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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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 edemagenic 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$_2$s), snake venom serine proteinases (SVSPs), acetylcholinesterase (AChE), L-amino acid oxidases (LAAs), 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 injury), 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 toxicologists worldwide as a tool for design of potent inhibitors against snake venom toxins. The potential advantages of antiophidian 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 antiophidian 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 antiophidian 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 antiophidian 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 "herbs" OR "decoction" OR "tea" OR "infusion" OR "macerate") AND (("snake venom" OR "snake" OR "snakes" OR "snakebite" OR "snakkebite" OR "snakebites" OR "antivenom" OR "antivenoms" OR "anti-venom" OR "anti-venoms" OR "anti-venin" OR "anti-venins" OR "anti-venin" OR "anti-venins" OR "antiophidian" OR "antiophidian"

snake venom neutralization") OR "snake venom inhibition") OR "snake venom neutralization") OR "snake toxins inhibition") OR "snake toxins neutralization") OR "viper" OR "viperidae" OR "crotalinae" OR "viperine" OR "elapidae" OR "pit-viper" OR "bothrops") OR "jalaraca") OR "crotalus" OR "micrurus" OR "lachesis" OR "cobra" OR "naja") OR "bitis" OR "viperina" OR "daboia") OR "trimere-
sus").

All abstracts and/or full-text data were considered, without language restriction. Then, the publications covering ethnobotanical and/or pharmacological studies of antiophidian 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 antivenomic 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 antivenomic 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 antivenomic 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 antivenomic agents, present a series of another popular uses (data not shown) in popular medicine, mainly anti-inflammatory activity. For example, Jatropha gossypiifolia (Euphorbiaceae) has antivenomic, 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 antivenomic 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 antivenomic activity.

The plant families with most vegetal species showing positive results in antivenomic 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 antivenomic plants.

