkia bigblosa	Stem bark, cortex	*N. nigricollis, B. arietans, E. ocellatus*	71, 86, 185
	Pentaclethra macroloba	ND	*B. jararacussu*	186
	Pentaclethra macroloba	Bark	*B. jararaca, B. jararacussu, B. moojeni, B. neuwiedi, B. pirajai*	186, 187
	Periandra mediterranea	Roots	*B. jaracaca*	114
	Periandra pujalu	Roots	*B. jaracaca*	114
	Plathymenia reticulata	Bark	*B. atrox, B. jararaca*	67, 101
	Platymiscium pleiostachyum	Leaves	*B. asper*	83
	Psoralea corylifolia	Seed	*N. n. karachiensis*	72
	Psoralea corylifolia	Seeds	*N. naja karachiensis*	72
	Schizolobium parahyba	Leaf	*B. alternatus, B. moojeni, B. pauloensis, C. d. terrificus*	188, 189
	Senna auriculata	Leaf	*E. carinatus*	190
	Senna dariensis	Whole plant	*B. atrox*	81
	Stryphnodendron adstringens	Root	*L. muta*	89
	Tamarindus indica	Root, seed, leaf,	*D. r. siamensis, D. russelii, N. nigricollis, B. arietans, Viper russelli*	71, 191-193
Gentianaceae	*Enicostemma hyssopifolium*	Whole plant	*N. n. karachiensis*	72
Heliconiaceae	*Heliconia curtispatha*	Rhizome	*V. russelli, B. atrox, B. asper*	99, 102, 103
	Heliconia latispatha	Rhizome	*B. asper*	194
Hymenophyllaceae	*Trichomanes elegans*	Whole plant	*V. russelli, B. atrox, B. asper*	99, 102, 103
Hypericaceae	*Hypericum brasiliense*	Whole plant	*B. jararaca*	195
	Psorospermum corymbiferum	Cortex, radix	*N.. Nigricollis, B. arietans*	71
Hypoxidaceae	*Curculigo orchioides*	Tuber	ND	69
	Milineria capitulate	Folium	*B.* arietans	71
Icacinaceae	*Casimirella ampla*	Root	*B. atrox, B. jararaca, B. jararacussu*	196
	Humirianthera ampla	Root	*B. atrox, B. jararaca, B. jararacussu*	196
Lamiaceae	*Hoslundia opposita*	Root, leaves	*N. naja*	197
	Leucas aspera	Leaf, root, whole plant	*N.* naja, *D. russelii*	97, 198, 199
	Leucas capitata	Complete plant	*N. n. karachiensis*	72
	Leucas cephalotes	Whole plant	*N. n. karachiensis*	72
	Leucas martinicensis	ND	*N. nigricollis*	71
	Marsypianthes ch amaedrys	Inflorescence, leaf	*B. atrox*	200

