Hindawi
Evidence-Based Complementary and Alternative Medicine
Volume 2017, Article ID 5748256, 52 pages
https://doi.org/10.1155/2017/5748256

Review Article

Medicinal Plants for the Treatment of Local Tissue Damage Induced by Snake Venoms: An Overview from Traditional Use to Pharmacological Evidence

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Received 23 February 2017; Accepted 9 July 2017; Published 21 August 2017

Academic Editor: Rainer W. Bussmann

Snakebites are a serious problem in public health due to their high morbimortality. Most of snake venoms produce intense local tissue damage, which could lead to temporary or permanent disability in victims. The available specific treatment is the antivenom serum therapy, whose effectiveness is reduced against these effects. Thus, the search for complementary alternatives for snakebite treatment is relevant. There are several reports of the popular use of medicinal plants against snakebites worldwide. In recent years, many studies have been published giving pharmacological evidence of benefits of several vegetal species against local effects induced by a broad range of snake venoms, including inhibitory potential against hyaluronidase, phospholipase, proteolytic, hemorrhagic, myotoxic, and edematogenic activities. In this context, this review aimed to provide an updated overview of medicinal plants used popularly as antiophidic agents and discuss the main species with pharmacological studies supporting the uses, with emphasis on plants inhibiting local effects of snake envenomation. The present review provides an updated scenario and insights into future research aiming at validation of medicinal plants as antiophidic agents and strengthens the potentiality of ethnopharmacology as a tool for design of potent inhibitors and/or development of herbal medicines against venom toxins, especially local tissue damage.

1. Introduction

Snakebites are a serious public health problem in many regions around the world, particularly in Africa, Asia, Latin America, and parts of Oceania [1]. Conservative data indicate that, worldwide, there are between 1.2 and 5.5 million snakebites every year, leading to 25,000 to 125,000 deaths [2]. Despite its significant impact on human health, this condition remains largely neglected by national and international health authorities, funding agencies, pharmaceutical companies, patients' organizations, and health advocacy groups [1]. Thus, snake envenomation is included since 2009 in World Health Organization (WHO) list of Neglected Tropical Diseases (NTDs) [3]. Envenoming and deaths resulting from snakebites are a particularly important public health problem in the rural tropics. Populations in these regions experience high morbidity and mortality because of poor access to health services, which are often suboptimal, as well as other NTDs, which are associated with poverty [3, 4].

Snakes with major clinical importance belong to 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) [5]. After production, snake venom is injected in the victim via tubular or channeled fangs [6]. Biochemically, venoms are complex mixtures of pharmacologically active proteins and polypeptides, acting in concert

to help in immobilizing the prey [7]. The most common toxins in snake venoms are snake venom metalloproteinases (SVMPs), phospholipases A_2 (PLA_2s), snake venom serine proteinases (SVSPs), acetylcholinesterase (AChE), L-amino acid oxidases (LAAOs), nucleotidases, and snake venom hyaluronidases (SVHs) [7].

Biological properties of snake venom components are peculiar to each species, but in general, the main clinical effects of snake envenomation are immediate and prominent local tissue damage (including myonecrosis, dermonecrosis, hemorrhage, and edema), coagulation disorders (consumption coagulopathy and spontaneous systemic bleeding), cardiovascular alterations (hypotension, hypovolemic shock, and myocardial damage), renal alterations (which could evolve into acute kidney injure), neurotoxic action (descending paralysis, progressing from ptosis and external ophthalmoplegia to bulbar, respiratory muscle, and total flaccid paralysis), generalized rhabdomyolysis with myoglobinuria, and intravascular haemolysis [5, 8].

The only available specific treatment is the antivenom serum therapy, which consists of a pool of neutralizing immunoglobulins, or immunoglobulin fragments, purified from the plasma of animals hyperimmunized against snake venoms or specific toxins. Its effectiveness consists in its ability to provide to the patient antibodies with a high affinity to snake venom, aiming to eliminate the toxins responsible for toxicity of the envenoming, mitigating the progress of toxic effects induced by snake venom components [9]. However, the antivenom has some limitations, such as poor ability to treat local effects, risk of immunological reactions, high cost, and difficult access in some regions [8–10]. If antivenom administration is initiated rapidly after envenomation, neutralization of systemic effects is usually achieved successfully; however, neutralization of local tissue damage is more difficult [8]. Furthermore, the availability and accessibility of antivenoms is limited in many regions, such as Sub-Saharan Africa, Asia, and, to a lesser extent, Latin America, which could aggravate even more this picture [1]. Thus, this inability to treat local effects, as well as the increased time between accident and treatment, is the main reason for the temporary or permanent disability observed in many victims, which can lead to serious social, economic, and health negative impacts, given that most victims live in rural areas [3].

In this context, the search for complementary therapies to treat snakebites is relevant and medicinal plants could be highlighted as a rich source of natural inhibitors and pharmacologically active compounds [6, 11–13]. There are several reports of the popular use of medicinal plants against snakebites around the world, especially in tropical and subtropical regions such as Asia, Africa, and South America [14, 15]. The rural and tribal people living in remote areas greatly depend on folk medicines for the treatment of bites from any venomous creatures [16]. The use of medicinal plants against snakebites is a historical practice throughout the human history, and this knowledge has been transferred among the rural communities from generation after generation [17]. Nowadays, these herbal antidotes used in folk traditional medicine gained much attention by toxinologists worldwide as a tool for design of potent inhibitors against snake venom toxins. The potential advantages of antiophidic plants are their possible low cost, easy access, stability at room temperature, and ability to neutralize a broad spectrum of toxins, including the local tissue damage [12, 15–17].

So, the objective of this review is to provide an updated overview of medicinal plants used popularly as antiophidic and discuss the main species with pharmacological studies supporting the uses, with emphasis on plants inhibiting local effects of snake envenomation, since this is a critical effect of snake venoms that could lead to relevant sequel to victims. A review of the main botanical families popularly used as antiophidic is presented, including the main species and forms of popular use of them. Then, studies supporting their popular use are discussed, as well as the advantages of this kind of approach for treatment of snake venom accident.

2. Methodology

An extensive review of the literature was undertaken in different scientific sources, such as PubMed (https://www.ncbi.nlm.nih.gov/pubmed), Science Direct (http://www.sciencedirect.com/), Scopus (https://www.scopus.com/), Web of Science (http://www.webofknowledge.com/), *"Literatura Latino-Americana e do Caribe em Ciências da Saúde"* (LILACS) (http://lilacs.bvsalud.org/), Scientific Electronic Library Online (SciELO) (http://www.scielo.org/), Google Scholar (https://scholar.google.com.br/), Cochrane Library (http://www.cochranelibrary.com/), and Centre for Reviews and Dissemination (CRD) (http://www.crd.york.ac.uk/CRDWeb).

The study database included original articles published in peer-reviewed journals, as well as books, thesis, dissertations, patents, and other reports covering antiophidic plants (ethnopharmacological surveys, original articles, or reviews), dated until December 2016. For the online search, where applicable, the following search strategy was employed: ("plant" OR "plants" OR "plant extract" OR "vegetal" OR "vegetal species" OR "vegetal extract" OR "traditional medicine" OR "alternative medicine" OR "complementary therapy" OR "natural medicine" OR "ethnopharmacology" OR "ethnobotany" OR "herbal medicine" OR "herb" OR "herbs" OR "decoction" OR "tea" OR "infusion" OR "macerate") AND ("snake venom" OR "snake" OR "snakes" OR "snakebite" OR "snakebites" OR "antivenom" OR "antivenoms" OR "anti-venom" OR "anti-venoms" OR "antivenin" OR "antivenins" OR "anti-venin" OR "anti-venins" OR "antiophidian" OR "antiophidic" OR "snake envenomation" OR "antitoxin" OR "antitoxins" OR "snake antidote" OR "snake antidotes" OR "snake venom neutralization" OR "snake venom inhibition" OR "snake toxins inhibition" OR "snake toxins neutralization" OR "viper" OR "viperidae" OR "crotalinae" OR "viperinae" OR "elapidae" OR "pit-viper" OR "bothrops" OR "jararaca" OR "crotalus" OR "micrurus" OR "lachesis" OR "cobra" OR "naja" OR "bitis" OR "vipera" OR "daboia" OR "trimeresus").

All abstracts and/or full-text data were considered, without language restriction. Then, the publications covering ethnobotanical and/or pharmacological studies of antiophidic plants were selected and carefully analyzed. With the information gathered in these studies, the actual scenario of

the use of plants against snake venom was pointed out. Main botanical families used, main countries where antiophidic plants are reported, and mode of use mostly employed in folk medicine were described. Regarding studies of pharmacological evidence, the snake species that were most studied, which plant species were tested and presented positive results, correlating with those species that also presented record of ethnopharmacological use, were also reported.

The accepted botanical name of each medicinal plant listed was confirmed in at least 2 botanical databases among the following ones: Flora do Brasil (http://www.floradobrasil.jbrj.gov.br/), Tropicos (http://www.tropicos.org/), The Plant List (http://www.theplantlist.org/), and NCBI Taxonomy Browser (https://www.ncbi.nlm.nih.gov/taxonomy). In some cases, where the same species was considered as different ones (different synonyms used) in different papers, the accepted name according to the botanical databases mentioned above was used in the present review, bringing the synonym used in the original work between parenthesis.

3. Medicinal Plants as a Popular Source of Antidotes for Snakebites: Traditional Use

According to the literature search performed, a lot of ethnopharmacological studies showing medicinal plants claimed as antiophidic were found. A summary of these vegetal species can be observed in Table 1.

Along our survey were found 150 botanical families containing plants with reputation against snakebites, among which the most cited ones were the families Fabaceae, Asteraceae, Apocynaceae, Lamiaceae, Rubiaceae, Euphorbiaceae, Araceae, Malvaceae, and Acanthaceae (Figure 1(a)). In a cross-cultural comparison of medicinal floras used against snakebites, Molander et al. [80] identified five countries with a high number of antiophidic plants and representing different cultures, geography, and floristic zones: Brazil, Nicaragua, Nepal, China, and South Africa. From these countries, some "hot" families were identified, which were Apocynaceae, Lamiaceae, Rubiaceae, and Zingiberaceae [80], similar to the present review, except for the Zingiberaceae family which was not so reported in our survey.

Medicinal plants with reputation against snakebites are found all over the world, especially in tropical or subtropical regions of Asia, Americas, and Africa (Figure 2). This fact may be associated with richness of flora of these regions, as well as with relative need of complementary therapies to treat snakebites, considering geographical features that could limit the distribution and availability of the antivenoms in these areas.

As observed in Figure 3(a), leaves and roots are the parts of plants most used in folk medicine. Regarding the mode of use, the most frequent one is the topical application of the vegetal products directly on the place of the bite (Figure 3(b)). This is interesting especially in snake venoms that cause serious local tissue damage, such as *Bothrops* and *Daboia* species. Since these snakes produce intense local tissue damage, which has a very rapid onset, a topical treatment could be interesting for a rapid inhibitory action. On the other hand, interestingly, the use of some plant species is made by internal and external routes simultaneously, while for some other species the route of administration could be chosen among internal or external use. However, since in several cases this information is not clear, this differentiation was not considered in data tables. Regarding the mode of preparation, in general, paste and decoction were the most cited forms of use. However, for most of the plants enlisted, the information of mode of preparation was missing or confusing.

It is important to emphasize that these plant species, in addition to their use as antiophidic agents, present a series of another popular uses (data not shown) in popular medicine, mainly anti-inflammatory activity. For example, *Jatropha gossypiifolia* (Euphorbiaceae) has antiophidic, anti-inflammatory, analgesic, antipyretic, healing, and antihemorrhagic uses, among others [81].

4. Antivenom Activities of Extracts of Medicinal Plants against Snake Venom Induced Local Tissue Damage

4.1. General Aspects. Until date, according to our database, only a few numbers (less than 20%) of the species with reputation against snakebites were tested in preclinical assays with different snake venoms, which shows that there is still a great road for the study of antiophidic plants. From these tested plants which have popular use documented in our database, more than a half (almost 60%) showed positive results, which shows that in fact ethnobotany could be a good tool for bioprospecting of plants with antiophidic activity. In addition, the fact that among the tested vegetal species very significative results were obtained strongly suggests the potentiality of these natural products as a future source for development of snake venom inhibitors.

The plant families with most vegetal species showing positive results in antiophidic tests were Fabaceae, Euphorbiaceae, Apocynaceae, Lamiaceae, Asteraceae, Malvaceae, Melastomaceae, and Sapindaceae (Figure 1(b)). Crossing the data of popular use (Figure 1(a)) and of positive activity (Figure 1(b)), we can highlight these families as "hot" ones, that is, families that might be preferred or prioritized in studies searching for antiophidic plants.

Snakes from the genus *Naja*, *Bothrops*, and *Bitis* were the most evaluated ones in these antiophidic assays. However, although *Naja* and *Bitis* comprise a large fraction of the studies, virtually most of them are only *in vitro* studies, dealing with the *in vitro* enzymatic inhibition of classes of venom toxins relevant to local tissue damage, such as phospholipases A_2 (PLA_2s), hyaluronidases (SVHs), and proteases. More particularly, the great majority of these studies with *Naja* and *Bitis* snakes are part of the work undertaken by Molander et al. [82], aiming to investigate whether plants used in traditional medicine systems would be active against necrosis-inducing enzymes of snake venoms, having tested a total of 226 extracts from 94 plants from the countries of Mali, Democratic Republic of Congo, and South Africa against PLA_2, SVHs, and proteases from *Bitis arietans* and *Naja nigricollis* (see Tables 2 and 4). Studies evaluating the inhibitory action of medicinal plants against these enzymes

Table 1: List of medicinal plants used against snakebites.