Snakes from the genus Naja, Bothrops, and Bitis were the most evaluated ones in these antivenomic assays. However, although Naja and Bothrops 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<sub>2</sub> (PLA<sub>2</sub>s), 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<sub>2</sub>, SVHs, and proteases from Bitis arietans and Naja nigriscollis (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) |
|--------------------------------|------------------------------------------------|-----------------------------------|---------|--------------|
| Acanthus arboreus              | Sri Lanka                                      | ND                                | I       | [18]         |
| Andrographis echioides (syn.  | India                                          | Shoot                            | ND      | [19]         |
| Indoneesiella echioides        |                                                 |                                   |         |              |
| 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 lapulina              | 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]         |
| Dictiperta paniculata (syn.    | India                                          | Root, whole plant                 | I, E    | [24, 25]     |
| Peristrophe paniculata         |                                                 |                                   |         |              |
| Fittonia albivenis             | Peru                                           | Aerial parts                      | E       | [29]         |
| Hygrophila auriculata          | India, Sri Lanka                               | Seed                              | I       | [18, 23]     |
| Justicia adhatoda (syn.        | India, Pakistan, Sri Lanka                     | Flower, leaf, root                | I, E    | [16–18, 30]  |
| Adhatoda vasica                | Lanna                                          |                                   |         |              |
| Justicia calyculata            | Kenya                                          | Aerial parts                      | E       | [31]         |
| Justicia gendarussa            | Bangladesh                                     | Leaf                              | I       | [30, 32]     |
| Justicia japonica (syn.        | India                                          | Leaf                              | I       | [23]         |
| Justicia simplex               |                                                 |                                   |         |              |
| 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]         |
| Acorus calamus                 | Bangladesh, India, Pakistan, Sri Lanka         | Rhizome                           | I, E    | [17, 18, 20, 22, 25, 32, 36] |
| Adoxaceae                      |                                                |                                   |         |              |
| Sambucus nigra                 | Spain                                          | Flower                            | E       | [37]         |
| Amaranthaceae                  |                                                |                                   |         |              |
| Achyranthes aspera (syn.       | Bangladesh, Colombia, India                    | Fruit, inflorescence, leaf, root,| I, E    | [17, 20, 22, 23, 25, 28, 30, 32, 35, 38–41] |
| Achyranthes porphyristachya)‡  |                                                | seed, stem, whole plant           |         |              |
| Aerva lanata                   | India, Sri Lanka                               | Rhizome                           | I       | [18, 20]     |
| Aerva sanguinolenta            | Bangladesh                                     | Leaf                              | ND      | [30]         |
| Alternanthera albotomentosa    | Colombia                                       | Leaf                              | E       | [34]         |
| Alternanthera brasiliiana      | 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, Sri Lanka         | Fruit, root, whole plant          | E       | [17, 32, 41] |
| Cyathula tomentosa             | India                                          | Leaf                              | ND      | [19]         |
| Dysphania ambrosioides (syn.    | Colombia                                       | Whole plant                       | E       | [34]         |
| Chenopodium ambrosioides       |                                                |                                   |         |              |
| Aerva sanguinolenta            | Bangladesh                                     | Leaf                              | ND      | [30]         |
| Alternanthera albotomentosa    | Colombia                                       | Leaf                              | E       | [34]         |
| Alternanthera brasiliiana      | 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, Sri Lanka         | Fruit, root, whole plant          | E       | [17, 32, 41] |
| Cyathula tomentosa             | India                                          | Leaf                              | ND      | [19]         |
| Dysphania ambrosioides (syn.    | Colombia                                       | Whole plant                       | E       | [34]         |
| Chenopodium ambrosioides       |                                                |                                   |         |              |
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 | Bulb, inflorescence, leaf | I, E | [18, 22, 23, 37, 44] |
| Ammochoris tineana        | 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 araliaecea  | 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, stem | 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]          |
| 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 viminaline (syn. Sarcoptemma viminalis) | India | Whole plant              | E   | [38] |
| Drecia volubilis (syn. Wattakaka volubilis) | India, Sri Lanka | Root                     | I, E | [18, 23] |
| Echidnopsis damannianiana   | 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 pucticulosa     | 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 paeonifolius | 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] |
| 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 croatti*       | 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 hedracingae  | 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 poepiggii      | Peru               | Stem             | E     | [57]         |
| Araliaceae                |                    |                  |       |              |
| Osmoxylon micranthum      | Papua New Guinea   | Latex            | E     | [46]         |
| Areca catechu             | Sri Lanka          | ND               | E     | [18]         |
| Carya toona             | 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             | E     | [16, 26]     |
| Asparagaceae              |                    |                  |       |              |
| Asparagus racemosus       | Bangladesh, Sri Lanka | Leaf, root        | E     | [18, 30, 32] |
| Drimia indica (syn. Urginea indica) | India               | Bulb             | E     | [25]         |
| 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                       | Pakistan           | Leaf       | ND  | [17]          |
| Asplenium dalhousiae (syn. Ceterach dalhousiae) | Pakistan           | Leaf       | ND  | [17]          |
| Asteraceae                         | Pakistan           | Inflorescence, leaf | E   | [17]          |
| Achillea millefolium               | India              | Whole plant | I   | [20]          |
| Acnema paniculata (syn. Spilanthes paniculata) | Sri Lanka           | ND         | I   | [18]          |
| Adenostemma foosbergii             | Ecuador            | Leaf       | I   | [61]          |
| Adenostemma lavenia                | Colombia           | Whole plant | E   | [35]          |
| Agaratum coryzoides                | Colombia, India, Bangladesh | Flower, leaf, root | E   | [19, 24, 32, 34] |
| Agaratum 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               | 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]          |
| Cladium 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]          |
| Gymnura hispida                   | Sri Lanka          | ND         | I   | [18]          |
| Helianthus annuus                  | India              | Seed       | E   | [20]          |
| Inula heleneium                    | Serbia             | Root       | E   | [58]          |
| Laggera alata                      | Sri Lanka          | ND         | E   | [18]          |
| Linzia glabra (syn. Vernonia glabra) | Kenya              | Leaf       | E   | [31]          |
| Microglossa pyriformia             | 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] |
| Neurolea 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]         |
| Sphagnetica 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]         |
| Dolicichandra unguis-catt (syn. Macfadyena unguis-catt) | Colombia     | Whole plant                       | E   | [35]         |
| Handroanthus barbatus (syn. Tabebuia barbata) | Brazil                | Leaf                              | I   | [33]         |
| Mansoa alliacea                         | Peru                       | Bark, root                        | I   | [57]         |
| Oroxyllum indicum                       | Bangladesh, Sri Lanka      | Bark                              | E   | [18, 32]     |
| Stereocpermum chelonoides               | Sri Lanka                  | ND                                | I   | [18]         |
| Stereocpermum 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]         |
| 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] |
| 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 rubicola       | 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]          |
| Clusiaceae               |                      |            |     |               |
| 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. Calycoperis 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]          |
| Cascula 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]          |
| 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 lasiis                    | 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 lacinata (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                      | Tubber              | I   | [38]         |
| Cucumis melo                     | Sri Lanka                  | ND                  | I   | [18]         |
| Cucurbita pepo                   | Spain                      | Flower              | E   | [37]         |
| Diploccylos palmatus             | India, Sri Lanka           | Leaf, tuber         | I, E| [18, 23, 66] |
| Fevilea cordifolia               | Colombia, Nicaragua        | Seed, whole plant   | I, E| [27, 35]     |
| Lagenaria sicervaria*            | Sri Lanka                  | ND                  | E   | [18]         |
| Luffa acutangula                 | India, Sri Lanka           | Fruit, whole plant  | I, E| [18, 19, 38] |
| Momordica balsamina              | India                      | ND                  | ND  | [40]         |
| Moonordica 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]         |
| Scydium 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 moncepha) | India                  | ND                  | ND  | [40]         |
| Dilieniaceae                     |                            |                     |     |              |
| Tetraera sarmentosa              | Sri Lanka                  | ND                  | I, E| [18]         |
| Dioscoreaceae                    |                            |                     |     |              |
| Dioscorea oppositifolia          | Sri Lanka                  | ND                  | I   | [18]         |
| Dioscorea pentaphylla            | India                      | Tuber               | I   | [38, 55]     |
| 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] |
| *Eucaea 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 nerifolia (syn. Euphorbia ligularia)* | India, Sri Lanka | Latex, leaf, stem | I, E | [18, 19, 22, 38] |
| *Euphorbia thyrmifolia* | 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 gossypifolia* | 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 | 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 lebbbeck*              | Bangladesh, Pakistan, Sri Lanka    | Bark, flower, fruit, leaf | I, E | [16–18, 23, 32, 40] |
| Albizia prodera                | 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]         |
| Bueta monosperma*              | India                              | Bark, leaf, resin, seed | 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]         |
| Cilantro ternate               | 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]         |
| Dalberga melanoxylon           | India                              | Bark       | I    | [20]         |
| Deguelia amazonica (syn. Derris amazonica) | Brazil      | Root       | ND   | [50]         |
| 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]     |
| *Diptyery odorata*       | Brazil                      | Seed                              | I    | [33, 50]     |
| *Entada lepistachys*     | Kenya                       | Latex                             | E    | [31]         |
| *Entada rhedefi* (syn. Entada pursaethi) | 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 septum*      | 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 cincinella*  | Kenya                       | Leaf                              | E    | [31]         |
| *Indigofera suffrutoso*  | 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 darsiensis*       | 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 sophora* (syn. Cassia sophora) | 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] |
| Plant name | Countries | Parts used | Use | Reference(s) |
|------------|-----------|------------|-----|--------------|
| Sesbania grandiflora | Sri Lanka | ND | I, E | [18] |
| Tatedahagitriquetrum (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**