	Marsypjanthes hyptoides	Herb	*B. jaracaca*	114
	Ocimum tenuiflorum	Whole plant	*N. n. karachiensis*	72
	Peltodon radicans	Flower, leaf, stem	*B. atrox*	201, 202
	Rotheca myricoides	Cortex	*B. arietans, N. nigricollis*	71
	Salvia leucantha	Leaves	*N. n. karachiensis*	203
	Tectona grandis	Stem bark		204
	Teucrium kraussii	Aerial parts, cortex	*N. nigricollis, B. arietans*	71
	Volkameria glabra	Radix, cortex	*N. nigricollis, B. arietans*	71
Lauraceae	*Aniba parviflora*	Bark, leaf	*B. atrox, B. jararaca*	67, 101
	Cassytha filiformis	Herbal	*N. nigricollis, B. arietans*	71
	Persea americana	Seeds	*B. asper*	83
Laurencieae	*Laurencia aldingensis*	Leaves	*L. muta and B. jararaca*	205, 206
Loganiaceae	*Strychnos decussata*	Radix	*B. arietans*	71
	Strychnos innocua	Folium	*N. nigricollis, B. arietans*	71
	Strychnos nux-vomic	Seed	*N. kaouthia, D. russelii*	207
	Strychnos pseudoquina	Leaf	*B. jararaca*	143
	Strychnos xinguensis	ND	*B. atrox*	81
	Struthanthus orbicularis	Branch, leaf	*V. russelli, B. atrox, B. asper*	99, 102, 103
Lorasaceae	*Nasa speciosa*	Leaf	*B. asper*	113
Magnoliaceae	*Magnolia espinalii*	Leaf, twig	*B. asper*	74
	Magnolia guatapensis	Leaf, twig	*B. asper*	74
	Magnolia hernandezii	Leaf, twig	*B. asper*	74
	Magnolia yarumalensis	Leaf, twig	*B. asper*	74
Malpighiaceae	*Byrsonima crassa*	Leaf	*B.* jararaca	143
Malvaceae	*Althaea officinalis*	Roots	*Naja naja karachiensis*	72
	Dombeya quinqueseta	Cortex	*Naja nigricollis, B. arietans*	71
	Grewia mollis	Cortex, folium,	*N. nigricollis, B. arietans*	71
	Hibiscus aethiopicus	Whole plant	*E. carinatus, E. ocellatus, N.* n. nigricollis	208, 209
	Pachira glabra	Root bark	*B. pauloensis*	157, 210
	Sterculia setigera	Stem-bark , Cortex	*N. nigricollis, E. ocellatus* and *B. arietans*	71, 86
	Waltheria indica	Radix	*N. nigricollis, B. arietans*	71
Melastomataceae	*Bellucia dich otoma*	Bark	*B. atrox, B. jararaca*	67, 101, 211
	Miconia albicans	Stem	*L. muta*	89
	Miconia fallax	Stem	*L. muta*	89
	Miconia sellowiana	ND	*L. muta*	89
	Tibouchina stenocarpa	Root	*L. muta*	89
	Mouriri pusa	Leaf	*B. jararaca*	143
Meliaceae	*Azadirachta indica*	Leaf	*N. naja, V. russelli*	212
	Carapa guianensis	Leaf, twig	*B. asper*	74
	Cedrela odorata	Leaf, twig	*B. asper*	74
	Cedrela tonduzii	Leaves, stems	*B. asper*	83
	Swietenia humilis	Leaf, twig	*B. asper*	74
	Swietenia macrophylla	Leaf, twig	*B. asper*	74
	Toona ciliata	Root	***N.*** *melanoleuca*	53
Menispermaceae	*Cissampelos mucronata*	Herbal	*N. nigricollis, B. arietans*	71
	Cissampelos pareira	Leaf	*B. asper*	213
	Cyclea peltata	Root	*N. Naja*	214
Moraceae	*Brosimum guianense*	Leaf	*B. atrox*	215
	Castilla elastica	Branch, leaf, stem	*B. atrox*	81
	Dorstenia brasiliensis	Roots	*B. jaracaca*	114
	Ficus iteophylla	Leaves	*N. mossandica*	104
	Ficus nymphaeifolia	ND	*V. russelli, B. atrox*	102, 99
	Ficus platyphylla	Folium	*N. nigricollis, B. arietans*	71
	Ficus nymph aefolia	Branch, leaf, stem	*B. asper, B. atrox*	81
	Morus alba	Leaf, stem	*D.* russelli, *B. jaracaca*	216
Moringaceae	*Moringa oleifera*	Leaves	*N. nigricollis*	69, 217
Musaceae	*Musa paradisiaca*	Stem	*B. jararacussu, B. jararaca B. neuwiedi*	218, 219
Myrtaceae	*Myrcia guianensis*	Leaf	*B. jararaca*	220
	Syzygium guineense	Leaves	*B. jararaca*	221
Olacaceae	*Olax viridis*	Leaves	*B. jararaca*	221