Plant name	Countries	Parts used	Use	Reference(s)
Acanthaceae				
Acanthus arboreus	Sri Lanka	ND	I	[18]
Andrographis echioides (syn. *Indoneesiella echioides*)	India	Shoot	ND	[19]
Andrographis lineata	India	Flower, leaf	I	[20]
Andrographis paniculata	India	Leaf, whole plant	I, E	[16, 20–26]
Barleria cristata	India, Pakistan	Leaf, root, seed, whole plant	E	[17, 19, 25]
Barleria lupulina	Sri Lanka	ND	I	[18]
Blechum pyramidatum	Nicaragua	Leaf, whole plant	I	[27]
Blepharis maderaspatensis	India	Leaf	I	[28]
Clinacanthus nutans	India	Leaf	E	[20]
Dicliptera paniculata (syn. *Peristrophe paniculata*)	India	Root, whole plant	I, E	[24, 25]
Fittonia albivenis	Peru	Aerial parts	E	[29]
Hygrophila auriculata	India, Sri Lanka	Seed	I	[18, 23]
Justicia adhatoda (syn. *Adhatoda vasica*)	India, Pakistan, Sri Lanka	Flower, leaf, root	I, E	[16–18, 30]
Justicia calyculata	Kenya	Aerial parts	E	[31]
Justicia gendarussa	Bangladesh	Leaf	I	[30, 32]
Justicia japonica (syn. *Justicia simplex*)	India	Leaf	I	[23]
Justicia pectoralis[*]	Brazil	Leaf	I	[33]
Justicia procumbens	Sri Lanka	ND	E	[18]
Justicia secunda[#]	Colombia	Flower, leaf, root, whole plant	I, E	[34, 35]
Rhinacanthus nasutus	India	Leaf, root	I, E	[16, 28]
Thunbergia alata	Colombia	Flower, leaf	E	[34]
Trichanthera gigantea	Colombia	Leaf, root	E	[34]
Acoraceae				
Acorus calamus	Bangladesh, India, Pakistan, Sri Lanka	Rhizome, root	I, E	[17, 18, 20, 22, 25, 32, 36]
Adoxaceae				
Sambucus nigra	Spain	Flower	E	[37]
Amaranthaceae				
Achyranthes aspera (syn. *Achyranthes porphyristachya*)[#]	Bangladesh, Colombia, India	Fruit, inflorescence, leaf, root, seed, stem, whole plant	I, E	[17, 20, 22, 23, 25, 28, 30, 32, 35, 38–41]
Aerva lanata	India, Sri Lanka	Rhizome	I	[18, 20]
Aerva sanguinolenta	Bangladesh	Leaf	ND	[30]
Alternanthera albotomentosa	Colombia	Leaf	E	[34]
Alternanthera brasiliana	Brazil	Flower	I	[33]
Alternanthera sessilis	Sri Lanka	ND	I	[18]
Amaranthus blitum	India	Root	I	[25]
Amaranthus dubius	Colombia	Fruit peel, leaf, root, seed	E	[34]
Amaranthus polygonoides	Sri Lanka	ND	E	[18]
Amaranthus spinosus	India	Leaf, root, stem, whole plant	E	[17, 19, 32, 42]
Amaranthus viridis	Bangladesh, India, Pakistan, Sri Lanka	Leaf, stem, whole plant	E	[17, 18, 30, 42, 43]
Chenopodium album	Bangladesh, India, Pakistan	Fruit, root, whole plant	E	[17, 32, 41]
Cyathula tomentosa	India	Leaf	ND	[19]
Dysphania ambrosioides (syn. *Chenopodium ambrosioides*)	Colombia	Whole plant	E	[34]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Amaryllidaceae				
Allium ascalonicum	Sri Lanka	ND	I	[18]
Allium cepa[*]	Bangladesh, Colombia, India, Kenya	Bulb, latex, leaf	E	[20, 25, 31, 32, 34, 40]
Allium sativum[*]	Colombia, India, Sri Lanka, Spain	Bulb, inflorescence, leaf	I, E	[18, 22, 23, 37, 44]
Ammocharis tinneana	Kenya	Latex	ND	[31]
Crinum asiaticum	Sri Lanka	ND	E	[18]
Crinum latifolium	Sri Lanka	ND	E	[18]
Hymenocallis littoralis	Nicaragua	Leaf, root	I, E	[27]
Anacardiaceae				
Anacardium occidentale[*]	India, Nicaragua	Bark, fruit, leaf, root	I, E	[27, 45]
Buchanania cochinchinensis (syn. *Buchanania lanzan*)	India	Bark	E	[24, 38]
Mangifera indica[*]	Bangladesh, Pakistan, Sri Lanka	Leaf	E	[17, 18, 32]
Mangifera minor	Papua New Guinea	Bark	I	[46]
Pistacia chinensis	Pakistan	Gall	E	[17]
Pistacia chinensis subsp. *integerrima*[*]	India, Pakistan	Gall, leaf	E	[17, 19]
Semecarpus anacardium	India	Root	I	[20]
Semecarpus coriacea	Sri Lanka	ND	E	[18]
Spondias dulcis	Sri Lanka	ND	E	[18]
Spondias mombin[*]	Peru	Bark	ND	[29]
Tapirira guianensis	Colombia	Oil	E	[34]
Annonaceae				
Annona montana[#]	Brazil	Leaf	I	[33, 47]
Annona muricata	Brazil	Leaf	ND	[48]
Annona senegalensis[*]	Kenya	Leaf	I, E	[31]
Annona squamosa	Bangladesh, India	Bark, fruit	I, E	[23, 32]
Polyalthia longifolia	Bangladesh	Whole plant	ND	[30]
Uvaria scheffleri	Kenya	Leaf, root	E	[31]
Apiaceae				
Centella asiatica	Sri Lanka	ND	E	[18]
Conium maculatum	Spain	Leaf	E	[37]
Coriandrum sativum	Sri Lanka	ND	I	[18]
Eryngium bourgatii	Spain	Aerial parts, root	E	[37]
Eryngium campestre	Spain	Aerial parts, root	E	[37]
Eryngium foetidum	Nicaragua, Sri Lanka	Leaf	I, E	[18, 27]
Steganotaenia araliacea	Kenya	Root	E	[31]
Trachyspermum ammi	Sri Lanka	ND	I	[18]
Trachyspermum roxburghianum	Sri Lanka	ND	I	[18]
Apocynaceae				
Allamanda cathartica[*]	Colombia	Aerial parts, branch, leaf, stem	I, E	[35, 44]
Alstonia scholaris	Bangladesh, India, Sri Lanka	Bark, flower, latex, leaf, root	I, E	[18, 19, 32]
Alstonia venenata	Sri Lanka	ND	E	[18]
Asclepias curassavica	Nicaragua	Bark, flower, latex, leaf, root, whole plant	I, E	[27]
Blepharodon mucronatum	Nicaragua	Leaf, whole plant	I, E	[27]
Calotropis acia	Sri Lanka	ND	I, E	[18]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Calotropis gigantea	Bangladesh, India, Sri Lanka	Latex, leaf, root	I, E	[16, 18, 20, 22, 23, 28, 32, 38, 49]
Calotropis procera[*]	Bangladesh, India, Pakistan	Flower, latex, leaf, root, shoot	I, E	[17, 25, 32, 38, 40, 41]
Cascabela thevetia (syn. *Thevetia peruviana*)	Brazil	Bark, seed	E	[50]
Catharanthus roseus	Bangladesh, Colombia	Flower, leaf	I, E	[32, 34]
Cerbera floribunda	Papua New Guinea	Latex	E	[46]
Cerbera odollam	Sri Lanka	ND	E	[18]
Cryptolepis dubia (syn. *Cryptolepis buchanani*)	India, Sri Lanka	Root	ND	[18, 19]
Cynanchum viminale (syn. *Sarcostemma viminale*)	India	Whole plant	E	[38]
Dregea volubilis (syn. *Wattakaka volubilis*)	India, Sri Lanka	Root	I, E	[18, 23]
Echidnopsis dammanniana	Ethiopia	Stem	E	[51]
Echites umbellatus	Nicaragua	Root	I	[27]
Gymnema sylvestre	India	Leaf, root	I, E	[19, 20, 22, 23, 28, 52]
Hemidesmus indicus[*]	Bangladesh, India, Sri Lanka	Root, whole plant	I, E	[18, 20, 22, 25, 28, 32, 38]
Holarrhena pubescens (syn. *Holarrhena antidysenterica*)	Bangladesh, India	Bark, root, stem	I, E	[24, 32, 38]
Hoya ovalifolia	Sri Lanka	ND	I	[18]
Hunteria zeylanica	Sri Lanka	ND	E	[18]
Ichnocarpus frutescens	Bangladesh	Root	I	[32]
Nerium oleander (syn. *Nerium indicum*)[#]	India, Pakistan, Sri Lanka	Leaf, root, seed	E	[17, 18, 20, 28, 41, 53]
Odontadenia puncticulosa	Nicaragua	Leaf	I	[27]
Pergularia daemia	India, Namibia	Leaf	I	[19, 28, 54]
Rauvolfia serpentina	Bangladesh, India, Sri Lanka	Flower, leaf, rhizome, root, seed	I, E	[18, 20, 22, 28, 30, 32]
Rauvolfia tetraphylla (syn. *Rauvolfia canescens*)[#]	Bangladesh, India	Root	E	[16, 30]
Tabernaemontana dichotoma	Sri Lanka	ND	E	[18]
Tabernaemontana divaricata	Sri Lanka	ND	I	[18]
Tabernaemontana sananho	Peru	Leaf	E	[29]
Tylophora indica[*]	Bangladesh, India	Leaf	I	[23, 30, 32]
Tylophora longifolia	India	Flower, leaf	ND	[20]
Vincetoxicum hirundinaria	India	Root	ND	[19]
Willughbeia edulis	Bangladesh	Stem	E	[32]
Wrightia antidysenterica	Sri Lanka	ND	E	[18]
Wrightia arborea	India	Bark	ND	[19]
Wrightia tinctoria	India	Leaf	ND	[38]
Aponogetonaceae				
Aponogeton crispus	Sri Lanka	ND	E	[18]
Araceae				
Alocasia cucullata[#]	Colombia	Rhizome, root	E	[35, 44]
Amorphophallus commutatus	India	Tuber	ND	[55]
Amorphophallus paeoniifolius	Sri Lanka	ND	I	[18]
Anaphyllum beddomei	India	Rhizome	E	[16]
Anthurium marmoratum	Colombia	Branch, leaf, stem	E	[35]
Arisaema concinnum	India	Fruit, tuber	ND	[19]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Arisaema flavum	Pakistan	Rhizome	ND	[17]
Arisaema jacquemontii	India, Pakistan	Flower, leaf, tuber	ND	[17, 19, 56]
Arisaema tortuosum	India	Bulb, tuber	I	[38, 55]
Caladium bicolor	Peru	Tuber	E	[57]
Dieffenbachia longispatha#	Colombia	Whole plant	I, E	[35]
Dieffenbachia parlatorei	Colombia	Root	E	[44]
*Dracontium croatii**	Colombia	Rhizome	I, E	[35]
Dracontium spruceanum	Colombia, Peru	Stem, tuber, root	E	[29, 34, 44, 57]
Dracunculus vulgaris	Spain	Bulb, flower	E	[37]
Homalomena aromatica	Bangladesh	Rhizome	E	[32]
Homalomena peltata	Colombia	Leaf	E	[44]
Homalomena picturata	Colombia	Leaf	E	[34]
Lasia spinosa	Sri Lanka	ND	E	[18]
Philodendron deltoideum	Peru	Aerial parts	I, E	[29]
Philodendron hederaceum	Nicaragua	Leaf, stem	I, E	[27]
Philodendron heleniae	Colombia	Leaf	E	[44]
*Philodendron megalophyllum**	Brazil	Vine	I	[33]
*Philodendron tripartitum**	Colombia	Branch, leaf	E	[35]
Pothos scandens	Sri Lanka	ND	I	[18]
Rhodospatha oblongata	Colombia	Rhizome	E	[35]
Sauromatum venosum	India, Pakistan	Leaf, tuber	I, E	[17, 38]
Typhonium roxburghii	Sri Lanka	ND	I	[18]
Xanthosoma poeppigii	Peru	Stem	E	[57]
Araliaceae				
Osmoxylon micranthum	Papua New Guinea	Latex	E	[46]
Arecaceae				
Areca catechu	Sri Lanka	ND	E	[18]
Caryota urens	Sri Lanka	ND	I	[18]
Cocos nucifera	Sri Lanka	ND	I	[18]
Corypha umbraculifera	Sri Lanka	ND	E	[18]
Euterpe edulis	Brazil	Latex	E	[50]
Euterpe oleracea	Brazil	Fruit	E	[33]
Phoenix pusilla	Sri Lanka	ND	I	[18]
Syagrus coronata	Brazil	Bark	ND	[47]
Aristolochiaceae				
Aristolochia birostris	Brazil	Whole plant	I	[47]
*Aristolochia bracteolata**	India, Sri Lanka	Fruit, leaf, whole plant	I, E	[18, 23, 38, 55]
Aristolochia clematitis	Serbia	Rhizome	ND	[58]
Aristolochia cordiflora	Colombia	Leaf, stem	I, E	[34, 44]
Aristolochia grandiflora#	Colombia	Whole plant	I, E	[35]
*Aristolochia indica**	Bangladesh, India	Leaf, root, whole plant	I, E	[16, 20, 22, 23, 28, 30, 32]
Aristolochia ovalifolia	Mexico	Root	ND	[59]
Aristolochia pilosa#	Colombia	Root	I, E	[35]
Aristolochia tagala	India	Whole plant	I, E	[16]
Aristolochia trilobata	Brazil, Nicaragua	Leaf, root, whole plant	I, E	[27, 50]
Thottea siliquosa	India	Leaf, root	E	[16, 26]
Asparagaceae				
Asparagus racemosus	Bangladesh, Sri Lanka	Leaf, root	E	[18, 30, 32]
Drimia indica (syn. *Urginea indica*)	India	Bulb	E	[25]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Peliosanthes teta	Bangladesh	Root	E	[32]
Sansevieria parva	Kenya	Latex	E	[31]
Sansevieria roxburghiana	India	Rhizome	I	[23]
Sansevieria trifasciata	Bangladesh, Colombia	Aerial parts, whole plant	E	[30, 34, 60]
Sansevieria zeylanica	Sri Lanka	ND	E	[18]
Aspleniaceae				
Asplenium dalhousiae (syn. *Ceterach dalhousiae*)	Pakistan	Leaf	ND	[17]
Asteraceae				
Achillea millefolium	India	Whole plant	I	[20]
Acmella paniculata (syn. *Spilanthes paniculata*)	Sri Lanka	ND	I	[18]
Adenostemma fosbergii	Ecuador	Leaf	I	[61]
Adenostemma lavenia[#]	Colombia	Whole plant	E	[35]
Ageratum conyzoides[#]	Colombia, India, Bangladesh	Flower, leaf, root	E	[19, 24, 32, 34]
Ageratum houstonianum	Pakistan	Inflorescence, leaf	E	[17]
Ambrosia peruviana (syn. *Ambrosia cumanensis*)	Colombia	Aerial parts, whole plant	I, E	[34, 44]
Artemisia maritima	Pakistan	Whole plant	E	[17]
Artemisia scoparia	India, Pakistan	Whole plant	E	[17, 40]
Austroeupatorium inulifolium	Colombia	Leaf	E	[34, 44]
Ayapana triplinervis (syn. *Eupatorium ayapana*, *Eupatorium triplinerve*)	Brazil	Leaf	I	[33, 50]
Baccharis inamoena (syn. *Baccharis trinervis*)	Colombia	Aerial parts, whole plant	E	[34]
Baccharoides anthelmintica (syn. *Centratherum anthelminticum*)	India	Seed	ND	[26]
Bidens biternata	India	Leaf	E	[25]
Bidens pilosa	Kenya	Leaf	E	[31]
Blumea axillaris	Sri Lanka	ND	I	[18]
Blumea brevipes (syn. *Laggera brevipes*)	Kenya	Root	ND	[31]
Calendula officinalis	India	Flower	I	[20, 28]
Chromolaena odorata	Colombia	Whole plant	E	[34]
Clibadium sylvestre[#]	Colombia	Whole plant	I, E	[35]
Conyza sumatrensis	Kenya	Leaf	I	[31]
Cyanthillium cinereum	Sri Lanka	ND	E	[18]
Eclipta prostrata (syn. *Eclipta alba*)[*]	Bangladesh, India, Pakistan, Sri Lanka	Leaf, whole plant	I, E	[17, 18, 20, 28, 30, 40]
Elephantopus scaber	Sri Lanka	ND	E	[18]
Emilia sonchifolia	Bangladesh, Colombia, India, Sri Lanka	Leaf, whole plant	I, E	[16, 18, 30, 34]
Erechtites valerianifolia[#]	Colombia	Branch, leaf, stem	I, E	[35]
Gnaphalium purpureum	Sri Lanka	ND	I, E	[18]
Gynura hispida	Sri Lanka	ND	I	[18]
Helianthus annuus	India	Seed	E	[20]
Inula helenium	Serbia	Root	E	[58]
Laggera alata	Sri Lanka	ND	E	[18]
Linzia glabra (syn. *Vernonia glabra*)	Kenya	Leaf	E	[31]
Microglossa pyrifolia	Kenya	Leaf	E	[31]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Mikania cordata	Bangladesh	Leaf	E	[32]
Mikania cordifolia	Nicaragua	Leaf, stem, whole plant	I, E	[27]
Mikania guaco[#]	Colombia, Nicaragua	Leaf, stem, whole plant	I, E	[27, 35, 44]
Neurolaena lobata[*]	Colombia, Nicaragua	Aerial parts, branch, leaf, stem	I, E	[27, 35, 44]
Pentanema indicum	India, Sri Lanka	Leaf, root	I	[18, 23]
Pluchea indica[*]	India	Flower, seed	I, E	[20]
Pseudelephantopus spicatus[*]	Colombia	Whole plant	E	[44]
Saussurea simpsoniana	India	Flower	ND	[19]
Senecio chrysanthemoides	Pakistan	Whole plant	E	[17]
Seriphidium brevifolium (syn. *Artemisia brevifolia*)	Pakistan	Flower, leaf	E	[17]
Solanecio mannii	Kenya	Leaf	E	[31]
Sphaeranthus africanus	Sri Lanka	ND	I	[18]
Sphaeranthus indicus	Sri Lanka	ND	I	[18]
Sphagneticola trilobata	Nicaragua	Flower, leaf, stem, whole plant	I	[27]
Tagetes minuta	Kenya	Leaf	E	[31]
Taraxacum officinale	Colombia, Pakistan	Leaf, root, whole plant	I, E	[17, 34]
Tithonia diversifolia	Colombia, Kenya	Leaf, whole plant	I, E	[31, 34]
Tricholepis glaberrima	India	Root	ND	[19]
Verbesina gigantea	Colombia	Root, stem	I, E	[34]
Vernonanthura patens	Colombia	Whole plant	E	[34]
Vernonia zeylanicum	Sri Lanka	ND	I, E	[18]
Wedelia calendulacea	India	Leaf	I	[20]
Wollastonia biflora (syn. *Wedelia biflora*)	Sri Lanka	ND	E	[18]
Xanthium strumarium	Pakistan	Aerial parts	E	[17]
Balsaminaceae				
Impatiens balsamina	Colombia	Flower	I, E	[34]
Begoniaceae				
Begonia annulata (syn. *Begonia barbata*)	Bangladesh	Leaf, stem	E	[32]
Berberidaceae				
Dysosma pleiantha	China, Taiwan	Rhizome	ND	[62]
Betulaceae				
Betula alnoides	India	Bark, leaf	ND	[19]
Bignoniaceae				
Crescentia cujete[#]	Colombia	Fruit	I	[35]
Dolichandra unguis-cati (syn. *Macfadyena unguis-cati*)[#]	Colombia	Whole plant	E	[35]
Handroanthus barbatus (syn. *Tabebuia barbata*)	Brazil	Leaf	I	[33]
Mansoa alliacea	Peru	Bark, root	I	[57]
Oroxylum indicum	Bangladesh, Sri Lanka	Bark	E	[18, 32]
Stereospermum chelonoides	Sri Lanka	ND	I	[18]
Stereospermum colais	Sri Lanka	ND	E	[18]
Tabebuia rosea[*]	Colombia	Bark	I, E	[35]
Bixaceae				
Bixa orellana[*]	Bangladesh, Colombia, Nicaragua	Branch, fruit, latex, leaf, root, stem	I, E	[27, 32]
Cochlospermum vitifolium	Colombia	Aerial parts	E	[34]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Boraginaceae				
Cordia dichotoma (syn. *Cordia obliqua*)	Pakistan	Bark, fruit	ND	[17]
Cordia spinescens (syn. *Varronia spinescens*)	Colombia	Leaf	E	[34]
Cynoglossum zeylanicum	India	Root	I	[63]
Echium vulgare	Spain	Aerial parts	ND	[37]
Ehretia microphylla (syn. *Ehretia buxifolia*)	India, Sri Lanka	Root	I, E	[18, 20]
Heliotropium europaeum	Pakistan	Whole plant	E	[17]
Heliotropium indicum[#]	Nicaragua	Leaf, whole plant	I	[27]
Tournefortia cuspidata[#]	Colombia	Branch, leaf, stem	E	[35]
Trichodesma indicum[*]	Pakistan	Leaf, root	ND	[17]
Trichodesma zeylanicum	India	Root	I, E	[20]
Brassicaceae				
Brassica juncea	Sri Lanka	ND	E	[18]
Brassica rapa (syn. *Brassica campestris*)	India	ND	E	[25]
Lepidium virginicum	Colombia	Whole plant	E	[34]
Bromeliaceae				
Ananas comosus	Nicaragua, Sri Lanka	Flower, leaf, root	I, E	[18, 27]
Bromelia pinguin	Nicaragua	Leaf	I, E	[27]
Burseraceae				
Boswellia serrata	India	Bark	I	[24]
Bursera simaruba	Nicaragua	Bark, whole plant	I	[27]
Canarium zeylanicum	Sri Lanka	ND	E	[18]
Cactaceae				
Opuntia ficus-indica (syn. *Opuntia vulgaris*)	India	Root	ND	[25]
Pereskia bleo[#]	Colombia	Leaf, stem	E	[35]
Calophyllaceae				
Calophyllum inophyllum	Sri Lanka	ND	E	[18]
Mesua ferrea	Sri Lanka	ND	I, E	[18]
Campanulaceae				
Hippobroma longiflora	Nicaragua	Leaf, root, whole plant	I, E	[27]
Cannabaceae				
Cannabis sativa	India, Sri Lanka	ND	I	[18, 40]
Cannaceae				
Canna indica	Sri Lanka	ND	E	[18]
Capparaceae				
Capparis decidua	Pakistan	Flower, shoot	E	[17]
Capparis moonii	Sri Lanka	ND	I	[18]
Capparis roxburghii	Sri Lanka	ND	E	[18]
Capparis zeylanica	Sri Lanka	ND	I, E	[18]
Carica papaya[#]	India	Fruit	ND	[41]
Crateva adansonii	Sri Lanka	ND	I	[18]
Crateva tapia (syn. *Crateva benthamii*)[#]	Brazil	Leaf	E	[33]
Cynophalla flexuosa (syn. *Capparis flexuosa*)	Brazil	Bark	I	[64]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Caprifoliaceae				
Nardostachys jatamansi	India	Root	ND	[19]
Valeriana jatamansi	Pakistan, Sri Lanka	Root	I, E	[17, 18]
Celastraceae				
Cassine glauca	India, Sri Lanka	Leaf	I	[18, 19]
Celastrus paniculatus	India	Bark, root, seed	I	[19, 38]
Gymnosporia emarginata	Sri Lanka	ND	I	[18]
Parnassia nubicola	India	Tuber	ND	[19]
Chrysobalanaceae				
Parinari capensis	Namibia	Root	ND	[65]
Cleomaceae				
Cleome gynandra	Sri Lanka	ND	E	[18]
Cleome viscosa	Sri Lanka	ND	I	[18]
Clusiaceae				
Garcinia morella	Sri Lanka	ND	I, E	[18]
Garcinia xanthochymus	Sri Lanka	ND	I, E	[18]
Colchicaceae				
Gloriosa superba[*]	India, Pakistan, Sri Lanka	Tuber	I, E	[17, 18, 20, 28, 38, 40]
Combretaceae				
Anogeissus latifolia	Bangladesh, India	Bark, whole plant	I, E	[25, 30, 38]
Combretum collinum	Kenya	Root	E	[31]
Combretum molle[*]	Kenya	Bark, root	I	[31]
Getonia floribunda (syn. *Calycopteris floribunda*)	Bangladesh	Root	E	[32]
Terminalia arjuna[*]	Bangladesh, India	Bark	I, E	[20, 32]
Terminalia bellirica	Sri Lanka	ND	I	[18]
Terminalia chebula	Sri Lanka	ND	I	[18]
Commelinaceae				
Callisia gracilis	Colombia	Flower, leaf	I, E	[34]
Commelina benghalensis	India, Sri Lanka	Root	ND	[18, 42]
Connaraceae				
Connarus favosus[*]	Brazil	Bark	I	[33]
Connarus monocarpus	Sri Lanka	ND	E	[18]
Convolvulaceae				
Argyreia nervosa (syn. *Argyreia speciosa*)	India	Root, seed	ND	[19]
Argyreia populifolia	Sri Lanka	ND	I	[18]
Cuscuta reflexa	Sri Lanka	ND	E	[18]
Dichondra repens	Kenya	Leaf	E	[31]
Evolvulus alsinoides	India, Sri Lanka	Root	I	[18, 23]
Ipomoea alba	Sri Lanka	ND	E	[18]
Ipomoea aquatica	Bangladesh	Leaf, whole plant	ND	[30]
Ipomoea asarifolia	Sri Lanka	ND	I, E	[18]
Ipomoea cairica[#]	Colombia	Branch, leaf, stem	E	[35]
Ipomoea mauritiana	Nicaragua	Leaf	I, E	[27]
Ipomoea pes-caprae	Nicaragua	Leaf, seed	I	[27]
Ipomoea pes-tigridis	India, Sri Lanka	Root	I, E	[18, 19, 24, 39]
Ipomoea setifera	Nicaragua	Leaf	I, E	[27]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Ipomoea triloba	Sri Lanka	ND	I	[18]
Operculina pteripes	Nicaragua	Leaf	E	[27]
Rivea hypocrateriformis	India	ND	I	[24]
Cornaceae				
Alangium salviifolium	India	Bark	I	[20, 23]
Costaceae				
Cheilocostus speciosus (syn. *Costus speciosus*)	Bangladesh, India, Sri Lanka	Bulb, leaf, stem, root, tuber	I, E	[18, 19, 32, 55]
Costus guanaiensis[#]	Colombia	Stem	I, E	[35]
Costus lasius[*]	Colombia	Branch, leaf, stem	I, E	[35]
Costus lima	Colombia	Stem	E	[34]
Crassulaceae				
Bryophyllum pinnatum (syn. *Kalanchoe pinnata*)[*]	India	Leaf	ND	[22, 42]
Kalanchoe laciniata (syn. *Kalanchoe brasiliensis*)[*]	Brazil	Leaf	E	[33]
Cucurbitaceae				
Benincasa hispida	Sri Lanka	ND	E	[18]
Citrullus colocynthis[*]	India, Pakistan	Fruit, root	ND	[17, 40, 41]
Coccinia grandis	Pakistan, Sri Lanka	Root	I, E	[17, 18]
Corallocarpus epigaeus	India	Tuber	I	[38]
Cucumis melo	Sri Lanka	ND	I	[18]
Cucurbita pepo	Spain	Flower	E	[37]
Diplocyclos palmatus	India, Sri Lanka	Leaf, tuber	I, E	[18, 23, 66]
Fevillea cordifolia	Colombia, Nicaragua	Seed, whole plant	I, E	[27, 35]
Lagenaria siceraria[#]	Sri Lanka	ND	E	[18]
Luffa acutangula	India, Sri Lanka	Fruit, whole plant	I, E	[18, 19, 38]
Momordica balsamina	India	ND	ND	[40]
Momordica charantia[*]	Colombia, India, Nicaragua, Sri Lanka	Aerial parts, branch, flower, fruit, leaf, stem, whole plant	I, E	[18, 20, 27, 34, 35]
Momordica dioica	Sri Lanka	ND	E	[18]
Sicydium tamnifolium	Mexico	Root	ND	[59]
Trichosanthes cucumerina	India, Sri Lanka	Leaf	I	[18, 38]
Trichosanthes tricuspidata	Bangladesh	Root	I	
Cycadaceae				
Cycas pectinata	Bangladesh	Flower	E	[32]
Cycas revoluta	Bangladesh	Whole plant	ND	[30]
Cyclanthaceae				
Cyclanthus bipartitus	Peru	Heart	E	[57]
Cyperaceae				
Cyperus kyllingia	Sri Lanka	ND	I	[18]
Cyperus rotundus	Bangladesh, India, Pakistan, Sri Lanka	Bulb, flower, leaf, rhizome, root, tuber	I, E	[17, 18, 20, 28, 32, 39]
Kyllinga odorata (syn. *Kyllinga monocephala*)	India	ND	ND	[40]
Dilleniaceae				
Tetracera sarmentosa	Sri Lanka	ND	I, E	[18]
Dioscoreaceae				
Dioscorea oppositifolia	Sri Lanka	ND	I	[18]
Dioscorea pentaphylla	India	Tuber	I	[38, 55]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Dipterocarpaceae				
Dipterocarpus lowii	Sri Lanka	ND	I	[18]
Dipterocarpus zeylanicus	Sri Lanka	ND	E	[18]
Droseraceae				
Drosera burmannii	Sri Lanka	ND	I, E	[18]
Drosera indica	Sri Lanka	ND	E	[18]
Ebenaceae				
Diospyros kaki	Malaysia	Fruit	I	[67]
Diospyros melanoxylon	India	Seed	E	[25]
Diospyros montana	India	Root	I	[38]
Diospyros vera (syn. *Maba buxifolia*)	Sri Lanka	ND	I, E	[18]
Euclea racemosa	Ethiopia	Leaf	I	[51]
Elaeagnaceae				
Elaeagnus latifolia	Sri Lanka	ND	I, E	[18]
Ericaceae				
Gaultheria trichophylla	India	Leaf	I	[66]
Erythroxylaceae				
Erythroxylum monogynum	Sri Lanka	ND	E	[18]
Euphorbiaceae				
Acalypha aristata (syn. *Acalypha arvensis*)	Nicaragua	Leaf, whole plant	I, E	[27]
Acalypha fimbriata	ND	ND	ND	[68]
*Acalypha indica**	Bangladesh, India, Sri Lanka	Leaf, whole plant	E	[18, 20, 32]
Acalypha phleoides	Mexico	ND	ND	[68]
Acalypha wilkesiana (syn. *Acalypha godseffiana*)	Sri Lanka	ND	E	[18]
Agrostistachys hookeri	Sri Lanka	ND	E	[18]
Baliospermum solanifolium (syn. *Baliospermum montanum*)	India	Leaf, root, seed	E	[19, 32]
Cnidoscolus aconitifolius	Colombia	Leaf, whole plant	I, E	[34]
Croton tiglium	Sri Lanka	ND	E	[18]
Croton trinitatis	Colombia	Whole plant	E	[34]
Euphorbia antiquorum	Sri Lanka	ND	E	[18]
*Euphorbia hirta**	Bangladesh, Brazil, India	Latex, root, whole plant	I	[19, 20, 32, 47]
Euphorbia milii	Bangladesh	Whole plant	ND	[30]
Euphorbia neriifolia (syn. *Euphorbia ligularia*)	India, Sri Lanka	Latex, leaf, stem	I, E	[18, 19, 22, 38]
Euphorbia thymifolia	Nicaragua	Latex, leaf, whole plant	I	[27]
Euphorbia tirucalli	Sri Lanka	ND	I	[18]
Euphorbia tithymaloides (syn. *Pedilanthus tithymaloides*)	Sri Lanka	ND	I, E	[18]
Euphorbia tortilis	Sri Lanka	ND	E	[18]
Hura crepitans	Peru	Latex	E	[57]
*Jatropha curcas**	Brazil, Nepal	Latex, root, stem	I	[47, 64, 69, 70]
*Jatropha gossypiifolia**	Bangladesh, Brazil	Latex, leaf, stem	I, E	[32, 50]
*Jatropha mollissima**	Brazil	Latex	ND	[47, 64]
Jatropha multifida	Sri Lanka	ND	E	[18]
Jatropha podagrica	Sri Lanka	ND	E	[18]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Jatropha ribifolia	Brazil	Latex	ND	[47]
Mallotus repandus	Sri Lanka	ND	E	[18]
Manihot esculenta	Brazil, Colombia, Nicaragua	Branch, leaf, root	I, E	[27, 33, 34]
Melanolepis multiglandulosa	Papua New Guinea	Latex	I	[46]
Phyllanthus acuminatus[#]	Colombia	Branch, leaf	I, E	[35]
Ricinus communis	Brazil, Pakistan, Sri Lanka	Fruit, latex, leaf, root, seed	I, E	[17, 18, 69, 71, 72]
Spirostachys africana	Namibia	Stem	ND	[65]
Tragia involucrata	India	Whole plant	I	[20, 28]
Trewia nudiflora	Bangladesh	Leaf	E	[32]
Fabaceae				
Abrus precatorius[*]	Bangladesh, India	Leaf, root, stem	I, E	[20, 21, 28, 32, 38]
Abrus pulchellus	Sri Lanka	ND	E	[18]
Acacia caesia	Sri Lanka	ND	I, E	[18]
Acacia cornigera	Mexico	Root	ND	[59]
Acacia leucophloea	India	Bark	I, E	[20, 63]
Acacia mellifera	Namibia	ND	ND	[54]
Acacia nilotica	India	Leaf	I, E	[38]
Acacia torta	India	Bark	I	[63]
Acosmium panamense	Mexico	Bark	ND	[59]
Adenanthera pavonina	Sri Lanka	ND	I, E	[18]
Albizia lebbeck[*]	Bangladesh, India, Pakistan, Sri Lanka	Bark, flower, fruit, leaf, seed	I, E	[16–18, 23, 32, 40]
Albizia procera	Bangladesh, Pakistan	Juicy parts, leaf, root	E	[17, 32]
Alysicarpus vaginalis	Sri Lanka	ND	I	[18]
Amburana cearensis	Brazil	Seed	ND	[71]
Bauhinia divaricata (syn. *Bauhinia retusa*)	India	Bark, flower, leaf	ND	[19]
Bauhinia guianensis	Nicaragua	Bark, stem	I, E	[27]
Bauhinia purpurea	India	Bark, flower, leaf	ND	[19]
Bauhinia racemosa	Sri Lanka	ND	E	[18]
Bauhinia variegata[*]	Bangladesh, Sri Lanka	Bulb, stem	E	[18, 32]
Brownea rosa-de-monte[*]	Colombia	Bark	I, E	[35]
Butea monosperma[*]	India	Bark, leaf, resin, seed	I, E	[24, 25, 38, 40, 41]
Caesalpinia bonduc	India, Nicaragua, Sri Lanka	Root, seed	I, E	[18, 20, 27, 38]
Caesalpinia coriaria	Sri Lanka	ND	E	[18]
Cajanus cajan	Bangladesh	Stem	E	[30, 32]
Canavalia gladiata	Sri Lanka	ND	E	[18]
Cassia fistula[*]	Bangladesh, Brazil, India, Sri Lanka	Bark, fruit, leaf, root, seed	I, E	[18, 19, 24, 25, 32, 33, 38, 40]
Centrosema pubescens	Colombia	Whole plant	E	[34]
Clitoria ternatea	Bangladesh, India, Sri Lanka	Flower, leaf, root, seed	I, E	[16, 18, 19, 32, 38, 39, 42, 60]
Crotalaria laburnifolia	Sri Lanka	ND	E	[18]
Crotalaria verrucosa	India	Seed	I	[23]
Dalbergia melanoxylon	India	Bark	I	[20]
Deguelia amazonica (syn. *Derris amazonica*)	Brazil	Root	ND	[50]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Derris floribunda	Brazil	Root	ND	[50]
Desmodium adscendens[#]	Colombia, Nicaragua	Leaf, root, whole plant	I, E	[27, 35]
Desmodium gangeticum	Bangladesh, India, Pakistan	Root, whole plant	I, E	[17, 32, 55]
Desmodium triflorum	Bangladesh, Sri Lanka	Shoot	I, E	[18, 32]
Dipteryx odorata[#]	Brazil	Seed	I	[33, 50]
Entada leptostachya	Kenya	Latex	E	[31]