| Plant name | Countries | Parts used | Use | Reference(s) |
|------------|-----------|------------|-----|--------------|
| 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**

| Plant name | Countries | Parts used | Use | Reference(s) |
|------------|-----------|------------|-----|--------------|
| Columnea pulcherrima* | Colombia | Whole plant | I, E | [35] |
| Columnea sanguinea (syn. Besleria sanguinea)* | Colombia | Whole plant | I, E | [35] |
| Episcia dianthiiflora* | Colombia | Whole plant | I, E | [35] |
| Gleicheniaceae | | | | |
| Gleichenella pectinata | Colombia | Whole plant | I | [34] |

**Haemodoraceae**

| Plant name | Countries | Parts used | Use | Reference(s) |
|------------|-----------|------------|-----|--------------|
| Xiphidium caeruleum* | Colombia, Nicaragua, Peru | Leaf, stem, whole plant | I, E | [27, 35, 44, 57] |

**Heliconiaceae**

| Plant name | Countries | Parts used | Use | Reference(s) |
|------------|-----------|------------|-----|--------------|
| Heliconia curtispatha* | Colombia | Rhizome | E | [35] |

**Hydroaceae**

| Plant name | Countries | Parts used | Use | Reference(s) |
|------------|-----------|------------|-----|--------------|
| Hydrolea zeylanica | Sri Lanka | ND | I | [18] |

**Hymenophyllaceae**

| Plant name | Countries | Parts used | Use | Reference(s) |
|------------|-----------|------------|-----|--------------|
| Trichomanes elegans* | Colombia | Whole plant | E | [35] |