	Ximenia americana	Folium	*N. nigricollis, B. arietans*	71
Passifloraceae	*Passiflora quadrangularis*	Branch, leaf	*B. atrox*	81
Pedaliaceae	*Ceratotheca sesamoides*	Herbal	*N. nigricollis*	71
Peraceae	*Clutia pulchella*	Radix	*N. nigricollis*	71
Phyllanthaceae	*Flueggea virosa*	Radix	*Naja nigricollis, B. arietans*	71
Pinaceae	*Cedrus deodara*	Bark	*N. n. karachiensis*	72
	Pinus roxburghii	Oleoresins	*N. naja karachiensis*	72
Piperaceae	*Piper longum*	Fruit	*D.. russelii*	222
	Piper arboreum	Branch, leaf	*B. atrox,*	81
	Piper pulch rum	Leaf, branch, stem	*B. atrox*	81
Poaceae	*Coix Lacrymajobi*	Roots	*D. russelli*	223
	Cymbopogon schoenanthus	Radix	*N. nigricollis*	71
Polygalaceae	*Bredemeyera floribunda*	Roots	*B. jaracaca*	114
Polypodiaceae	*Pleopeltis percussa*	Branch, leaf, stem, whole plant	*B. asper, B. atrox*	81, 99
Primulaceae	*Maesa lanceolata*	Cortex	*N. nigricollis, B. arietans*	71
Rhamnaceae	*Ziziphus mucronata*	Radix	*N. nigricollis, B. arietans*	71
	Ziziphus spina-christi	Cortex	*N. nigricollis, B. arietans*	71
Rhodomelaceae	*Palisada flagellifera*	ND	*L. muta, B. jararaca*	224
Rubiaceae	*Crossopteryx febrifuga*	Cortex	*N. nigricollis, B. arietans*	71
	Diodia scundens	Aerial part	*E. carinatus*	225
	Gonzalagunia panamensis	Branch, leaf, stem	*B. asper, B. atrox*	81, 99
	Ophiorrhiza mungos	Root, leaf	*V. russelli, D. russelii*	226
	Pentanisia prunelloides	Radix	*N. nigricollis, B. arietans*	71
	Pentas zanzibarica	Folium	*N. nigricollis, B. arietans*	71
	Randia aculeata	Fruit	*B. asper, C. simus*	227
	Rubia cordifolia	Stem	*N. nigricollis, Naja naja karachiensis*	71, 72
	Schuanniophyton magnificum	Root bark	*N. melanoleuca, Naja kaouthia, B. gabonica*	228
	Uncaria tomentosa	Root	*B. asper*	113
	Chiococca brachiata	Roots	*B. jaracaca*	114
Rutaceae	*Aegle marmelos*	Leaves, stem,root bark	*N. naja*	69, 229
	Citrus limon	Root, ripe fruits	*V. russelli, B. atrox, B. asper, N. karachiensis, L muta*	72, 99, 102
	Murraya paniculata	Leaf, twig	*B. asper*	74
	Zanthoxylum capense	Radix	*N. nigricollis, B. arietans*	71
	Zanthoxylum monogynum	Radix	*N. nigricollis, B. arietans*	230
Salicaceae	*Casearia sylvestris*	Stems, leaves, seeds, roots	*B. jaracaca, B. asper, B. jararacussu, B. moojeni, B. neuwiedi, B. pirajai, L. muta, N. Kaouthia*	114, 231, 232
	Casearia grandiflora	Leaf	*B. moojeni, B., neuwiedi*	233
Salvadoraceae	*Azima tetracantha*	Leaf	*D. Russelii, Bungarus caeruleus*	2, 81, 107
Sapindaceae	*Billia hippocastanum*	Leaf, twig	*B. asper,*	74
	Cupania americana	Leaf, twig	*B. asper,*	74
	Paullinia pinnata	Root, folium	*N. nigricollis, B. arietans, E. carniatus*	71, 170
	Sapindus mukorossi	Fruits	*N. naja karachiensis*	72
	Sapindus saponaria	Whole plant,	*C. d. terrificus*	74, 234
	Serjania erecta	Aerial parts	*B. jararacussu*	235
Sapotaceae	*Manilkara subsericea*	Leaf, stem	*L. muta*	236
Scrophulariaceae	*Buddleja nitida*	Leaves	*B. asper*	83
Simaroubaceae	*Picrasma quassioides*	Leaves	*N. naja*	237
Siparunaceae	*Siparuna th ecaph ora*	Branch, leaf, stem	*B. atrox*	81
Solanaceae	*Brunfelsia unifora*	Leaves	*B. jaracaca*	114
	Capsicum annuum	Ripe fruit	*B. atrox*	81
	Nicotiana rustica	Leaf	*N. nigricollis*	141
	Schwenckia americana	Folium	*N. nigricollis, B. arietans*	71
	Solanum dasyphyllum	Leaves, Fruits	*N. naja*	238
	Solanum incanum L.	Root	*N. naja*	239
	Solanum xanthocarpum	Roots	*N. naja*	56
	Withania Somnifera	Roots	*E. carinatus, N. naja*	98, 240
Symplocaceae	Symplocos racemosa	Bark	*N. naja*	241, 242
Theaceae	*Camellia sinensis*	Leaves	*N. naja kaouthia, Calloselasmarhodostoma*	243, 244
Thymelaeaceae	*Gnidia anthylloides*	Radix	*N. nigricollis*	71
	Gnidia kraussiana	Radix	*N. nigricollis*	71
	Gnidia splendens	Radix	*N. nigricollis*	71