Entada rheedii (syn. *Entada pursaetha*)	Bangladesh, India, Sri Lanka	Leaf, seed	I, E	[18, 32, 49]
Erythrina americana	Mexico	Leaf, seed	ND	[59]
Erythrina excelsa	India, Kenya	Bark, latex	ND	[20, 31]
Erythrina fusca	Sri Lanka	ND	I, E	[18]
Erythrina subumbrans	Sri Lanka	ND	I	[18]
Erythrina variegata	India	Bark	ND	[19]
Gliricidia sepium	Colombia	Leaf, stem	I, E	[34]
Glycine max	India	Seed	I	[20]
Glycyrrhiza glabra	Sri Lanka	ND	E	[18]
Humboldtia decurrens	India	Root	E	[16]
Humboldtia laurifolia	Sri Lanka	ND	E	[18]
Indigofera circinella	Kenya	Leaf	E	[31]
Indigofera suffruticosa	Colombia, Nicaragua	Aerial parts, seed, whole plant	I, E	[27, 34]
Indigofera tinctoria[#]	India	Root	I	[16]
Leucaena leucocephala	Sri Lanka	ND	E	[18]
Libidibia ferrea[#]	Brazil	Seed	I	[33]
Machaerium ferox	Brazil	Leaf	E	[33]
Macrotyloma uniflorum	Sri Lanka	ND	I	[18]
Mimosa pudica[*]	Bangladesh, India	Leaf, root, whole plant	I, E	[16, 19, 20, 22, 23, 28, 32]
Mucuna pruriens[#]	Bangladesh, India, Nepal, Sri Lanka	Fruit, seed, stem, whole plant	I, E	[18, 19, 28, 32, 69]
Mucuna sloanei	Ecuador	Seed	I	[61]
Mucuna urens	Nicaragua	Seed	E	[27]
Parkinsonia aculeata	Brazil	Seed	ND	[47]
Pentaclethra macroloba[*]	Nicaragua	Bark	I, E	[27]
Plathymenia reticulata[*]	Brazil	Bark	I	[33]
Pongamia pinnata	Sri Lanka	ND	I, E	[18]
Pterocarpus santalinus	Sri Lanka	ND	E	[18]
Saraca asoca	Sri Lanka	ND	I	[18]
Senna alata (syn. *Cassia alata*)	India, Nicaragua, Sri Lanka	Flower, leaf, whole plant	I, E	[18, 20, 27, 28]
Senna auriculata[*]	Sri Lanka	ND	E	[18]
Senna dariensis[*]	Colombia	Whole plant	I, E	[35]
Senna hirsuta	Bangladesh	Leaf	E	[32]
Senna occidentalis (syn. *Cassia occidentalis*)	Bangladesh, India, Nicaragua, Sri Lanka	Leaf, root, whole plant	I, E	[18, 27, 32, 40]
Senna reticulata (syn. *Cassia reticulata*)	Brazil, Nicaragua	Leaf, root, whole plant	I	[27, 50]
Senna siamea	Kenya	Root	ND	[31]
Senna sophera (syn. *Cassia sophera*)	Bangladesh	Leaf, root	I	[30, 32]
Senna tora (syn. *Cassia tora*)	Bangladesh, India	Leaf, root, seed, stem	I, E	[20, 24, 25, 28, 32, 42]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Sesbania grandiflora	Sri Lanka	ND	I, E	[18]
Tadehagi triquetrum (syn. *Desmodium triquetrum*)	India	Whole plant	ND	[19]
Tamarindus indica[*]	Bangladesh, India, Sri Lanka	Seed, whole plant	I, E	[18, 22, 25, 32, 38]
Tephrosia purpurea	Bangladesh, India	Root, whole plant	I, E	[19, 20, 24, 32]
Trigonella foenum-graecum	Sri Lanka	ND	I	[18]
Uraria lagopodioides	India	Bark	I, E	[49]
Uraria picta	Bangladesh, India	Root, whole plant	I	[24, 30]
Vigna luteola	Colombia	Whole plant	E	[34]
Vigna radiata	Sri Lanka	ND	I	[18]
Gentianaceae				
Chelonanthus alatus (syn. *Irlbachia alata*)[#]	Colombia	Branch, leaf	E	[35]
Enicostema axillare[*]	India	Whole plant	I	[23, 45]
Fagraea ceilanica	Sri Lanka	ND	E	[18]
Hoppea dichotoma	India	Shoot	ND	[19]
Huperzia phlegmaria	Sri Lanka	ND	E	[18]
Potalia amara	Peru	Aerial parts	ND	[29]
Gesneriaceae				
Columnea pulcherrima[#]	Colombia	Whole plant	I, E	[35]
Columnea sanguinea (syn. *Besleria sanguinea*)[#]	Colombia	Whole plant	I, E	[35]
Episcia dianthiflora[#]	Colombia	Whole plant	I, E	[35]
Gleicheniaceae				
Gleichenella pectinata	Colombia	Whole plant	I	[34]
Haemodoraceae				
Xiphidium caeruleum[#]	Colombia, Nicaragua, Peru	Leaf, stem, whole plant	I, E	[27, 35, 44, 57]
Heliconiaceae				
Heliconia curtispatha[*]	Colombia	Rhizome	E	[35]
Hydroleaceae				
Hydrolea zeylanica	Sri Lanka	ND	I	[18]
Hymenophyllaceae				
Trichomanes elegans[*]	Colombia	Whole plant	E	[35]
Hypoxidaceae				
Curculigo orchioides	Bangladesh, India	Bulb, leaf, rhizome	I	[32, 73]
Iridaceae				
Iris kemaonensis	India	Rhizome	ND	[66]
Sisyrinchium micranthum	Colombia	Whole plant	E	[34]
Lamiaceae				
Aegiphila panamensis[#]	Colombia	Leaf, branch, stem	E	[35]
Anisochilus velutinus	Sri Lanka	ND	E	[18]
Anisomeles indica	India, Sri Lanka	Whole plant	ND	[18, 19]
Anisomeles malabarica	Bangladesh, India	Whole plant	I	[28, 30, 60]
Callicarpa tomentosa	Sri Lanka	ND	E	[18]
Clerodendrum cordatum (syn. *Clerodendrum viscosum*)	Bangladesh	Flower, leaf	E	[32]
Clerodendrum phlomidis	Sri Lanka	ND	E	[18]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Fuerstia africana	Kenya	Leaf	I	[31]
Gmelina arborea	Bangladesh	Root	I	[32]
Gmelina asiatica	Sri Lanka	ND	I, E	[18]
Hyptis capitata[#]	Colombia	Branch, leaf, stem	I, E	[35]
Hyptis suaveolens	Bangladesh	Leaf	E	[32]
Leonotis leonurus	South Africa	Flower, leaf	I	[74]
Leucas aspera[*]	Bangladesh, India	Leaf, root, stem	I	[23, 24, 28, 30, 32]
Leucas cephalotes[*]	India	Bark, leaf, whole plant	I, E	[19, 20, 40, 49]
Marsypianthes chamaedrys[*]	Brazil	Leaf	I	[33]
Mentha × *piperita*	Colombia	Leaf	E	[34]
Mentha pulegium	Colombia	Leaf	E	[34]
Ocimum basilicum[#]	Bangladesh, Colombia, India	Branch, leaf, stem, whole plant	I, E	[20, 32, 35]
Ocimum campechianum (syn. *Ocimum micranthum*)	Colombia, Nicaragua	Aerial parts, leaf, whole plant	I, E	[27, 44]
Ocimum tenuiflorum (syn. *Ocimum sanctum*)[*]	India, Sri Lanka	Leaf, root, whole plant	I, E	[16, 18, 20, 28, 40, 41]
Origanum vulgare	Serbia	Flower, leaf	ND	[58]
Plectranthus amboinicus	Sri Lanka	ND	I	[18]
Plectranthus hadiensis	Sri Lanka	ND	I	[18]
Plectranthus monostachyus	Brazil	Leaf	I	[33]
Pogostemon cablin	Malaysia	ND	ND	[75]
Pogostemon heyneanus	Sri Lanka	ND	E	[18]
Premna esculenta	Bangladesh	Leaf	E	[32]
Premna serratifolia (syn. *Premna integrifolia*)	Bangladesh	Leaf, root	I, E	[36]
Rosmarinus officinalis	Colombia	Whole plant	E	[34]
Rotheca serrata (syn. *Clerodendrum serratum*)	India	Leaf, root	ND	[19, 39]
Tectona grandis	India	Bark	I	[25]
Teucrium chamaedrys	Serbia	Flower	ND	[58]
Thymus vulgaris	India, Spain	Aerial parts, whole plant	I, E	[20, 37]
Vitex negundo[*]	Bangladesh, India, Sri Lanka	Leaf, rhizome, root	I, E	[18, 20, 22, 32]
Vitex trifolia	India	Leaf	I	[28]
Volkameria eriophylla (syn. *Clerodendrum eriophyllum*)	Kenya	Leaf, root	ND	[76]
Lauraceae				
Aniba parviflora (syn. *Aniba fragrans*)[*]	Brazil	Bark	I	[33]
Cinnamomum verum	Sri Lanka	ND	I, E	[18]
Litsea glutinosa	Sri Lanka	ND	E	[18]
Litsea longifolia	Sri Lanka	ND	I, E	[18]
Persea macrantha	Sri Lanka	ND	E	[18]
Lecythidaceae				
Careya arborea	Sri Lanka	ND	E	[18]
Couroupita guianensis	Bangladesh	Bark, leaf	ND	[30]
Linderniaceae				
Lindernia diffusa[#]	Colombia	Whole plant	E	[35]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Loganiaceae				
Strychnos nux-vomica[*]	India	Bark, root, seed	I, E	[16, 20, 49]
Strychnos potatorum	Sri Lanka	ND	E	[18]
Strychnos xinguensis[*]	Colombia	Stem	E	[35]
Loranthaceae				
Struthanthus cassythoides	Nicaragua	Leaf, whole plant	I, E	[27]
Struthanthus orbicularis[*]	Colombia	Branch, leaf	E	[35]
Lycopodiaceae				
Huperzia pulcherrima	Sri Lanka	ND	E	[18]
Lygodiaceae				
Lygodium heterodoxum	Nicaragua	Leaf	I, E	[27]
Lygodium venustum	Colombia, Mexico, Nicaragua	Aerial parts, leaf, stem, whole plant	I, E	[27, 34, 59]
Lythraceae				
Lawsonia inermis	India	Bark	ND	[25]
Punica granatum	India, Sri Lanka	Whole plant	I, E	[18, 20, 28]
Trapa natans (syn. *Trapa bispinosa*)	Sri Lanka	ND	I	[18]
Magnoliaceae				
Magnolia champaca (syn. *Michelia champaca*)	Sri Lanka	ND	E	[18]
Malpighiaceae				
Bronwenia cornifolia (syn. *Banisteriopsis cornifolia*)	Nicaragua	Bark, leaf, stem	E	[27]
Byrsonima crassifolia	Brazil, Nicaragua	Bark, leaf	I	[27, 47]
Stigmaphyllon puberum	Nicaragua	Leaf, stem	I, E	[27]
Malvaceae				
Abelmoschus moschatus	Bangladesh, India, Sri Lanka	Fruit, leaf, seed	I, E	[18, 32, 38]
Abroma augusta	Bangladesh	Leaf, root, stem	E	[32]
Abutilon hirtum (syn. *Abutilon heterotrichum*)	Sri Lanka	ND	I, E	[18]
Abutilon indicum	India, Sri Lanka	Fruit, leaf	I	[18, 20]
Ceiba pentandra	Sri Lanka	ND	I	[18]
Corchorus trilocularis	Kenya	Leaf	E	[31]
Firmiana simplex (syn. *Sterculia urens*)	India	Bark, latex	I	[38, 55]
Gossypium arboreum	Sri Lanka	ND	E	[18]
Gossypium herbaceum	India	Seed	ND	[41]
Gossypium hirsutum	Brazil	Leaf	I	[33]
Grewia damine	Sri Lanka	ND	E	[18]
Grewia nervosa (syn. *Microcos paniculata*)	Sri Lanka	ND	E	[18]
Helicteres isora	Bangladesh, India	Fruit, root	I	[23, 25, 32]
Hibiscus rostellatus (syn. *Hibiscus furcatus*)	Sri Lanka	ND	E	[18]
Hibiscus surattensis	Sri Lanka	ND	E	[18]
Hibiscus tiliaceus	Mexico	Seed	ND	[59]
Melochia corchorifolia	Bangladesh, Sri Lanka	Leaf, whole plant	I, E	[18, 32]
Sida acuta[#]	Bangladesh, Colombia, India, Sri Lanka	Leaf, whole plant	I, E	[18, 32, 35, 39, 44]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Sida cordata	Sri Lanka	ND	I	[18]
Sida cordifolia	Bangladesh	Leaf	I	[32]
Sida rhombifolia	Bangladesh, Nicaragua, Sri Lanka	Leaf, stem	I, E	[18, 27, 32]
Thespesia populnea	Sri Lanka	ND	I	[18]
Triumfetta rhomboidea	Kenya	Root	E	[31]
Urena lobata	Bangladesh	Root	I	[32]
Wissadula periplocifolia	Bangladesh, Sri Lanka	Leaf, root	E	[18, 30, 60]
Marantaceae				
Ischnosiphon rotundifolius	Brazil	Leaf	ND	[47]
Martyniaceae				
Martynia annua	India, Sri Lanka	Fruit	E	[18, 25]
Melastomataceae				
Osbeckia octandra	Sri Lanka	ND	E	[18]
Bellucia dichotoma[*]	Brazil	Bark	I	[33]
Melastoma malabathricum	Bangladesh	Leaf	E	[32]
Memecylon umbellatum	India	Leaf	I	[63]
Meliaceae				
Azadirachta indica	India, Sri Lanka	Bark, flower, latex, leaf, seed	I, E	[18, 20, 22, 28, 39–41]
Cipadessa baccifera	India	Leaf, root	I	[63]
Melia azedarach	India, Sri Lanka	Bark, leaf	I, E	[18, 41]
Munronia pinnata	Sri Lanka	ND	I, E	[18]
Menispermaceae				
Cissampelos fasciculata	Colombia	Leaf	I	[44]
Cissampelos pareira[*]	Bangladesh, India, Mexico, Nicaragua, Sri Lanka	Leaf, root, whole plant	I, E	[18, 19, 23, 25, 27, 32, 38, 55, 59]
Cocculus acuminatus	India	Stem	E	[16]
Cocculus hirsutus (syn. *Cocculus villosus*)	India	Leaf	I	[38, 40]
Coscinium fenestratum	Sri Lanka	ND	I	[18]
Cyclea peltata	Sri Lanka	ND	I	[18]
Odontocarya tenacissima[#]	Colombia	Whole plant	I, E	[35]
Tinospora cordifolia	Bangladesh, India, Sri Lanka	Fruit, root, stem	I	[18, 22, 23, 32]
Menyanthaceae				
Nymphoides indica	Nicaragua, Sri Lanka	Leaf, root	I, E	[18, 27]
Monimiaceae				
Hortonia angustifolia	Sri Lanka	ND	E	[18]
Moraceae				
Artocarpus heterophyllus	Sri Lanka	ND	E	[18]
Artocarpus nobilis	Sri Lanka	ND	I, E	[18]
Broussonetia zeylanica	Sri Lanka	ND	I, E	[18]
Castilla elastica[*]	Colombia	Branch, leaf, stem	I, E	[35]
Dorstenia contrajerva	Mexico, Nicaragua	Leaf, whole plant	I, E	[27, 59]
Ficus benghalensis	India	ND	ND	[40]
Ficus drupacea	Sri Lanka	ND	E	[18]
Ficus hispida	Sri Lanka	ND	E	[18]
Ficus nymphaeifolia[*]	Colombia	Branch, leaf, stem	I, E	[35]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Ficus racemosa	Bangladesh, India, Sri Lanka	Bark, shoot	I, E	[18, 32, 38]
Ficus religiosa	India, Sri Lanka	Bark	I, E	[18, 49]
Morus alba[*]	India	Leaf	I	[20]
Plecospermum spinosum	Sri Lanka	ND	I, E	[18]
Streblus asper	Bangladesh	Root	E	[32]
Moringaceae				
Moringa oleifera[#]	India, Sri Lanka	Bark, root, seed	I, E	[16, 18, 20, 22, 24, 28]
Musaceae				
Ensete ventricosum (syn. *Ensete edule*)	Kenya	Latex	E	[31]
Musa × *paradisíaca*[*]	Ecuador, India, Nicaragua, Sri Lanka	Bark, flower, latex	I, E	[18, 20, 27, 28, 61]
Myristicaceae				
Myristica fragrans	Sri Lanka	ND	I	[18]
Myrtaceae				
Myrcia bracteata (syn. *Eugenia bracteata*)	Sri Lanka	ND	I, E	[18]
Syzygium aromaticum	Sri Lanka	ND	I	[18]
Syzygium caryophyllatum	Sri Lanka	ND	E	[18]
Syzygium cumini (syn. *Eugenia jambolana*)	India, Pakistan, Sri Lanka	Bark, leaf	I	[17, 18, 20]
Syzygium zeylanicum	Sri Lanka	ND	E	[18]
Nelumbonaceae				
Nelumbo nucifera	Sri Lanka	ND	I	[18]
Nepenthaceae				
Nepenthes distillatoria	Sri Lanka	ND	E	[18]
Nyctaginaceae				
Boerhavia coccinea	Pakistan	Whole plant	E	[17]
Boerhavia diffusa	Brazil, India, Sri Lanka	Leaf, root, whole plant	E	[18, 24, 25, 39, 41, 50]
Boerhavia procumbens	Pakistan	Leaf	E	[17]
Mirabilis jalapa	Bangladesh, Sri Lanka	Leaf	I, E	[18, 32]
Nymphaeaceae				
Nymphaea nouchali	Sri Lanka	ND	E	[18]
Nymphaea pubescens	Sri Lanka	ND	I	[18]
Ochnaceae				
Ochna jabotapita	Sri Lanka	ND	I	[18]
Sauvagesia erecta	Nicaragua	Whole plant	I, E	[27]
Oleaceae				
Jasminum officinale	Sri Lanka	ND	E	[18]
Jasminum sambac	Sri Lanka	ND	E	[18]
Nyctanthes arbor-tristis	India, Sri Lanka	Root	I	[18, 49]
Olea europaea	Spain	Oil	ND	[37]
Opiliaceae				
Opilia amentacea	Kenya	Root	E	[31]
Orchidaceae				
Vanda tessellata	India	Root	E	[25]
Zeuxine regia	Sri Lanka	ND	E	[18]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Oxalidaceae				
Averrhoa carambola	Sri Lanka	ND	I	[18]
Biophytum reinwardtii	Sri Lanka	ND	I	[18]
Oxalis corniculata	Bangladesh, Sri Lanka	Leaf	I, E	[18, 32]
Pandanaceae				
Pandanus kaida	Sri Lanka	ND	I	[18]
Pandanus odorifer (syn. *Pandanus odoratissimus*)	India	Root	ND	[19]
Papaveraceae				
Argemone mexicana	Bangladesh, India	Leaf, root, seed, stem	I, E	[20, 32, 38, 42]
Papilionaceae				
Desmodium elegans	Pakistan	Root	E	[17, 53]
Passifloraceae				
Adenia hondala	Sri Lanka	ND	E	[18]
Passiflora quadrangularis[*]	Colombia	Branch, leaf	E	[34, 35]
Phyllanthaceae				
Antidesma bunius	India	Leaf	ND	[77]
Bridelia retusa	Sri Lanka	ND	I, E	[18]
Cleistanthus collinus	Sri Lanka	ND	I	[18]
Glochidion zeylanicum	Sri Lanka	ND	I	[18]
Margaritaria indica	Sri Lanka	ND	I, E	[18]
Phyllanthus acidus	India	Root	ND	[77]
Phyllanthus debilis	Sri Lanka	ND	I	[18]
Phyllanthus emblica (syn. *Emblica officinalis*)[*]	Bangladesh, India, Sri Lanka	Bark, fruit, root	I, E	[18, 20, 22, 30]
Phyllanthus niruri	India	Flower	E	[20]
Phyllanthus reticulatus	India	Leaf	I	[20]
Phyllanthus urinaria	Sri Lanka	ND	I, E	[18]
Phytolaccaceae				
Petiveria alliacea[#]	Colombia, Nicaragua	Branch, leaf, root, whole plant	I, E	[27, 34, 35]
Pinaceae				
Pinus roxburghii[*]	Pakistan	Oil, resin, wood	E	[17, 53]
Piperaceae				
Peperomia elsana[#]	Colombia	Whole plant	E	[35]
Peperomia pellucida	Nicaragua, Sri Lanka	Whole plant	I, E	[18, 27]
Piper amalago	Mexico, Nicaragua	Leaf, root	I	[27, 59]
Piper arboreum[*]	Colombia	Branch, leaf	E	[35]
Piper auritum[#]	Colombia, Nicaragua	Branch, leaf, stem, whole plant	I, E	[27, 34, 35, 44]
Piper betle	Sri Lanka	ND	I, E	[18]
Piper chuvya	Sri Lanka	ND	E	[18]
Piper confusionis	Peru	Leaf	E	[57]
Piper coruscans[#]	Colombia	Branch, leaf, stem	I, E	[35]
Piper hispidum[#]	Colombia	Branch, leaf, stem	I, E	[35]
Piper longivillosum[#]	Colombia	Whole plant	E	[35]
Piper longum[*]	Bangladesh, Sri Lanka	Flower, fruit, Latex, root	E	[18, 30]
Piper marginatum[#]	Brazil, Colombia	Branch, leaf, root, stem	I, E	[35, 50]
Piper multiplinervium[#]	Colombia	Branch, leaf, stem	I, E	[35]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Piper nigrum	Bangladesh, India, Sri Lanka	Floral bud, flower, fruit, root	I, E	[18, 20, 28, 32, 52]
Piper peltatum[#]	Colombia, Nicaragua	Branch, leaf, stem, whole plant	I, E	[27, 35]
Piper pulchrum[*]	Colombia	Branch, leaf, stem	I, E	[35]
Piper reticulatum[#]	Colombia	Branch, leaf, stem	I, E	[35]
Piper tricuspe[#]	Colombia	Branch, leaf, stem	E	[35]
Piper umbellatum	Sri Lanka	ND	I, E	[18]
Pittosporaceae				
Pittosporum neelgherrense	India	Bark	I, E	[16]
Pittosporum tetraspermum	India	Bark	I	[26]
Plantaginaceae				
Bacopa monnieri	Bangladesh, India, Sri Lanka	Leaf, root, whole plant	I	[18, 23, 32, 39, 41]
Plantago australis	Colombia	Whole plant	E	[34]
Plantago major	Colombia	Aerial parts, leaf	I, E	[44]
Scoparia dulcis[#]	Colombia, Nicaragua	Aerial parts, branch, leaf, root, whole plant	I, E	[27, 34, 35, 44]
Platanaceae				
Platanus orientalis	Pakistan	Bark	I, E	[17]
Plumbaginaceae				
Plumbago indica	Sri Lanka	ND	I, E	[18]
Plumbago zeylanica	Bangladesh, India, Sri Lanka	Root	I, E	[18, 23, 32]
Poaceae				
Chrysopogon zizanioides (syn. *Vetiveria zizanioides*)	India, Sri Lanka	Root	I, E	[16, 18]
Cymbopogon citratus	Colombia	Leaf	E	[34]
Cynodon dactylon	Bangladesh, India, Sri Lanka	Leaf, root, whole plant	E	[18, 19, 32]
Drynaria quercifolia	Sri Lanka	ND	I	[18]
Eleusine coracana	Sri Lanka	ND	I	[18]
Gynerium sagittatum	Nicaragua	Leaf, root	I	[27]
Heteropogon contortus	India, Sri Lanka	Root	I, E	[18, 38, 55]
Isachne globosa	Sri Lanka	ND	E	[18]
Oryza punctata	Sri Lanka	ND	I, E	[18]
Oryza sativa	Sri Lanka	ND	I	[18]
Pogonatherum paniceum	Sri Lanka	ND	E	[18]
Saccharum arundinaceum	Sri Lanka	ND	I	[18]
Saccharum officinarum	Colombia, Sri Lanka	Stem	I, E	[18, 34, 44]
Polygalaceae				
Polygala abyssinica	Pakistan	Root	I	[17]
Polygala crotalarioides	India	Leaf, root	ND	[19]
Polygala paniculata	Brazil	Root	E	[47]
Polygala spectabilis	Brazil	Root	I, E	[47]
Polygonaceae				
Persicaria barbata (syn. *Polygonum barbatum*)	India	Leaf	I, E	[38]
Persicaria chinensis (syn. *Polygonum chinense*)	Bangladesh	Leaf	E	[32]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Persicaria ferruginea (syn. *Polygonum ferrugineum*)	Colombia	Aerial parts	E	[34]
Persicaria glabra (syn. *Polygonum glabrum*)	India	Root	E	[25]
Polypodiaceae				
Pleopeltis percussa[*]	Colombia	Branch, leaf, stem	I, E	[35]
Pyrrosia piloselloides	Sri Lanka	ND	E	[18]
Pontederiaceae				
Monochoria hastata	Sri Lanka	ND	I, E	[18]
Portulacaceae				
Portulaca pilosa	Brazil	Leaf	I	[33]
Primulaceae				
Aegiceras corniculatum	Sri Lanka	ND	E	[18]
Anagallis arvensis	Serbia	Aerial parts	ND	[58]
Ardisia humilis	Sri Lanka	ND	E	[18]
Maesa lanceolata[*]	Kenya	Root	ND	[31]
Myrsine coriacea	Colombia	Whole plant	E	[34]
Pteridaceae				
Acrostichum aureum	Nicaragua	Leaf, root	I, E	[27]
Adiantum capillus-veneris	Pakistan	Frond	E	[17]
Pellaea viridis	Kenya	Leaf	E	[31]
Ranunculaceae				
Clematis brachiata (syn. *Clematis triloba*)	India	Root	E	[25]
Delphinium denudatum	India	Root	ND	[19]
Delphinium vestitum	India	Whole plant	ND	[19]
Rhamnaceae				
Alphitonia incana	Papua New Guinea	Oil	E	[46]
Ziziphus jujuba (syn. *Ziziphus mauritiana*)	Sri Lanka	ND	E	[18]
Ziziphus oenoplia	India, Sri Lanka	Leaf	I, E	[18, 49]
Rhizophoraceae				
Rhizophora mangle	Nicaragua	Bark	I, E	[27]
Rosaceae				
Crataegus monogyna	Spain	Thorn	ND	[37]
Potentilla sundaica	India	Root, stem	ND	[19]
Prunus persica	Ethiopia	Leaf	I	[51]
Prunus walkeri	Sri Lanka	ND	E	[18]
Pyrus communis	Pakistan	Fruit, leaf	I	[17]
Sanguisorba officinalis	Serbia	Rhizome	ND	[58]
Rubiaceae				
Catunaregam spinosa (syn. *Randia dumetorum*)	India	Root	I	[23]
Ceriscoides turgida (syn. *Gardenia turgida*)	India	Bark, root	I	[24, 38]
Chiococca alba	Brazil, Nicaragua	Leaf, root	I	[27, 47]
Clausena dentata	Sri Lanka	ND	E	[18]
Gonzalagunia panamensis[*]	Colombia	Branch, leaf, stem	I, E	[35]
Hamelia axillaris	Nicaragua	Leaf, whole plant	I, E	[27]
Hamelia barbata	Nicaragua	Leaf, whole plant	I, E	[27]
Hamelia patens	Nicaragua	Leaf, whole plant	I, E	[27]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Hamelia rovirosae	Nicaragua	Flower, leaf, stem	I, E	[27]
Hedyotis scandens	Bangladesh	Leaf, stem	E	[32]
Ixora coccinea	Sri Lanka	ND	I, E	[18]
Ixora cuneifolia	Bangladesh	Bark	E	[32]
Ixora pavetta (syn. *Ixora arborea*)	India	Leaf, rood, seed	ND	[19]
Mitragyna parvifolia	India	Bark, stem	I, E	[38, 63]
Morinda angustifolia	Bangladesh	Leaf	I	[32]
Morinda citrifolia	Bangladesh	Root	ND	[30]
Morinda coreia	Sri Lanka	ND	I, E	[18]
Morinda persicifolia	Bangladesh	Leaf	E	[32]
Mussaenda frondosa	Sri Lanka	ND	I	[18]
Mussaenda roxburghii	Bangladesh	Leaf	E	[32]
Nauclea orientalis	Sri Lanka	ND	E	[18]
Neonauclea purpurea (syn. *Anthocephalus chinensis*)	Bangladesh	Bark, leaf	ND	[30]
Oldenlandia diffusa	India	Whole plant	E	[20]
Oldenlandia umbellata	India	Leaf, root	E	[20]
Ophiorrhiza mungos[*]	India	Root	I	[16, 20]
Paederia foetida	Sri Lanka	ND	I, E	[18]
Palicourea croceoides	Colombia	Bark	I	[34]
Pavetta indica	Sri Lanka	ND	I, E	[18]
Psychotria elata	Nicaragua	Flower, leaf, root, stem, whole plant	I, E	[27]
Psychotria flavida	India	Root	I	[63]
Psychotria poeppigiana[#]	Colombia, Nicaragua, Sri Lanka	Branch, leaf, stem, whole plant	I, E	[18, 27, 35]
Randia aculeata[*]	Mexico	Fruit, whole plant	I	[59, 78]
Rubia cordifolia[*]	Nepal, Pakistan	Leaf, root, stem	I	[17, 69]
Rubia manjith	India	Root, stem	ND	[19]
Spermacoce remota (syn. *Borreria assurgens*)	Nicaragua	Leaf, root	I, E	[27]
Tamilnadia uliginosa	Sri Lanka	ND	I	[18]
Wendlandia exserta	India	Root	I	[49]
Rutaceae				
Acronychia pedunculata	Sri Lanka	ND	E	[18]
Aegle marmelos	Bangladesh, India, Sri Lanka	Bark, whole plant	I, E	[18, 20, 30, 32, 41]
Atalantia ceylanica	Sri Lanka	ND	I, E	[18]
Citrus aurantiifolia	Sri Lanka	ND	I, E	[18]
Citrus aurantium	Sri Lanka	ND	I, E	[18]
Citrus japonica (syn. *Citrus madurensis*)	Sri Lanka	ND	I, E	[18]
Citrus limon[*]	Colombia, India, Sri Lanka	Fruit, leaf, root	I, E	[18, 20, 28, 34, 35]
Citrus maxima (syn. *Citrus grandis*)	Sri Lanka	ND	I, E	[18]
Glycosmis pentaphylla	India	Leaf	I, E	[16]
Limonia acidissima (syn. *Feronia limonia*)	India, Sri Lanka	Root	I	[18, 20]
Murraya koenigii	India, Sri Lanka	Bark, leaf	I, E	[18, 28]
Murraya paniculata[*]	Sri Lanka	ND	E	[18]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Naringi crenulata	India	Fruit	ND	[19]
Pamburus missionis	Sri Lanka	ND	E	[18]
Ruta chalepensis	Colombia	Whole plant	E	[34]
Toddalia asiatica	India, Sri Lanka	Root	I, E	[18, 63]
Salicaceae				
Casearia grandiflora[*]	ND	Bark, leaf	ND	[79]
Casearia nigrescens (syn. *Casearia elliptica*)	India	Bark, leaf	ND	[19]
Casearia sylvestris[*]	Brazil	Leaf, whole plant	ND	[47, 79]
Casearia tomentosa	India	Bark, root	I, E	[49, 79]
Flacourtia indica	Bangladesh	Leaf	E	[32]
Santalaceae				
Santalum album	Sri Lanka	ND	E	[18]
Sapindaceae				
Allophylus cobbe	Sri Lanka	ND	I, E	[18]
Cardiospermum halicacabum	India, Sri Lanka	Leaf	I, E	[18, 28]
Dodonaea viscosa	India	Leaf	E	[28]
Harpullia arborea	Sri Lanka	ND	I, E	[18]
Sapindus emarginatus	India	Bark	I	[20]
Sapindus mukorossi	India, Pakistan	Fruit, leaf, root, seed	E	[17, 25]
Sapotaceae				
Madhuca longifolia (syn. *Madhuca indica*)	India, Sri Lanka	Bark, fruit, leaf, nut, root, seed	I, E	[18, 20, 23, 25, 32, 38]
Manilkara zapota	Mexico	Root	ND	[59]
Mimusops elengi	Sri Lanka	ND	I	[18]
Scrophulariaceae				
Verbascum thapsus	India	Leaf	ND	[66]
Selaginellaceae				
Selaginella articulata[#]	Colombia	Whole plant	I, E	[35]
Simaroubaceae				
Ailanthus excelsa	India	Bark	I	[38]
Quassia amara[#]	Colombia, Nicaragua	Root, stem, whole plant	I, E	[27, 35]
Quassia indica	Sri Lanka	ND	I	[18]
Simaba cedron[#]	Colombia	Seed, whole plant	I, E	[34, 35, 44]
Siparunaceae				
Siparuna gesnerioides	Colombia	Leaf, root	I	[34, 44]
Siparuna thecaphora[*]	Colombia	Branch, leaf, stem	I, E	[35]
Smilacaceae				
Smilax regelii	Nicaragua	Root	I	[27]
Smilax spinosa	Nicaragua	Root	I	[27]
Solanaceae				
Atropa acuminata	Pakistan	Leaf, root	E	[17]
Capsicum annuum (syn. *Capsicum frutescens*)[*]	Bangladesh, Colombia, India, Sri Lanka	Fruit, root	I, E	[18, 19, 25, 32, 34, 35]
Datura metel	Bangladesh, Colombia, India, Sri Lanka	Bark, flower, fruit, leaf, root, seed	I, E	[18, 22, 23, 25, 28, 30, 34]
Datura stramonium[#]	India	Root	I, E	[38]
Lycopersicon esculentum	Colombia	Leaf, stem, whole plant	E	[34]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Nicotiana tabacum	Colombia, India, Nicaragua	Leaf	I, E	[20, 27, 44]
Solanum allophyllum[#]	Colombia	Branch, leaf, stem	I, E	[35]
Solanum americanum (syn. *Solanum nigrum*)	Colombia, India, Sri Lanka	Fruit, leaf, whole plant	I, E	[18, 25, 34, 38]
Solanum capsicoides	Bangladesh	Seed	ND	[30]
Solanum incanum	Kenya	Fruit, stem	E	[31]
Solanum melongena	Sri Lanka	ND	I	[18]
Solanum nudum[#]	Colombia	Branch, fruit, leaf, stem	I, E	[35]
Solanum ochraceo-ferrugineum	Mexico	Whole plant	ND	[59]
Solanum torvum	Bangladesh, India, Nicaragua	Flower, leaf, root	I, E	[20, 27, 30, 32]
Solanum verbascifolium	Mexico	Whole plant	ND	[59]
Solanum virginianum (syn. *Solanum xanthocarpum*)	India, Sri Lanka	Root	I	[18, 41]
Withania somnifera	Bangladesh, India, Sri Lanka	Root	I, E	[18, 22, 32]
Sterculiaceae				
Byttneria pilosa	Bangladesh	Leaf, stem	E	[32]
Symplocaceae				
Symplocos cochinchinensis	Sri Lanka	ND	E	[18]
Symplocos racemosa	Sri Lanka	ND	I, E	[18]
Talinaceae				
Talinum paniculatum	Sri Lanka	ND	E	[18]
Thymelaeaceae				
Daphne papyracea	Pakistan	Leaf, root, stem	ND	[17]
Triuridaceae				
Sciaphila purpurea	Colombia	Whole plant	I, E	[35]
Urticaceae				
Boehmeria nivea	Sri Lanka	ND	E	[18]
Cecropia obtusifolia	Nicaragua	Leaf	I	[27]
Cecropia peltata	Bangladesh, Nicaragua	Leaf, whole plant	I	[27, 30]
Girardinia diversifolia	Sri Lanka	ND	E	[18]
Pouzolzia zeylanica (syn. *Pouzolzia indica*)	Bangladesh, India	Leaf, whole plant	E	[32, 42]
Verbenaceae				
Aloysia triphylla	Colombia	Aerial parts	E	[34]
Lantana camara	Bangladesh, Colombia, India, Sri Lanka	Flower, leaf, root, stem	I, E	[18, 32, 34, 39, 41]
Lippia alba	Colombia	Aerial parts, leaf, whole plant	I, E	[34]
Lippia grandis	Brazil	Leaf	I	[33]
Stachytarpheta cayennensis	Colombia	Whole plant	E	[34]
Verbena litoralis	Colombia	Fruit peel, leaf, root, seed	E	[34]
Verbena officinalis	Pakistan	Root, whole plant	E	[17, 53]
Vitaceae				
Ampelocissus latifolia	India	Root	I	[49]
Cayratia pedata (syn. *Cissus pedata*)	Bangladesh	Leaf	ND	[30]
Cayratia trifolia (syn. *Vitis trifolia*)	Bangladesh, India	Leaf, root	I, E	[36, 38]