**Hyoxidaceae**

| Plant name | Countries | Parts used | Use | Reference(s) |
|------------|-----------|------------|-----|--------------|
| Curculigo orchioides | Bangladesh, India | Bulb, leaf, rhizome | I | [32, 73] |

**Iridaceae**

| Plant name | Countries | Parts used | Use | Reference(s) |
|------------|-----------|------------|-----|--------------|
| Iris kemaonensis | India | Rhizome | ND | [66] |
| Sisyrinchium micranthum | Colombia | Whole plant | E | [34] |

**Lamiaceae**

| Plant name | Countries | Parts used | Use | Reference(s) |
|------------|-----------|------------|-----|--------------|
| 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] |
| 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 chamaedryss | 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 | 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 | Sri Lanka | ND | E   | [18] |
| Couroupita guianensis | Bangladesh | Bark, leaf | ND  | [30] |
| Linderniaceae | Colombia | Whole plant | E   | [35] |

* Indicates plants with antihypertensive properties.
| 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 cassyoides*  | Nicaragua               | Leaf, whole plant   | I, E  | [27]         |
| *Struthanthus orbicularis* | Colombia                | Branch, leaf        | E     | [35]         |
| Loranthaceae               |                         |                     |       |              |
| *Huperzia pulcherrima*     | Nicaragua               | ND                  | E     | [18]         |
| Loranthaceae               |                         |                     |       |              |
| *Lygodium heterodoxum*     | Colombia, Mexico,       | Leaf                | I, E  | [27]         |
| Lygodialiceae              | 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              |                         |                     |       |              |
| *Bromweina 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 damina*            | 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 rosthelatus* (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             |                            |            |     |               |
| Obeckia 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       | I   | [63]          |
| Melia azedarach             | India, Sri Lanka           | Bark, leaf | I, E | [18, 41]      |
| Munronia pinnata            | Sri Lanka                  | ND         | I, E| [18]          |
| Menispermaeae               |                            |            |     |               |
| 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 pelitula             | Sri Lanka                  | ND         | I   | [18]          |
| Odontocaryta 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 nympheifolia*         | Colombia                   | Branch, leaf, stem | I, E| [35]          |
Table I: 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]         |
| *Strybus 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 × paradisiaca*        | 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 zeilanicum*       | 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 jacobapita*          | 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                  |                            |                  |     |              |
| *Opili 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** | | | | |
| *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 arborescens* | 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 chuuya* | 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 longifilum* | 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 multiervalvatum* | Colombia | Branch, leaf, stem | I, E | [35] |
| 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*<sup>2</sup> | Colombia, Nicaragua       | Branch, leaf, stem, whole plant | I, E | [27, 35] |
| *Piper pulchrum*<sup>+</sup> | Colombia                   | Branch, leaf, stem          | I, E | [35] |
| *Piper reticulatum*<sup>4</sup> | Colombia                   | Branch, leaf, stem          | I, E | [35] |
| *Piper tricuspe*<sup>6</sup> | Colombia                   | Branch, leaf, stem          | E   | [35] |
| *Piper umbellatum*          | Sri Lanka                  | ND                          | I, E | [18] |
| **Pittosporaceae**          |                            |                             |     |              |
| *Pittosporum neelgherrense* | India                      | Bark                        | I, E | [16] |
| *Pittosporum tetraspernum*  | 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*<sup>3</sup> | 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 crotalariaioides* | India                      | Leaf, root                  | ND   | [19] |
| *Polygala paniculata*       | Brazil                     | Root                        | E    | [47] |
| *Polygala spectabilis*      | Brazil                     | Root                        | I, E | [47] |
| **Polygononaceae**          |                            |                             |     |              |
| *Persicaria barbata* (syn. Polygonum barbatum) | India                     | Leaf                        | I, E | [38] |
| *Persicaria chinensis* (syn. Polygonum chinense) | Bangladesh | Leaf                        | E    | [32] |
| 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] |
| *Pyrrhoa 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 densatum*                             | 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]          |
| *Cerisoides 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]          |
| *Gonzalaguinia 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] |
| 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]         |
| Ophiopogon mungos*            | India         | Root            | I   | [16, 20]     |
| Paederia foetida              | Sri Lanka     | ND              | I, E | [18]         |
| Palicourea crocoides          | 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            | ND  | [19]         |
| Spermatoce remota (syn. Borreria assurgens) | Nicaragua | Leaf, root    | I, E | [27]         |
| Tamilnadia uliginosa           | Sri Lanka     | ND              | I   | [18]         |
| Wendlandia exserta            | India         | Root            | I   | [49]         |
| Rutaceae                      | India         | Root            | I   | [49]         |
| Acronychia pedunculata         | Sri Lanka     | ND              | E   | [18]         |
| Aegle marmelos                | Bangladesh, India, Sri Lanka | Bark, whole plant | I, E | [18, 20, 30, 32, 41] |
| Atalanta ceylanica            | Sri Lanka     | ND              | I, E | [18]         |
| Citrus aurantifolia           | 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]         |
| 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]      |
| Placourtia 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]          |
| 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]         |
| *Leeca 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 purpurea*          | 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 alpina*          | Colombia      | Rhizome, stem | I, E | [34, 35] |
| *Renealmia thyrsoida*       | 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).
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 effectiveness 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 gossypifolia (Euphorbiaceae), a medicinal plant studied very much by our research group, has 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],