Urticaceae	*Urera baccifera*	Leaf	*B. asper*	113
Velloziaceae	*Vellozia squamata*	Leaf	*B. jararacussu*	245
	Vernonia cinerea	Whole plant		246
Verbenaceae	*Citharexylum macrodenium*	Leaves	*B. asper*	83
	Clerodendrum serratum	Leaves	*Bungarus caeruleus, D. russelli*	247
	Clerodendrum viscosum	Root	*N. naja*	248
	Lantana trifolia	Cortex	*N. nigricollis, B. arietans*	71
	Stachytarpheta dichotoma	Herb	*B. jaracaca*	114
	Vitex negundo	Roots, leaves	*V. russelli, E. carinatus, N. naja, N. kaouthia, Bungarus caeruleus, D. russelli*	55, 152, 249
Vitaceae	*Cissus populnea*	Stem	*N. nigricollis, B. arietans*	71
	Vitis vinefera	Grape eed,	*E. carinatus, D. russelii*	176, 250
Vivianiaceae	*Caesarea mariquitensis*	Leaves	*B. neuwiedi pauloensis*	251
Zingiberaceae	*Costus Afer*	Leaves		252
	Costus spicatus	Leaf	*B. atrox*	253
	Costus l sius	ND	*B. atrox*	81
	Curcuma longa	Rhizome	*Naja* sp, *B. alternatus*	254, 93
	Curcuma zedoaria	Root	*D. russellii, E. carinatus, N. kaouthia, O. hannah*	55
	Renealmia alpinia	Leaf, rhizome	*B. asper, B. atrox*	81, 99, 255
	urcuma aromatica	Root	*D. russellii, E. carinatus, N. kaouthia, O. hannah*	55
	Zingiber capitatum	Rhizome	ND	69
	Zingiber officinalis	Rhyzome	*N. n. karachiensis*	72
Zygophyllaceae	*Fagonia cretica*	Leaf, stem	*N. n. karachiensis*	72

ND = Not described

III. Anti-Snake Venom Terpenoids From Plants

Terpenoids have been reported to have numerous pharmacological properties such as antimicrobial, antifungal, antiparasitic, antiviral, antiallergenic, antispasmodic, antihyperglycemic, anti-inflammatory, and immunomodulatory. They have also been found to be helpful in the prevention and treatment of a number of diseases, including cancer [256]. Despite the abundant ethnomedicinal and pharmacological information on the efficay of plant extracts as antivenons, the progress in isolation and characterization of the bioactive compounds is not impressive.

Triterpenes and sterols with antivenom properties (Table 2) include sitosterol, stigmasterol, lupeol, lupeol acetate, lupenone, 28-hydroxylupenone, betulin, betulinic acid, friedelin, β-amyrin, arjunolic acid, oleanolic acid, 11-deoxoglycyrrhetinic acid, glycyrrhizin, quinovic acid, and ursolic acid [88, 109, 230, 257]. For example, β-sitosterol and stigmasterol protected mice against lethal doses of *C. durissus terrificus, B. jararaca, B. jararacussu, and L. muta* venom and also reduced lethality caused by *D. russelli and N. kaouthia* venoms [120, 258]. Stigmasterol exhibited inhibitory effects on enzymatic and myotoxic activities of PLA2 from *Sapindus saponaria* [234]. Lupeol was found to be capable of interacting and altering the activity of the thrombin-like toxin Jararacussin-I, and capable of interacting with the BthA-I acidic PLA_2, both from *Bothrops* snakes venom [259 230]. Lupeol acetate inhibited lethality, hemorrhage, defibrinogenation, edema and phospholipase A2 (PLA_2) activity induced by *Daboia russelii* venom[108]. Lupeol acetate also inhibited lethality, cardiotoxicity and neurotoxicity in mice induced by *Naja kaouthia venom* [108]. The triterpenoids lupeol, lupenone, 28-hydroxylupenone and betulin from *Dipteryx alata* prevented the irreversible neuromuscular blockade caused *Bothrops jararacussu* and *Crotalus durissus terrificus* venom [259]. Betulin showed the best protective effect against neuromuscular blockade and myotoxicity caused by both snake venoms [259]. Betulinic acid, oleanolic acid and ursolic acid showed the enzymatic, hemorrhagic, myotoxic and edema-inducing activities against *Bothrops atrox* venom [260]. Quinovic acid and its glycosides (quinovin glycoside C, quinovic acid-3-O-α-L-rhamnopyranoside, quinovic acid-3-O-β-D-fucopyranoside and quinovic acid-3-O-β-D-glucopyranosyl (1-4)-β-D-fucopyranoside showed significant inhibitory activity against snake venom phosphodiesterase-I [261, 262].

Some diterpenes have also been reported to exhibit antivenom properties including labdane lactone, labdane trialdehyde, labdane dialdehyde and corticosterone [263-265]. For example, labdane dialdehyde isolated from *Curcuma zedoaroides* was found active *in vitro* and *in vivo* for antivenom activity against the King cobra venom [264].