Table 1: Continued.

Plant name	Countries	Parts used	Use	Reference(s)
Cissus adnata	Bangladesh	Leaf	E	[32]
Cissus javana	Bangladesh	Leaf, stem	E	[32]
Cissus quadrangularis[#]	Sri Lanka	ND	E	[18]
Leea indica	Sri Lanka	ND	E	[18]
Vitis heyneana (syn. *Vitis lanata*)	Bangladesh	Leaf	E	[32]
Xanthorrhoeaceae				
Aloe harlana	Ethiopia	Leaf	I	[51]
Aloe littoralis	Pakistan	Whole plant	E	[17]
Aloe vera	Nicaragua, Sri Lanka	Leaf	I, E	[18, 27]
Zingiberaceae				
Alpinia calcarata	Sri Lanka	ND	I, E	[18]
Alpinia galanga	Sri Lanka	ND	I	[18]
Alpinia nigra	Sri Lanka	ND	E	[18]
Alpinia purpurata	Colombia	Leaf	E	[44]
Curcuma angustifolia	India	Rhizome	E	[28]
Curcuma longa[*]	Bangladesh, India, Sri Lanka	Rhizome	I, E	[16, 18, 20, 30]
Elettaria cardamomum	Sri Lanka	ND	I	[18]
Globba marantina (syn. *Globba bulbifera*)	India	Rhizome	I	[49]
Hedychium coronarium	Colombia, Nicaragua	Root, whole plant	E	[27, 34]
Renealmia alpinia[*]	Colombia	Rhizome, stem	I, E	[34, 35]
Renealmia thyrsoidea	Colombia	Leaf, stem	I	[34]
Zingiber officinale[*]	Ecuador, Nicaragua, Sri Lanka	Rhizome, root	I, E	[18, 27, 61]
Zygophyllaceae				
Balanites aegyptiaca[#]	India	Bark, fruit	E	[38]

In parentheses is the synonym used in the original work; out of the parentheses is the accepted name (in case of more than one paper treating the same species with different names); ND = information not described in the work; I = internal use; E = external use. [*]Species evaluated on antiophidic activities in previous studies (see Tables 2–8) showing good inhibitory potential against venom induced local effects. [#]Species evaluated on antiophidic activities in previous studies, however, with poor inhibition potential against venom induced local effects.

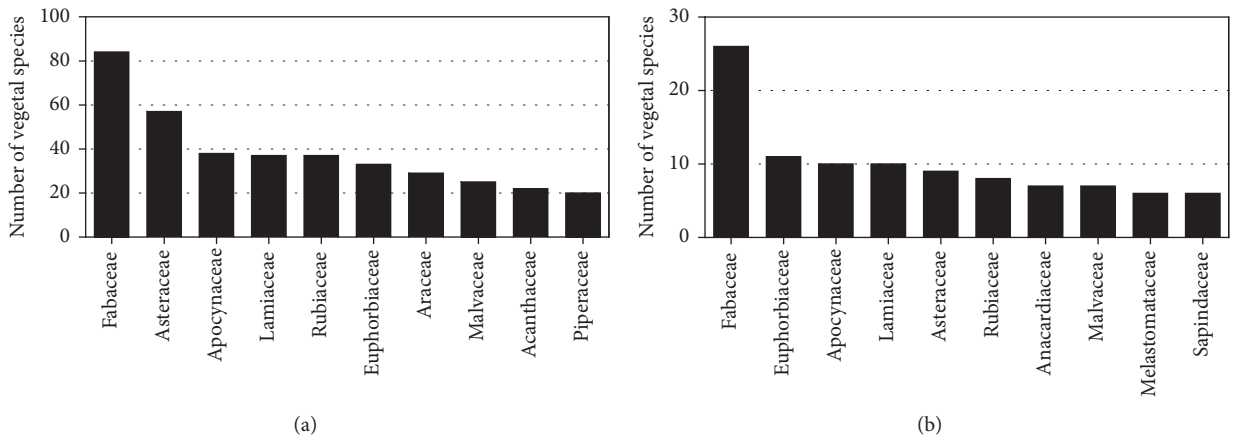

Figure 1: "Hot families" with antiophidic potential. Main related botanical families in ethnopharmacological surveys as antiophidic (a) and main botanical families that were evaluated in antiophidic assay (inhibition of local tissue damage) and presented positive results (b).

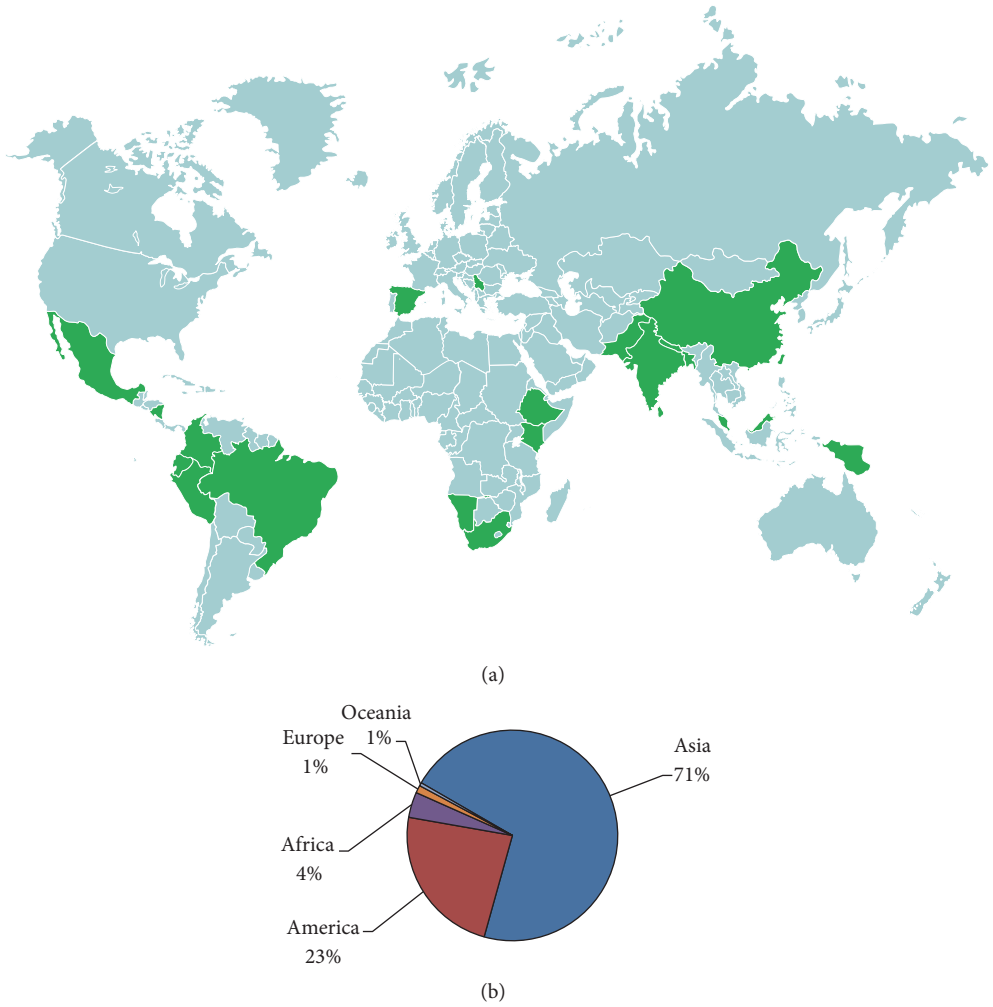

Figure 2: Distribution of medicinal plants used against snakebite around the world. World map highlighting the countries where antiophidic plants were related in ethnopharmacological surveys (a) and number of vegetal species per continent (b).

are very relevant, since they are involved in several pathological mechanisms produced by snake venoms; however, *in vivo* preclinical assays or, even better, clinical assays are essential for giving even stronger evidences of the effectivity of the use of medicinal plants against snakebites. In this scenario, the study of anti-*Bothrops* plants is more advanced, since quantitatively a higher number of *in vivo* scientific evidences are found in literature. Going the same way, studies with plants inhibiting local tissue damage of *Daboia*/*Vipera*, *Lachesis*, and *Crotalus* snakes could be also highlighted. However, studies of antiophidic medicinal plants in humans are very scarce: only one clinical study was found in literature, evaluating the inhibitory properties of a polyherbal formulation against local effects from Chinese cobra bite (see Section 4.9).

Hereafter, we describe the main plants with inhibitory potential against local tissue damage induced by snake venoms. It is important to emphasize that the focus of this review is plants against local tissue damage, mainly due to severity of these effects (which could cause permanent disabilities in victims) and the poor effectiveness of available antivenoms against them. So, studies with plants against systemic effects induced by snake were not considered; in addition some plants herein described possess inhibitory action upon systemic effects, although not stated here. For example, the vegetal species *Jatropha gossypiifolia* (Euphorbiaceae), a medicinal plant studied very much by our research group, had showed significative inhibitory action upon hemostatic disorders induced by *B. jararaca* snake venom [96]. So, the antiophidic potential of this species (as well as some others) lies beyond the capacity of inhibit local tissue damage provoked by *B. jararaca* venom, although not described in this review.