IV. Conclusion

The results from this study show that plant posses potent snake venom neutralizing activity and could provide an alternative way to inhibit venom toxins in snakebite. A huge number of plant extracts have been

studied for antivenom properties. However, information on antivenom compounds from plants is scanty. Further research to identify the anti snake venom drugs and formulations is of importance.

Table 2: Some compound with antivenom activity against anake venoms

Compound	**Plant name**	Molecula Formula	**Snake venom**	**Activity Inhibited**	**Ref.**
β-Sitosterol	*Eclipta prostrata, Mimosa pudica, Pluchea indica, Erythroxylum subsessile, E. ovalifolium*	$C_{29}H_{50}O$	*Crotalus durissus terrificus, B. jararaca, B. jararacussu, L. muta, D. russelli, Deinagkistrodon acutus*, N. kaouthia	Lethality, hemorrhagic, defibrogenation, cardiotoxicity, neurotoxicity, edematogenous, enzimatic	2, 88, 109, 120, 146, 147
Stigmasterol	Cyclea peltata, *Eclipta prostrata, Pluchea indica*	$C_{29}H_{48}O$	*C. d. terrificus, B. jararaca, B. jararacussu, L. muta, D. russelli, Deinagkistrodon acutus, N. kaouthia*	Lethality, hemorrhagic, defibrogenation, cardiotoxicity, neurotoxicity, edematogenous, enzimatic	2, 88, 120, 214
Lupeol	*Humirianthera ampla, Hemidesmus indicus, Erythroxylum subsessile, E. ovalifolium, Zanthoxylum monogynum*	$C_{30}H_{50}O$	*B. atrox; B. jararaca;B. jararacussu, L. muta, D. russelli; N. kaouthia*	Proteolytic, hemolytic, hemorrhagic	108, 146, 147, 196, 230, 259
Lupeol acetate	*H. indicus*	$C_{32}H_{52}O_2$	*B. neuwiedi, B. jararacussu, D. russelii* and *N. kaouthia*	Lethality, hemorrhagic, desfibrogenation, edematogenous, enzymatic, cardiotoxicity, neurotoxicity	1082
Lupenone	*Dipteryx alata*	$C_{30}H_{48}O$	*B. jararacussu*	Myotoxicity, neurotoxicity	259
28-OH-Lupenone	*Dipteryx alata*	$C_{30}H_{48}O_2$	*B. jararacussu*	Myotoxicity, neurotoxicity	259
Betulin	*Betula alba, D. alata*	$C_{30}H_{50}O_2$	*B. jararacussu*	Myotoxicity, neurotoxicity	259, 266, 267
Betulinic acid	Betula alba	$C_{30}H_{48}O_3$	*B. atrox*	Proteolytic enzymatic, hemorrhagic, myotoxic and edema-inducing activities	260, 266
Friedelin	*Albizia chevalieri, Erythroxylum ovalifolium*	$C_{30}H_{50}O$	*L. muta*	hemorrhagic	146, 147
β-Amyrin	*Apuleia leiocarpa*	$C_{30}H_{50}O$	*B. jararaca*	Lethality	109, 114
Arjunolic acid	*Combretum leprosum*	$C_{30}H_{48}O_5$	*B. jararacussu, B. jararaca*	Lethality, hemorrhagic, myotoxicity	137
Oleanolic acid	*Baccharis uncinella*	$C_{30}H_{48}O_3$	*D. russelii, N. naja, B. atrox, C. d.terrificus*	Enzimatic, proteolytic, hemorrhagic, edematogenous	260, 268, 269
11-deoxoglycyrrhetinic acid	*Clematis gouriana*	$C_{30}H_{48}O_3$	*D. russelii, N. naja*	-	270
Ursolic acid	*B. uncinella*	$C_{30}H_{48}O_3$	*B. atrox, V. russelii, N. naja*	Proteolytic, enzimatic, edematogenous, hemorrhagic, myotoxic and edema-inducing activities	260, 268, 269
Quinovic acid	*Mitragyna stipulosa*	$C_{30}H_{46}O_5$	*C. d.terrificus*	Enzimatic	261
Labdane lactone	*C. antinaia, C. contravenenum, C. zedoaroides*	$C_{20}H_{30}O_3$	*O. hannah*	Lethality	263
Labdane trialdehyde	*C. antinaia, C. contravenenum, C. zedoaroides*	$C_{20}H_{30}O_3$	*O. hannah*	Diaphragmatic, neurotoxic	263, 264
Labdane dialdehyde	*C. zedoaroides*	$C_{20}H_{30}O_2$	*B. asper, B. atrox*	Lethality	264

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