In addition, it is important to analyze critically some works dealing with antiophidic activity of plant extracts, since some of them have limitations that could reduce, at least partially, the potentiality of these species. The major limitation is that various studies, especially the early ones, make the evaluation of the plants using a preincubation approach, which consists in the previous inactivation of venom by preincubating it with different proportions of the tested extracts. Although scientifically valid and even recommended by WHO for assessing antiophidic antivenoms [97],

Table 2: List of medicinal plants with inhibitory potential against local effects induced by *Naja* snakes.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Acanthaceae					
Andrographis stenophylla	Leaf	*N. naja*	—	Hemorrhage	[83]
Amaranthaceae					
Pupalia lappacea	Herbal	*N. nigricollis*	SVH	—	[82]
Amaryllidaceae					
Allium cepa[#]	Bulb	*N. n. karachiensis*	PLA_2	—	[84]
Allium sativum[#]	Bulb	*N. n. karachiensis*	PLA_2	—	[84]
Anacardiaceae					
Lannea acida	Cortex	*N. nigricollis*	SVH	—	[82]
Pistacia chinensis subsp.*integerrima*[#]	Gall	*N. n. karachiensis*	PLA_2	—	[84]
Sclerocarya birrea	Cortex	*N. nigricollis*	SVH	—	[82]
Spondias mombin[#]	Cortex, radix	*N. nigricollis*	SVH	—	[82]
Annonaceae					
Annona senegalensis[#]	Cortex	*N. nigricollis*	SVH	—	[82]
Apiaceae					
Cuminum cyminum	Seed	*N. n. karachiensis*	PLA_2	—	[84]
Apocynaceae					
Acokanthera oppositifolia	Radix	*N. nigricollis*	SVH	—	
Calotropis procera[#]	Flower, latex	*N. n. karachiensis*	PLA_2	—	[84]
Strophanthus sarmentosus	Folium	*N. nigricollis*	SVH	—	[82]
Strophanthus speciosus	Radix	*N. nigricollis*	SVH	—	[82]
Tylophora indica[#]	Leaf, root	*N. naja*	PLA_2	Hemorrhage	[85]
Araceae					
Colocasia esculenta	Tuber	*N. nigricollis*	SVH	—	[82]
Araliaceae					
Polyscias fulva	Cortex	*N. nigricollis*	SVH	—	[82]
Aristolochiaceae					
Aristolochia bracteolata[#]	Leaf, root	*N. naja*	PLA_2	Hemorrhage	[85]
Asteraceae					
Callilepis laureola	Radix	*N. nigricollis*	SVH	—	[82]
Bignoniaceae					
Kigelia africana	Cortex, folium	*N. nigricollis*	SVH	—	[82]
Tecoma stans (syn. *Stenolobium stans*)	Root	*N. n. karachiensis*	PLA_2	—	[84]
Bixaceae					
Cochlospermum tinctorium	Radix	*N. nigricollis*	SVH	—	[82]
Boraginaceae					
Cordia macleodii	Bark	*N. naja*	—	Edema, hemorrhage[*], necrosis[*]	[86]
Trichodesma indicum[#]	Whole plant	*N. n. karachiensis*	PLA_2	—	[84]
Capparaceae					
Capparis tomentosa	Radix	*N. nigricollis*	SVH	—	[82]
Colchicaceae					
Gloriosa superba[#]	Radix	*N. nigricollis*	SVH	—	[82]
Combretaceae					
Combretum molle[#]	Folium	*N. nigricollis*	SVH	—	[82]
Guiera senegalensis	Radix	*N. nigricollis*	SVH	—	[82]
Terminalia arjuna[#]	Bark	*N. n. karachiensis*	PLA_2	—	[84]

Table 2: Continued.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Convolvulaceae					
Ipomoea rubens	Seed	*N. nigricollis*	SVH	—	[82]
Cucurbitaceae					
Citrullus colocynthis[#]	Fruit	*N. n. karachiensis*	PLA_2	—	[84]
Luffa cylindrica (syn. *Luffa aegyptiaca*)	Leaf	*N. nigricollis*	Proteolytic	—	[87]
Momordica charantia[#]	Fruit	*N. n. karachiensis*	PLA_2	—	[84]
Ebenaceae					
Diospyros mespiliformis	Cortex	*N. nigricollis*	SVH	—	[82]
Euphorbiaceae					
Alchornea laxiflora	Cortex	*N. nigricollis*	SVH	—	[82]
Clutia cordata	Radix	*N. nigricollis*	SVH	—	[82]
Euphorbia hirta[#]	Whole plant	*N. naja*	PLA_2, proteolytic, SVH	Edema[*]	[88]
Jatropha curcas[#]	Leaf, root, stem	*N. naja*	PLA_2	—	[89]
Jatropha gossypiifolia[#]	Leaf, root, stem	*N. naja*	PLA_2	—	[89]
Manihot foetida (syn. *Jatropha foetida*)	Leaf, stem	*N. naja*	PLA_2	—	[89]
Fabaceae					
Abrus precatorius[#]	Radix	*N. nigricollis*	SVH	—	[82]
Argyrolobium stipulaceum	Radix	*N. nigricollis*	SVH	—	[82]
Bauhinia thonningii	Cortex, radix	*N. nigricollis*	SVH	—	[82]
Bauhinia variegata[#]	Root	*N. n. karachiensis*	PLA_2	—	[84]
Bobgunnia madagascariensis (syn. *Swartzia madagascariensis*)	Folium, radix	*N. nigricollis*	SVH	—	[82]
Burkea africana	Cortex	*N. nigricollis*	SVH	—	[82]
Cullen corylifolium (syn. *Psoralea corylifolia*)	Seed	*N. n. karachiensis*	PLA_2	—	[84]
Dichrostachys cinerea	Folium	*N. nigricollis*	SVH	—	[82]
Entada africana	Radix	*N. nigricollis*	SVH	—	[82]
Mimosa pudica[#]	Root	*N. kaouthia, N. naja*	PLA_2, proteolytic, SVH	Edema[*], myotoxicity[*]	[90–92]
Parkia biglobosa	Cortex, stem bark	*N. nigricollis*	Cytotoxicity against muscle cells, SVH		[82, 93]
Stylosanthes erecta	Folium	*N. nigricollis*	SVH	—	[82]
Tamarindus indica[#]	Folium, radix	*N. nigricollis*	SVH	—	[82]
Gentianaceae					
Enicostema axillare (syn. *Enicostema hyssopifolium*)[#]	Whole plant	*N. n. karachiensis*	PLA_2	—	[84]
Hypericaceae					
Psorospermum corymbiferum	Cortex, radix	*N. nigricollis*	SVH	—	[82]
Lamiaceae					
Leucas aspera[#]	Leaf, root, whole plant	*N. naja*	PLA_2, proteolytic, SVH	Hemorrhage	[85, 94]
Leucas cephalotes (syn. *Leucas capitata*)[#]	Whole plant	*N. n. karachiensis*	PLA_2	—	[84]
Leucas martinicensis	ND	*N. nigricollis*	SVH	—	[82]
Ocimum tenuiflorum (syn. *Ocimum sanctum*)[#]	Whole plant	*N. n. karachiensis*	PLA_2	—	[84]
Rotheca myricoides (syn. *Clerodendrum myricoides*)	Cortex	*N. nigricollis*	SVH	—	[82]

Table 2: Continued.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Teucrium kraussii	Aerial parts, cortex	*N. nigricollis*	SVH	—	[82]
Volkameria glabra (syn. *Clerodendrum glabrum*)	Radix	*N. nigricollis*	SVH	—	[82]
Lauraceae					
Cassytha filiformis	Herbal	*N. nigricollis*	SVH	—	[82]
Loganiaceae					
Strychnos innocua	Folium	*N. nigricollis*	SVH	—	[82]
Strychnos nux-vomica[#]	Seed	*N. kaouthia*	PLA_2	—	[95]
Malvaceae					
Althaea officinalis	Root	*N. n. karachiensis*	PLA_2	—	[84]
Dombeya quinqueseta	Cortex	*N. nigricollis*	SVH	—	[82]
Grewia mollis	Cortex, folium, radix	*N. nigricollis*	SVH	—	[82]
Sterculia setigera	Cortex	*N. nigricollis*	SVH	—	[82]
Waltheria indica	Radix	*N. nigricollis*	SVH	—	[82]
Menispermaceae					
Cissampelos mucronata	Herbal	*N. nigricollis*	SVH	—	[82]
Moraceae					
Ficus platyphylla	Folium	*N. nigricollis*	SVH	—	[82]
Olacaceae					
Ximenia americana	Folium	*N. nigricollis*	SVH	—	[82]
Pedaliaceae					
Ceratotheca sesamoides	Herbal	*N. nigricollis*	SVH	—	[82]
Peraceae					
Clutia pulchella	Radix	*N. nigricollis*	SVH	—	[82]
Phyllanthaceae					
Flueggea virosa (syn. *Securinega virosa*)	Radix	*N. nigricollis*	SVH	—	[82]
Pinaceae					
Cedrus deodara	Bark	*N. n. karachiensis*	PLA_2	—	[84]
Pinus roxburghii[#]	Oleoresin	*N. n. karachiensis*	PLA_2	—	[84]
Poaceae					
Cymbopogon schoenanthus	Radix	*N. nigricollis*	SVH	—	[82]
Primulaceae					
Maesa lanceolata[#]	Cortex	*N. nigricollis*	SVH	—	[82]
Rhamnaceae					
Ziziphus mucronata	Radix	*N. nigricollis*	SVH	—	[82]
Ziziphus spina-christi	Cortex	*N. nigricollis*	SVH	—	[82]
Rubiaceae					
Crossopteryx febrifuga	Cortex	*N. nigricollis*	SVH	—	[82]
Pentanisia prunelloides	Radix	*N. nigricollis*	SVH	—	[82]
Pentas zanzibarica	Folium	*N. nigricollis*	SVH	—	[82]
Rubia cordifolia[#]	Stem				
Rutaceae					
Citrus limon[#]	Fruit	*N. n. karachiensis*	PLA_2	—	[84]
Zanthoxylum capense	Radix	*N. nigricollis*	SVH	—	[82]
Sapindaceae					
Paullinia pinnata	Folium	*N. nigricollis*	SVH	—	[82]
Sapindus mukorossi	Fruit	*N. n. karachiensis*	PLA_2	—	[84]

Table 2: Continued.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Solanaceae					
Nicotiana rustica	Leaf	*N. nigricollis*	Proteolytic	—	[87]
Schwenckia americana	Folium	*N. nigricollis*	SVH	—	[82]
Thymelaeaceae					
Gnidia anthylloides	Radix	*N. nigricollis*	SVH	—	[82]
Gnidia kraussiana	Radix	*N. nigricollis*	SVH	—	[82]
Gnidia splendens	Radix	*N. nigricollis*	SVH	—	[82]
Verbenaceae					
Lantana trifolia	Cortex	*N. nigricollis*	SVH	—	[82]
Vitaceae					
Cissus populnea	Stem	*N. nigricollis*	SVH	—	[82]
Zingiberaceae					
Zingiber officinale[#]	Rhizome	*N. n. karachiensis*	PLA_2	—	[84]
Zygophyllaceae					
Fagonia cretica	Leaf, stem	*N. n. karachiensis*	PLA_2	—	[84]

ND = information not described in the work; PLA_2 = snake venom phospholipase A_2; SVH = snake venom hyaluronidase. [#]Vegetal species with related folk use as antiophidic agents, as showed in Table 1. [*]Studies where inhibitory activity was assessed only by preincubation of venom with extract (see Section 4.1 for details).

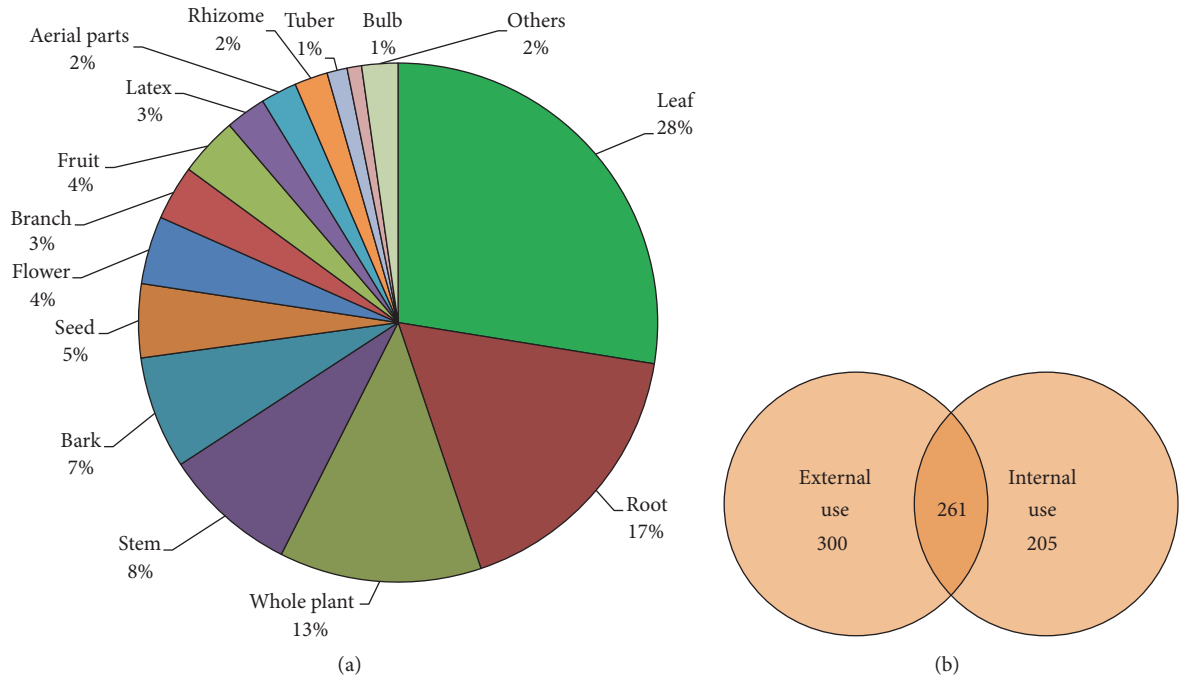

Figure 3: Mode of utilization of antiophidic plants reported by folk medicine. Main plant parts used (a) and Venn diagram showing the number of species enlisted having external use, internal use, or both (b).

this preincubation approach makes a scenario unlikely to be possible in the field, where the medicine would be delivered after the snakebite. In fact, a recent study evaluated the inhibitory action of the medicinal plant *Bellucia dichotoma* (Melastomataceae) against *Bothrops atrox* snake venom using different protocols: preincubation, pretreatment, and post-treatment [98]. The authors observed that while the extract was greatly active when preincubated, this inhibitory activity was drastically reduced or even lost when the extract was injected independently of venom, simulating traditional use. The authors observed that the extract has great amounts of tannins, which are compounds known to precipitate proteins. So, it was concluded that the "pseudo-inhibition" observed after preincubation may be due to the presence of these compounds, suggesting that the preincubation protocol overestimates inhibitory potential of medicinal plants, and for this reason, this kind of approach must be analyzed with caution for estimation of inhibitory potential of medicinal plants [13, 98]. In this sense, many recent studies have been done using protocols of pre- and/or posttreatment, to ensure the potentiality of antiophidic plants, and for most of them, positive results have been found [96, 98–102]. For this reason, studies using preincubation protocol are marked in the tables, for a critical analysis.

Also, it is interesting to note that several of the plants with inhibitory potential against snake venom local toxicities also present other relevant pharmacological activities. This is interesting since it is often discussed in the literature that several antiophidic plants did not neutralize snake venoms per se, but could have antiophidic use once they could relieve some of the symptoms of snake envenoming, especially the local effects. It is related that the presence of tranquilizing, antioxidant, immunostimulating, and/or anti-inflammatory activities in certain plants could be of great interest in the alleviation of snake envenoming symptoms [103, 104]. For example, some studies have shown that anti-inflammatory drugs could inhibit the edematogenic and other snake venom effects related to inflammation, such as necrosis and myotoxicity, induced by *Bothrops* venoms [105, 106]. In fact, many medicinal plants with antiophidic activity also possess significant anti-inflammatory activity *in vivo* [83, 96, 107–110]. Following the same reasoning, some plants with antioxidant activity also possess significant antiophidic effects [95, 96, 104, 111]. In fact, some authors suggest that molecules with antioxidant and/or anti-inflammatory effects could be interesting along with antivenom therapy, helping to reduce the occurrence of secondary/long term complication due to snakebites [112].

Bacterial infection secondary to snakebites is a common complication in envenomed victims [113, 114]. The main source of bacteria is the oral cavity of snakes, but the microbiota in the different layers of the victim's skin or even microorganisms from victim's clothes could also contribute [115, 116]. Abscess formation is a common complication found in patients bitten by Viperidae snakes, being a risk factor for amputation in these patients, and it may be associated with sepsis [113, 114, 117]. A large number of bacteria, including anaerobic species, aerobic gram-negative rods, and a small proportion of gram-positive cocci could be inoculated with snakebites and have been isolated from the abscesses of bitten patients [113, 114]. Microorganisms such as *Staphylococcus*, *Pseudomonas*, *Salmonella*, *Escherichia*, *Providencia*, *Proteus*, *Enterococcus,* and *Bacillus* were already identified in oral cavity of certain snakes [116]. The use of antibiotics following snakebites is often recommended, usually therapeutically than prophylactically, mainly to avoid complications due to infections [114, 118]. In this context, medicinal plants presenting antimicrobial activities, especially against those microorganisms usually detected in snakebite victims' abscesses, could be interesting [115].

Medicinal plants having antimicrobial activities in association with some of the pharmacological properties discussed above (such as anti-inflammatory and antioxidant, e.g.) could be of great value to relieve especially local effects induced by snake venom. In another point of view, it is possible that several related plants in folk medicine as antiophidic agents do not act directly upon venom toxins but indirectly on its symptoms. Anyway, some studies have shown the potentiality of some vegetal species acting in two ways: directly, neutralizing venom toxins, or indirectly, by having some of the pharmacological activities mentioned above. For example, *Jatropha gossypiifolia* (Euphorbiaceae), a plant species studied very much in our research group, showed significant antiophidic properties, inhibiting biological and enzymatic activities from *Bothrops* venoms [96, 119], and presented anti-inflammatory, antioxidant, anticoagulant, and antimicrobial properties in preclinical assays [81]. So, plants which possess these biological activities determined in previous studies might be preferred or prioritized in studies searching for antiophidic plants.

The mechanism by which medicinal plants neutralize the toxic venom constituents is still unknown, but many hypotheses have been proposed, such as protein precipitation, enzyme inactivation, proteolytic degradation, metal chelation, antioxidant action, and a combination of these mechanisms [15]. In this context, some improvements in this understanding have been achieved in the last years, through the use of *in silico* methods (e.g., docking simulations) to analyze the interaction of compounds isolated from plants and certain classes of snake venom toxins such as PLA_2 and SVMP [120–122].

The use of medicinal plants may present several advantages, such as low cost, being easily available, being stable at room temperature, and possibility of neutralization of a wide range of venom components [15]. In addition, since medicinal plants are an extremely complex mixture, it is possible that there may be a synergistic action of different compounds in plant, acting in distinct targets, inhibiting a broad spectrum of venom toxins [12, 15]. According to literature, interestingly, there are some plants in which the crude extract is more active than the isolated constituents [15], which supports the hypothesis of the synergistic action of plant components.

4.2. Plants Inhibiting Naja Snakes. A summary of active plants against *Naja* snakes local effects is presented in Table 2. *Naja* species are commonly called cobras. They typically occur in regions throughout Africa and Southern Asia. The outcomes of venom toxicity include nephro-, neuro-, and

Table 3: List of medicinal plants with inhibitory potential against local effects induced by *Bothrops* snakes.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Acanthaceae					
Justicia pectoralis[#]	Leaf	*B. jararaca*	—	Hemorrhage[*]	[33]
Amaranthaceae					
Blutaparon portulacoides	Aerial parts	*B. jararacussu*	—	Edema	[109]
Anacardiaceae					
Anacardium excelsum	Leaf, twig	*B. asper*	PLA_2	—	[111]
Annonaceae					
Ephedranthus columbianus	Leaf, twig	*B. asper*	PLA_2	—	[111]
Sapranthus isae	Leaf, twig	*B. asper*	PLA_2	—	[111]
Apocynaceae					
Allamanda cathartica[#]	Branch, leaf, stem	*B. atrox*	—	Hemorrhage[*]	[124]
Fernaldia pandurata (syn. *Mandevilla velutina*)	Leaf, stem, subterranean system	*B. alternatus, B. jararacussu, B. moojeni, B. pirajai*	PLA_2	Edema[*], hemorrhage[*], myotoxicity[*]	[125]
Tabernaemontana catharinensis	Root bark	*B. jararacussu*	Myotoxicity	Myotoxicity[**]	[126]
Araceae					
Dracontium croatii[#]	Rhizome	*B. asper*	—	Edema[*]	[127]
Philodendron megalophyllum[#]	Liana, vine	*B. atrox, B. jararaca*	PLA_2	Edema[*], hemorrhage[*]	[33, 128]
Philodendron tripartitum[#]	Branch, leaf	*B. atrox*	—	Hemorrhage[*]	[124]
Asteraceae					
Chaptalia nutans	Leaf	*B. asper*	—	Edema	[129]
Eclipta prostrata (syn. *Eclipta alba*)[#]	Aerial parts	*B. jararaca, B. jararacussu*	Myotoxicity	Myotoxicity	[130]
Mikania glomerata	Leaf	*B. jararaca*	—	Edema[*], hemorrhage[*], peritonitis	[131, 132]
Neurolaena lobata[#]	Branch, leaf, stem	*B. atrox*	—	Hemorrhage[*]	[124]
Pseudelephantopus spicatus[#]	Whole plant	*B. atrox*	—	Hemorrhage[*]	[124]
Bignoniaceae					
Fridericia chica (syn. *Arrabidaea chica*)	Leaf	*B. atrox*	—	Edema	[133]
Tabebuia aurea	Stem bark	*B. neuwiedi*	H_2O_2 production by peritoneal macrophages	Edema, hemorrhage[*], myonecrosis[*], peritonitis	[110]
Tabebuia rosea[#]	Stem bark	*B. asper, B. atrox*	PLA_2	Edema[**], Hemorrhage[*]	[124, 127, 134]
Bixaceae					
Bixa orellana[#]	Branch, leaf	*B. asper, B. atrox*	PLA_2	Edema[**], hemorrhage[*]	[124, 127, 134]
Boraginaceae					
Cordia verbenacea	Leaf	*B. jararacussu*	—	Edema[*]	[135]
Clusiaceae					
Clusia fluminensis	Fruit	*B. jararaca*	Proteolytic	Hemorrhage[**]	[136]
Combretaceae					
Combretum leprosum	Root	*B. jararaca, B. jararacussu*	Collagenase, myotoxicity, PLA_2, proteolytic	Edema, hemorrhage[*], myotoxicity[**]	[99]

Table 3: Continued.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Connaraceae					
Connarus favosus[#]	Bark	*B. atrox, B. jararaca*	PLA_2, proteolytic	Edema[*], hemorrhage[***]	[33, 115, 128]
Costaceae					
Costus lasius[#]	ND	*B. atrox*	PLA_2	—	[134]
Costus spicatus	Leaf	*B. atrox*	—	Edema[*], hyperalgesia[*]	[137]
Crassulaceae					
Bryophyllum pinnatum (syn. *Kalanchoe pinnata*)[#]	Leaf	*B. jararaca*	PLA_2	Edema, hemorrhage	[138]
Kalanchoe laciniata (syn. *Kalanchoe brasiliensis*)[#]	Leaf	*B. jararaca*	PLA_2	Edema, hemorrhage[***]	[33, 138]
Dicranaceae					
Dicranum frigidum	Whole plant	*B. asper*	PLA_2	—	[111]
Dilleniaceae					
Davilla elliptica	Leaf	*B. jararaca*	—	Hemorrhage[*]	[139]
Euphorbiaceae					
Croton urucurana	Stem bark	*B. jararaca*	—	Hemorrhage[*]	[140]
Hevea nitida	Leaf, twig	*B. asper*	PLA_2	—	[111]
Jatropha gossypiifolia[#]	Leaf	*B. erythromelas, B. jararaca*	PLA_2, proteolytic, SVH	Edema, hemorrhage, myotoxicity	[96, 119]
Jatropha mollissima[#]	Leaf	*B. erythromelas, B. jararaca*	—	Edema, hemorrhage, myotoxicity, peritonitis	[141]
Fabaceae					
Abarema cochliacarpos	Stem bark	*B. leucurus*	—	Decreased motor function, edema, hyperalgesia, myotoxicity	[101]
Brownea ariza	Bark, leaf	*B. asper*	PLA_2, proteolytic	—	[142]
Brownea rosa-de-monte[#]	Leaf, stem bark	*B. asper, B. atrox*	PLA_2, proteolytic	Edema[***], hemorrhage[***]	[124, 127, 134, 143]
Cassia fistula[#]	Seed	*B. jararaca*	—	Hemorrhage[*]	[33]
Dipteryx alata	Bark	*B. jararacussu*	Myotoxicity	—	[144]
Pentaclethra macroloba[#]	Bark	*B. alternatus, B. asper, B. atrox, B. jararaca, B. jararacussu, B. moojeni, B. neuwiedi, B. pirajai*	PLA_2	Edema[*], hemorrhage[*], myotoxicity[*]	[145]
Plathymenia reticulata[#]	Bark	*B. atrox, B. jararaca*	PLA_2	Edema[*], hemorrhage[*]	[33, 128]
Schizolobium parahyba	Leaf	*B. alternatus, B. moojeni, B. pauloensis*	PLA_2	Hemorrhage[*], myotoxicity[***]	[146, 147]
Senna dariensis[#]	Whole plant	*B. atrox*	PLA_2	Hemorrhage[*]	[124, 134]
Heliconiaceae					
Heliconia curtispatha[#]	Rhizome	*B. asper, B. atrox*	PLA_2, proteolytic	Edema[***], hemorrhage[*]	[124, 127, 134, 148]
Heliconia latispatha	Rhizome	*B. asper*	PLA_2, proteolytic	—	[148]
Heliconia wagneriana	Rhizome	*B. asper*	PLA_2, proteolytic	—	[148]

Table 3: Continued.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Hymenophyllaceae					
Trichomanes elegans[#]	Whole plant	*B. asper, B. atrox*	PLA_2	Edema[***], hemorrhage[*]	[124, 127, 134]
Hypericaceae					
Hypericum brasiliense	Whole plant	*B. jararaca*	Proteolytic	Edema[*], hemorrhage[*]	[149]
Icacinaceae					
Casimirella ampla (syn. *Humirianthera ampla*)	Root	*B. atrox, B. jararaca, B. jararacussu*	Myotoxicity, PLA2, proteolytic	Edema[***], hemorrhage[**], myotoxicity[*]	[102]
Lamiaceae					
Marsypianthes chamaedrys[#]	Inflorescence, leaf	*B. atrox*	PLA_2	Peritonitis	[108]
Peltodon radicans	Flower, leaf, stem	*B. atrox*	—	Edema	[150]
Lauraceae					
Aniba parviflora (syn. *Aniba fragrans*)[#]	Bark, leaf	*B. atrox, B. jararaca*	PLA_2	Edema[*], hemorrhage[*]	[33, 128]
Loasaceae					
Nasa speciosa (syn. *Loasa speciosa*)	Leaf	*B. asper*	—	Edema	[129]
Loganiaceae					
Strychnos pseudoquina	Leaf	*B. jararaca*	—	Hemorrhage[*]	[139]
Strychnos xinguensis[#]	ND	*B. atrox*	PLA_2	—	[134]
Loranthaceae					
Struthanthus orbicularis[#]	Branch, leaf	*B. asper, B. atrox*	PLA_2	Edema[**], hemorrhage[*]	[124, 127, 134]
Magnoliaceae					
Magnolia espinalii (syn. *Talauma espinalii*)	Leaf, twig	*B. asper*	PLA_2	—	[111]
Magnolia guatapensis (syn. *Dugandiodendron guatapense*)	Leaf, twig	*B. asper*	PLA_2	—	[111]
Magnolia hernandezii (syn. *Talauma hernandezii*)	Leaf, twig	*B. asper*	PLA_2	—	[111]
Magnolia yarumalensis (syn. *Dugandiodendron yarumalense*)	Leaf, twig	*B. asper*	PLA_2	—	[111]
Malpighiaceae					
Byrsonima crassa	Leaf	*B. jararaca*	—	Hemorrhage[*]	
Malvaceae					
Pachira glabra (syn. *Bombacopsis glabra*)	Root bark	*B. pauloensis*	—	Hemorrhage	[151]
Melastomataceae					
Bellucia dichotoma[#]	Bark	*B. atrox, B. jararaca*	PLA_2	Edema[***], hemorrhage[**]	[33, 98, 128, 152]
Mouriri pusa	Leaf	*B. jararaca*	—	Hemorrhage[*]	[139]
Meliaceae					
Carapa guianensis	Leaf, twig	*B. asper*	PLA_2	—	[111]
Cedrela odorata	Leaf, twig	*B. asper*	PLA_2	—	[111]
Swietenia humilis	Leaf, twig	*B. asper*	PLA_2	—	[111]
Swietenia macrophylla	Leaf, twig	*B. asper*	PLA_2	—	[111]
Swietenia mahagoni	Leaf, twig	*B. asper*	PLA_2	—	[111]

Table 3: Continued.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Menispermaceae					
Cissampelos pareira[#]	Leaf	*B. asper*	—	Hemorrhage[*]	[153]
Moraceae					
Brosimum guianense	Leaf	*B. atrox*	—	Hemorrhage[*], pain[*]	[154]
Castilla elastica[#]	Branch, leaf, stem	*B. atrox*	—	Hemorrhage[*]	[124]
Ficus nymphaeifolia[#]	Branch, leaf, stem	*B. asper, B. atrox*	—	Edema[**], hemorrhage[*]	[124, 127]
Musaceae					
Musa × *paradisíaca*[#]	Exudate	*B. jararacussu*	PLA_2	Hemorrhage[**], myonecrosis[**]	[155]
Myrtaceae					
Myrcia guianensis	Leaf	*B. jararaca*	PLA_2	Hemorrhage[*]	[156]
Passifloraceae					
Passiflora quadrangularis[#]	Branch, leaf	*B. atrox*	—	Hemorrhage[*]	[124]
Piperaceae					
Piper arboreum[#]	Branch, leaf	*B. atrox*	PLA_2	Hemorrhage[*]	[124, 134]
Piper pulchrum[#]	Leaf, branch, stem	*B. atrox*	—	Hemorrhage[*]	[124]
Polypodiaceae					
Pleopeltis percussa[#]	Branch, leaf, stem, whole plant	*B. asper, B. atrox*	PLA_2, proteolytic	Edema[**], hemorrhage[*]	[124, 127, 134]
Rubiaceae					
Gonzalagunia panamensis[#]	Branch, leaf, stem	*B. asper, B. atrox*	PLA_2	Edema[**], hemorrhage[*]	[124, 127, 134]
Randia aculeata[#]	Fruit	*B. asper*	—	Myotoxicity	[78]
Uncaria tomentosa	Root	*B. asper*	—	Edema	[129]
Rutaceae					
Citrus limon[#]	Ripe fruit	*B. asper, B. atrox*	—	Edema[***], hemorrhage[*]	[124, 127]
Murraya paniculata[#]	Leaf, twig	*B. asper*	PLA_2	—	[111]
Salicaceae					
Casearia grandiflora[#]	Leaf	*B. moojeni, B. neuwiedi*	PLA_2	Myotoxicity[*]	[157]
Casearia sylvestris[#]	Leaf	*B. asper, B. jararacussu, B. moojeni, B. neuwiedi, B. pirajai*	Myonecrosis, neuromuscular blockade	Edema[*], hemorrhage[*], myotoxicity[*]	[158–160]
Sapindaceae					
Billia hippocastanum	Leaf, twig	*B. asper*	PLA_2	—	[111]
Cupania americana	Leaf, twig	*B. asper*	PLA_2	—	[111]
Sapindus saponaria	*In vitro* cultivated callus, leaf, twig	*B. alternatus, B. asper, B. jararacussu, B. moojeni*	PLA_2	Hemorrhage[*]	[111, 161]
Serjania erecta	Aerial parts	*B. jararacussu*	PLA_2	Edema[*], hemorrhage[*], myotoxicity[*]	[162]

Table 3: Continued.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Siparunaceae					
Siparuna thecaphora[#]	Branch, leaf, stem	*B. atrox*	—	Hemorrhage[*]	[124]
Solanaceae					
Capsicum annuum (syn. *Capsicum frutescens*)[#]	Ripe fruit	*B. atrox*	—	Hemorrhage[*]	[124]
Urticaceae					
Urera baccifera	Leaf	*B. asper*	—	Edema	[129]
Velloziaceae					
Vellozia squamata (syn. *Vellozia flavicans*)	Leaf	*B. jararacussu*	Neuromuscular blockade and cell damage	—	[163]
Zingiberaceae					
Curcuma longa[#]	Rhizome	*B. alternatus*	—	Edema, hemorrhage, necrosis	[164]
Renealmia alpinia[#]	Leaf, rhizome	*B. asper, B. atrox*	PLA_2, proteolytic	Edema[**], hemorrhage	[107, 127, 134, 165, 166]

ND = information not described in the work; PLA_2 = snake venom phospholipase A_2; H_2O_2: hydrogen peroxide. [#]Vegetal species with related folk use as antiophidic agents, as showed in Table 1. [*]Studies where inhibitory activity was assessed only by preincubation of venom with extract (see Section 4.1 for details). [**]Active in preincubation tests but inactive or only poorly active when extract was used independently of venom (pre-, co-, or posttreatment protocols). [***]Active in preincubation tests and when used independently of venom (pre-, co-, or posttreatment protocols).

cardiotoxicity, respiratory and circulatory collapse, necrosis, hemorrhage, and edema [13]. A great number of the plants showed in this review were tested against *Naja* species. However, it is important to mention that only a very small number of these plants were assessed *in vivo*, and so the scientific evidences of antiophidic activities of these species are based on enzymatic *in vitro* assays, especially against SVHs, a class of toxin particularly relevant in cobras. The study of Molander et al. [82] presented several medicinal plants identified as potent inhibitors of *N. nigricollis* SVHs, PLA_2, and proteases, which could indicate a potential rich source of inhibitors of necrosis induced by these venom, which must be evaluated *in vivo* later [82]. The same group, in a more recent study [123], investigated the skin permeation, *ex vivo* inhibition of venom induced tissue destruction, and wound healing potential of African plants used against snakebite, which included the most potent inhibitors identified in the previous work [82]. A total of 30 plant species were tested against *Naja nigricollis* and *Bitis arietans* employing *in vitro* and *ex vivo* models [123]. However, although plant extracts have showed potential in inhibiting snake venom enzymes, this study showed no effect against cell death and tissue damage.

4.3. Plants Inhibiting Bothrops Snakes. A summary of active plants against *Bothrops* snakes local effects is presented in Table 3. More than 90% of the snakebites reported every year in Latin America are caused by *Bothrops* species [8]. Envenomation by *Bothrops* snakes is characterized by a prominent and complex series of local pathological alterations, which appear rapidly after the bite in the anatomical site where venom is inoculated [168]. In a number of *Bothrops* bite cases, lack of neutralization of local effects results in permanent sequelae, with significative tissue loss [8]. So, the use of a therapeutic approach with high inhibitory potential and easy access and disponibility to victims, which could neutralize rapidly the onset of these local manifestations, is interesting. Most of the inhibitory studies with *Bothrops* snakes were performed in Brazil, which could be associated with richness of Brazilian flora as well as the epidemiological aspects of this country. The work performed by De Moura et al. [33] could be highlighted, where these authors performed an ethnopharmacological-guided screening of plants with reputation against snakebite in Santarém, Western Pará, Brazil. Twelve species were evaluated against *Bothrops jararaca* snake venom induced hemorrhage and some of them presented very significative results, showing, thus, the relevance of traditional knowledge in the survey of antiophidic plants [33].

4.4. Plants Inhibiting Bitis Snakes. A summary of active plants against *Bitis* snakes local effects is presented in Table 4. Snakes belonging to the genus *Bitis* are implicated in many accidents with humans in Africa. The envenomation by *Bitis* often results in severe local damage, hypotension, coagulopathy, thrombocytopenia, and spontaneous local bleeding and, in the absence of antivenom therapy, the accident can be fatal. *Bitis arietans* is one of the three species of snakes of medical importance in Africa and its venom is considered the most

Table 4: List of medicinal plants with inhibitory potential against local effects induced by *Bitis* snakes.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Amaranthaceae					
Pupalia lappacea	Herbal	*B. arietans*	SVH	—	[82]
Amaryllidaceae					
Crinum jagus	Bulb	*B. arietans*	—	Myotoxicity*	[167]
Anacardiaceae					
Lannea acida	Cortex	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Sclerocarya birrea	Cortex	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Spondias mombin#	Cortex, radix	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Annonaceae					
Annona senegalensis#	Cortex	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Apocynaceae					
Strophanthus speciosus	Radix	*B. arietans*	SVH	—	[82]
Araliaceae					
Polyscias fulva	Cortex	*B. arietans*	SVH	—	[82]
Bignoniaceae					
Kigelia africana	Cortex	*B. arietans*	PLA_2, SVH	—	[82]
Bixaceae					
Cochlospermum tinctorium	Radix	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Capparaceae					
Capparis tomentosa	Radix	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Colchicaceae					
Gloriosa superba#	Radix	*B. arietans*	SVH	—	[82]
Combretaceae					
Combretum molle#	Folium	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Guiera senegalensis	Radix	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Ebenaceae					
Diospyros mespiliformis	Cortex	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Euphorbiaceae					
Alchornea laxiflora	Cortex	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Fabaceae					
Bauhinia thonningii	Cortex, radix	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Bobgunnia madagascariensis (syn. *Swartzia madagascariensis*)	Folium, radix	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Burkea africana	Cortex	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Dichrostachys cinerea	Folium	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Entada africana	Radix	*B. arietans*	SVH	—	[82]
Parkia biglobosa	Cortex	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Stylosanthes erecta	Folium	*B. arietans*	SVH	—	[82]
Tamarindus indica#	Cortex, folium	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Hypericaceae					
Psorospermum corymbiferum	Cortex, radix	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Hypoxidaceae					
Molineria capitulata (syn. *Curculigo recurvata*)	Folium	*B. arietans*	SVH	—	[82]

Table 4: Continued.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Lamiaceae					
Rotheca myricoides (syn. *Clerodendrum myricoides*)	Cortex	*B. arietans*	SVH	—	[82]
Teucrium kraussii	Aerial parts, cortex	*B. arietans*	SVH	—	[82]
Volkameria glabra (syn. *Clerodendrum glabrum*)	Cortex	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Lauraceae					
Cassytha filiformis	Herbal	*B. arietans*	SVH	—	[82]
Loganiaceae					
Strychnos decussata	Radix	*B. arietans*	Proteolytic	—	[82]
Strychnos innocua	Folium	*B. arietans*	Proteolytic, SVH	—	[82]
Malvaceae					
Dombeya quinqueseta	Cortex	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Grewia mollis	Cortex, folium, radix	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Sterculia setigera	Cortex	*B. arietans*	PLA_2, SVH	—	[82]
Waltheria indica	Radix	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Menispermaceae					
Cissampelos mucronata	Herbal	*B. arietans*	Proteolytic, PLA_2	—	[82]
Moraceae					
Ficus platyphylla	Folium	*B. arietans*	PLA_2, SVH	—	[82]
Olacaceae					
Ximenia americana	Folium	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Phyllanthaceae					
Flueggea virosa (syn. *Securinega virosa*)	Radix	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Primulaceae					
Maesa lanceolata[#]	Cortex	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Rhamnaceae					
Ziziphus mucronata	Radix	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Ziziphus spina-christi	Cortex	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Rubiaceae					
Crossopteryx febrifuga	Cortex	*B. arietans*	PLA_2, SVH	—	[82]
Pentanisia prunelloides	Radix	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Pentas zanzibarica	Folium	*B. arietans*	PLA_2	—	[82]
Rutaceae					
Zanthoxylum capense	Radix	*B. arietans*	PLA_2, proteolytic	—	[82]
Sapindaceae					
Paullinia pinnata	Folium, radix	*B. arietans*	PLA_2, proteolytic, SVH	—	[82]
Solanaceae					
Schwenckia americana	Folium	*B. arietans*	SVH	—	[82]
Verbenaceae					
Lantana trifolia	Cortex	*B. arietans*	PLA_2, SVH	—	[82]
Vitaceae					
Cissus populnea	Stem	*B. arietans*	SVH	—	[82]

PLA_2 = snake venom phospholipase A_2; SVH = snake venom hyaluronidase. [#]Vegetal species with related folk use as antiophidic agents, as showed in Table 1.
[*]Studies where inhibitory activity was assessed only by preincubation of venom with extract (see Section 4.1 for details).

toxic venom of the viper group [169]. Regarding the plants with inhibitory action upon *Bitis* snakes, only one *in vivo* study of antiophidic activity was found until date. Although many works have been showing the potential of medicinal plants against several snake venoms, only three works were identified evaluating the action of plants against *Bitis*, from which two are the same screening studies of plants against *Naja* snake venom discussed before (Section 4.2) [82, 123].

4.5. Plants Inhibiting Daboia/Vipera Snakes. A summary of active plants against *Daboia/Vipera* snakes local effects is presented in Table 5. The *Daboia* genus is represented by a single species, named *Daboia russelii,* also popularly known as Russell's viper. This species is widespread in many parts of Asia and is responsible for large morbimortality due to snakebites in this continent [183, 184]. Russell's viper was formerly classified in *Vipera* genus and is therefore better known as *Vipera russelii*, since the new accepted nomenclature *(Daboia russelii)* is not yet universally followed [184]. For this reason, to avoid confounding, we use the term *Daboia/Vipera* in some occasions.

In humans, Russell's viper bite causes severe local tissue damage; more frequently the necrosis results in an irreversible loss of tissue and requires amputation of the affected limb [182, 183, 185]. As observed with *Bothrops* snakes, several studies have showed the inhibitory potential of medicinal plants against local effects of Russell's viper venom, including several preclinical *in vivo* studies.

4.6. Plants Inhibiting Lachesis Snakes. A summary of active plants against *Lachesis* snakes local effects is presented in Table 6. *Lachesis muta* is the longest venomous snake in the Americas and is distributed in the equatorial forests east of the Andes, ranging from eastern Ecuador, Colombia, Peru, northern Bolivia, and eastern and northern Venezuela, to Guyana, French Guyana, Surinam, and northern Brazil [100, 186]. *L. muta* snakebites are mainly characterized by systemic (generalized bleeding, coagulopathy, renal failure, and shock) and local effects (pain, hemorrhage, edema, and necrosis). In South America, *Bothrops* species has a higher incidence of accidents than *L. muta*, but, on the other hand, *Lachesis* bites led to more severe symptoms and have lethality indexes significantly higher than *Bothrops* [100, 186, 187]. Thus, the study of medicinal plants against these snakes, too, is of very much relevance. However, only a few studies were detected with plants against *Lachesis* snakes.

4.7. Plants Inhibiting Crotalus Snakes. A summary of active plants against *Crotalus* snakes local effects is presented in Table 7. Snakes from *Crotalus durissus* complex, popularly known as rattlesnakes, are dispersed northward into North America and southward into South America. Species of the *Crotalus durissus* complex pose a serious medical problem in many parts of the America [199]. Crotalic venom is considered highly toxic and more lethal in comparison with that of the genus *Bothrops*, having three main actions: neurotoxic, myotoxic, and coagulant [200, 201]. The crotalic accident is characterized by local and systemic manifestations, but while the local alterations are only discrete, the systemic manifestations are severe, leading to high chances of death [201]. Probably due to this low local effect in envenomed victims, the inhibition of these effects by plants is, until now, little investigated, especially when compared to other species with characteristic severe local effects.

4.8. Plants Inhibiting Other Snakes. Besides the snakes discussed above, some other studies are found with plants inhibiting other snake species, such as those from *Echis* and *Bungarus* genus. For other snakes species such as *Calloselasma rhodostoma*, *Philodryas olfersii,* and *Montivipera xanthina*, only isolated studies with a single plant, in each one, were found. These plants are summarized in Table 8. Many reasons may be stated for this lack of studies, such as low level of local effects, incidence restricted to a small region of the world, and usual low efficacy of plant extracts due to possible extremely high toxicity. However, it is important to highlight that the lack of studies does not mean a lower medical relevance of these species. For example, the saw-scaled viper *(Echis carinatus)* and the common Indian krait *(Bungarus caeruleus)*, along with spectacled cobra *(Naja naja)* and Russell's viper *(Daboia russelii)*, are included among the referred "Big Four" venomous snakes of India, being responsible for the majority of morbid complications, characterized by persistent and progressive tissue necrosis even after treatment with antivenom [195, 202]. Therefore, future studies with plants aiming at the inhibition of the local effects induced by these snakes are encouraged.

4.9. Studies in Humans. Along our antiophidic plants database, only one clinical study was found in literature, evaluating the inhibitory properties of a polyherbal formulation, externally applied, against soft-tissue necrosis after *Naja atra* (Chinese cobra) bite [203]. This polyherbal formulation, known in China as Jidesheng antivenom, is composed of the following ingredients: Ganchan *(Succys Bufo)*, Dijincao *(Herba Euphorbiae Humifusae)*, Chonglou *(Rhizoma Paridis Chonglou)*, and Wugong *(Scolopendra)*. This was a retrospective study performed with 126 patients with skin and soft-tissue necrosis due cobra bite, with the control group being treated externally with 40% glyceride magnesium sulfate ($n = 52$) and the treatment group performed by application of Jidesheng antivenom externally ($n = 74$). The authors observed statistically significant differences in maximum local necrotic area of skin and soft tissues, healing time, and skin-grafting rate between the control and treatment groups ($P < 0.05$), thus indicating that external application of Jidesheng antivenom may help to promote wound healing and reduce the skin-grafting rate in cases of skin and soft-tissue necrosis due to Chinese cobra bite [203]. Considering the composition of the Jidesheng antivenom, the authors discuss that each ingredient in this product may exert antipyretic, antidotal, antiphlogistic, and analgesic effects, according to previous results with each ingredient isolated, which could contribute to the inhibitory effect observed by the formulation [203]. The result obtained in this clinical study is very promising, since it shows that a plant-derived product

Table 5: List of medicinal plants with inhibitory potential against local effects induced by *Daboia/Vipera* snakes.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Anacardiaceae					
Anacardium occidentale[#]	Bark	*D. russelli*	PLA_2, proteolytic, SVH	Edema, hemorrhage, myotoxicity	[170]
Mangifera indica[#]	Stem bark	*D. russelii*	LAAO, PLA_2, SVH, proteolytic	Edema[*], hemorrhage[*], myotoxicity[*]	[171]
Apocynaceae					
Hemidesmus indicus[#]	Root	*D. russelli*	—	Hemorrhage	[172]
Tylophora indica[#]	Leaf, root	*D. russelli*	PLA_2	Hemorrhage	[85]
Aristolochiaceae					
Aristolochia bracteolata[#]	Leaf, root	*D. russelli*	PLA_2	Hemorrhage	[85]
Aristolochia indica[#]	Root	*D. russelii*	LAAO, proteolytic	—	[173]
Asteraceae					
Pluchea indica[#]	Root	*D. russelli*	—	Hemorrhage	[172]
Euphorbiaceae					
Acalypha indica[#]	Leaf	*D. r. russelli*	—	Hemorrhage, necrosis	[174]
Fabaceae					
Butea monosperma[#]	Stem bark	*D. russelii*	SVH	Hemorrhage[*]	[175]
Mimosa pudica[#]	Root	*D. russelii*	Proteolytic, SVH	—	[91]
Tamarindus indica[#]	Seed	*D. r. siamensis, D. russelii*	LAAO, PLA_2, SVH, proteolytic	Edema[*], hemorrhage[*], myotoxicity[*]	[176, 177]
Lamiaceae					
Leucas aspera[#]	Leaf, root	*D. russelii*	PLA_2	Hemorrhage	[85]
Vitex negundo[#]	Root	*D. russelii*	—	Edema, hemorrhage	[178]
Loganiaceae					
Strychnos nux-vomica[#]	Seed	*D. russelii*	PLA_2	Hemorrhage[*]	[95]
Moraceae					
Morus alba[#]	Leaf	*D. russelii*	Proteolytic, SVH	Edema[*], hemorrhage[*], myotoxicity[*]	[179]
Phyllanthaceae					
Phyllanthus emblica (syn. *Emblica officinalis*)[#]	Root	*D. russelii*	—	Edema, hemorrhage	[178]
Piperaceae					
Piper longum[#]	Fruit	*D. russelii*	Hemorrhage	Edema, hemorrhage, myotoxicity, necrosis	[104]
Rubiaceae					
Ophiorrhiza mungos[#]	Root	*D. russelii*	Hemorrhage	—	[180]
Salvadoraceae					
Azima tetracantha	Leaf	*D. russelii*	SVH	—	[181]
Vitaceae					
Vitis vinifera	Seed	*D. russelii*	Proteolytic, SVH	Edema[*], hemorrhage[*], myonecrosis[*]	[182]

LAAO = L-amino acid oxidase; PLA_2 = snake venom phospholipase A_2; SVH = snake venom hyaluronidase. [#]Vegetal species with related folk use as antiophidic agents, as showed in Table 1. [*]Studies where inhibitory activity was assessed only by preincubation of venom with extract (see Section 4.1 for details).

Table 6: List of medicinal plants with inhibitory potential against local effects induced by *Lachesis* snakes.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Apocynaceae					
Fernaldia pandurata (syn. *Mandevilla velutina*)	Root	*L. muta*	Proteolytic, PLA_2	Hemorrhage*	[188]
Asteraceae					
Eclipta prostrata (syn. *Eclipta alba*)#	Aerial parts, root	*L. muta*	Myotoxicity, proteolytic, PLA_2	Hemorrhage*, myotoxicity	[130, 188]
Mikania glomerata	Root	*L. muta*	Proteolytic, PLA_2	—	[188]
Erythroxylaceae					
Erythroxylum ovalifolium	Stem	*L. muta*	Proteolytic, PLA_2	Edema***, hemorrhage***	[189]
Erythroxylum subsessile	Stem	*L. muta*	Proteolytic, PLA_2	Edema***, hemorrhage***	[189]
Euphorbiaceae					
Jatropha elliptica	Root, stem	*L. muta*	Proteolytic, PLA_2	Hemorrhage*	[188]
Fabaceae					
Pentaclethra macroloba#	Bark	*L. muta*	—	Hemorrhage*	[145]
Stryphnodendron adstringens (syn. *Stryphnodendron barbatimam*)	Root	*L. muta*	Proteolytic, PLA_2	Hemorrhage*	[188]
Melastomataceae					
Miconia albicans	Stem	*L. muta*	Proteolytic, PLA_2	Hemorrhage*	[188]
Miconia fallax	Stem	*L. muta*	Proteolytic, PLA_2	Hemorrhage*	[188]
Miconia sellowiana	ND	*L. muta*	Proteolytic, PLA_2	Hemorrhage*	[188]
Tibouchina stenocarpa	Root	*L. muta*	Proteolytic, PLA_2	Hemorrhage*	[188]
Salicaceae					
Casearia sylvestris#	Root	*L. muta*	Proteolytic	Hemorrhage*	[188]
Sapotaceae					
Manilkara subsericea	Leaf, stem	*L. muta*	Proteolytic, PLA_2	Edema**, hemorrhage**	[100]

ND = information not described in the work; PLA_2 = snake venom phospholipase A_2. #Vegetal species with related folk use as antiophidic agents, as showed in Table 1. *Studies where inhibitory activity was assessed only by preincubation of venom with extract (see Section 4.1 for details). **Active in preincubation tests but inactive or only poorly active when extract was used independently of venom (pre-, co-, or posttreatment protocols). ***Active in preincubation tests and when used independently of venom (pre-, co-, or posttreatment protocols).

showed significant results in humans, thus pointing to the potentiality of this kind of product in treatment of snake venom induced local effects. However, only one study is insufficient to ensure the potentiality of medicinal plants against snakebites, with performing more clinical studies, preferentially controlled and randomized ones, to bring more evidences of the viability of the approach for future safe and effective use in humans being necessary. So, more clinical studies, especially ones with those plants highlighted in this review and those presenting good preclinical *in vivo* evidences of antiophidic efficacy, are highly encouraged.

5. Concluding Remarks

The popular use of vegetal species does not necessarily imply efficacy, but it gives a selected list of medicinal plants that can be primarily studied in pharmacologic assays for possible antiophidic effects, directing future studies in this area. In fact, a great number of these species that have been evaluated against local tissue damage induced by several snake species showed inhibitory potential against hyaluronidase, phospholipase, proteolytic, hemorrhagic, myotoxic, and edematogenic activities, among others. Therefore, considering the limitations of conventional antivenom serotherapy, especially

Table 7: List of medicinal plants with inhibitory potential against local effects induced by *Crotalus* snakes.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Apocynaceae					
Fernaldia pandurata (syn. *Mandevilla velutina*)	Leaf, stem, subterranean system	*C. d. terrificus*	PLA_2	Edema*, myotoxicity*	[125]
Mandevilla illustris	Subterranean system	*C. d. terrificus*	PLA_2	—	[190]
Asteraceae					
Eclipta prostrata (syn. *Eclipta alba*)#	Aerial parts	*C. d. terrificus*	Myotoxicity	Myotoxicity*	[11]
Bignoniaceae					
Fridericia chica (syn. *Arrabidaea chica*)	Leaf	*C. d. ruruima*	—	Edema	[133]
Fabaceae					
Pentaclethra macroloba#	Bark	*C. atrox*	—	Hemorrhage*	[145]
Schizolobium parahyba	Leaf	*C. d. terrificus*	PLA_2	Edema*	[146, 147]
Musaceae					
Musa × *paradisiaca*#	Exudate	*C. d. terrificus*	PLA_2	—	[155]
Rubiaceae					
Randia aculeata#	Fruit	*C. simus*	—	Myotoxicity	[78]
Sapindaceae					
Sapindus saponaria	*In vitro* cultivated callus	*C. d. terrificus*	PLA_2	—	[161]

PLA_2 = snake venom phospholipase A_2. #Vegetal species with related folk use as antiophidic agents, as showed in Table 1. *Studies where inhibitory activity was assessed only by preincubation of venom with extract (see Section 4.1 for details).

its poor efficacy against local effects, the treatment with medicinal plants may provide a potential adjuvant alternative to treat snakebites, being used to complement the activity and effectiveness of available snake venom therapy. The main potential advantages of antiophidic plants are their low cost, easy access, stability at room temperature, and ability to neutralize a broad spectrum of toxins, including the local tissue damage.

Interestingly, some studies have showed that the crude extracts are more powerful than the individual herbal compounds, which could, at a certain extent, justify the development of herbal products containing these plants instead of medicines containing isolated compounds, which in turn could be more rapidly available in market, after proof of safety, effectiveness, and quality of these products. However, despite the existence of many plants with great potential, no natural antiophidic product is available in market, which points to question of the need for further studies. Only a few numbers of patents regarding herbal products against snakebites were found in literature. Some patents regarding the use of Chinese medicinal plants against snake and bug bites were found. In our research group, two patents were deposited concerning the processes of obtaining extracts, fraction, isolated compounds, and pharmaceutical compositions of some plants studied by our group applied in the treatment of accidents with venomous animals (BR 10 2013 034046 4 A2 and BR 10 2012 026958 9 A2). Thus, the number of patents with antiophidic herbal products is still relatively small. For this reason, we encourage pharmacologists and toxinologists around the world to intensify studies with antiophidic plants, especially prioritizing those with the greatest number of indications in traditional medicine and emphasizing clinical studies with the most active plants in preclinical studies, given that the low number of human studies is one of the major obstacles for the future application of herbal products with antiophidic potential. No less important, toxicological studies are also extremely necessary to ensure the safety of these products.

In conclusion, the data presented in this review provides an updated scenario for and insights into future research aiming at validation of medicinal plants as antiophidic agents and, based on scientific evidences, strengthens the potentiality of medicinal plants and ethnopharmacological knowledge as a tool for design of potent inhibitors and/or herbal medicines against venom toxins.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Acknowledgments

Matheus de Freitas Fernandes-Pedrosa is CNPq fellowship-honored researcher. Juliana Félix-Silva acknowledges CAPES for the Ph.D. scholarship.

Table 8: List of medicinal plants with inhibitory potential against local effects induced by other snakes.

Plant name	Part used	Snake venom	Inhibited activities		Reference(s)
			In vitro	*In vivo*	
Amaryllidaceae					
Crinum jagus	Bulb	*Echis ocellatus*	Hemorrhage	Myotoxicity**	[167, 191]
Asteraceae					
Artemisia absinthium	Aerial parts	*Montivipera xanthina*	—	Edema	[192]
Mikania laevigata	Leaf	*Philodryas olfersii*	Inflammation, myotoxicity	—	[193]
Fabaceae					
Albizia lebbeck#	Seed	*Echis carinatus*	Proteolytic, SVH	Hemorrhage, myotoxicity	[194]
Mimosa pudica#	Root	*Bungarus caeruleus, Echis carinatus*	PLA_2, proteolytic, SVH	Edema*	[91, 92]
Parkia biglobosa	Stem bark	*Echis ocellatus*	Cytotoxicity against muscle cells, hemorrhage	—	[93]
Pentaclethra macroloba#	Bark	*Calloselasma rhodostoma*	—	Hemorrhage*	[145]
Senna auriculata (syn. *Cassia auriculata*)	Leaf	*Echis carinatus*	PLA_2, proteolytic, SVH	Edema***, hemorrhage***, myotoxicity***	[195]
Malvaceae					
Hibiscus aethiopicus	Whole plant	*Echis carinatus, Echis ocellatus*	Cytotoxicity against muscle cells, hemorrhage	Edema***, hemorrhage***	[196, 197]
Salvadoraceae					
Azima tetracantha	Leaf	*Bungarus caeruleus*	PLA_2	—	[181]
Vitaceae					
Vitis vinifera	Seed	*Echis carinatus*	Proteolytic, SVH	Edema*, hemorrhage*, myotoxicity*	[198]

PLA_2 = snake venom phospholipase A_2; SVH = snake venom hyaluronidase. #Vegetal species with related folk use as antiophidic agents, as showed in Table 1. *Studies where inhibitory activity was assessed only by preincubation of venom with extract (see Section 4.1 for details). **Active in preincubation tests but inactive or only poorly active when extract was used independently of venom (pre-, co-, or posttreatment protocols). ***Active in preincubation tests and when used independently of venom (pre-, co-, or posttreatment protocols).

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