![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).](image-url)
| Plant name                  | Part used | Snake venom     | Inhibited activities | Reference(s) |
|-----------------------------|-----------|-----------------|----------------------|---------------|
| Acanthaceae                 |           |                 |                      |               |
| Andrographis stenophylla    | Leaf      | N. naja         | —                    | [83]          |
| Amaranthaceae               |           |                 |                      |               |
| Pupalia lappa              | Herbal    | N. nigrigollis  | SVH                  | [82]          |
| Amaryllidaceae             |           |                 |                      |               |
| Allium cepa                | Bulb      | N. n. karachiensis | PLA₂ | —     | [84]          |
| Allium sativum             | Bulb      | N. n. karachiensis | PLA₂ | —     | [84]          |
| Anacardiaceae              |           |                 |                      |               |
| Lannea acida               | Cortex    | N. nigrigollis  | SVH                  | [82]          |
| Pistacia chinensis subsp. integerrima | Gall | N. n. karachiensis | PLA₂ | —     | [84]          |
| Sclerocarya birrea         | Cortex, radix | N. nigrigollis | SVH                  | [82]          |
| Spondias mombin            | Cortex    | N. nigrigollis  | SVH                  | [82]          |
| Annona senegalensis        | Cortex    | N. nigrigollis  | SVH                  | [82]          |
| Apioideae                  |           |                 |                      |               |
| Cuminum cyminum            | Seed      | N. n. karachiensis | PLA₂ | —     | [84]          |
| Apocynaceae                |           |                 |                      |               |
| Acokanthera oppositifolia  | Radix     | N. nigrigollis  | SVH                  | [82]          |
| Calotropis procera         | Flower, latex | N. n. karachiensis | PLA₂ | —     | [84]          |
| Strophanthus sermentosus   | Folium    | N. nigrigollis  | SVH                  | [82]          |
| Strophanthus speciosus     | Radix     | N. nigrigollis  | SVH                  | [82]          |
| Tylophora indica           | Leaf, root | N. naja         | PLA₂ Hemorrhage      | [85]          |
| Araceae                    |           |                 |                      |               |
| Colocasia esculenta        | Tuber     | N. nigrigollis  | SVH                  | [82]          |
| Araliaceae                 |           |                 |                      |               |
| Polyscias fulva            | Cortex    | N. nigrigollis  | SVH                  | [82]          |
| Aristolochiaceae           |           |                 |                      |               |
| Aristolochia bracteolata   | Leaf, root | N. naja         | PLA₂ Hemorrhage      | [85]          |
| Asteraceae                 |           |                 |                      |               |
| Callilepis laurcera        | Radix     | N. nigrigollis  | SVH                  | [82]          |
| Bignoniaceae               |           |                 |                      |               |
| Kigelia africana           | Cortex, folium | N. nigrigollis | SVH                  | [82]          |
| Tecoma stans (syn. Stenolobium stans) | Root | N. n. karachiensis | PLA₂ | —     | [84]          |
| Bixaceae                   |           |                 |                      |               |
| Cochlospermum tinctorium   | Radix     | N. nigrigollis  | SVH                  | [82]          |
| Boraginaceae               |           |                 |                      |               |
| Cordia macleodii           | Bark      | N. naja         | —                    | Edema, hemorrhage, necrosis | [86] |
| Trichodesma indicum        | Whole plant | N. n. karachiensis | PLA₂ | —     | [84]          |
| Capparaceae                |           |                 |                      |               |
| Capparis tomentosa         | Radix     | N. nigrigollis  | SVH                  | [82]          |
| Colchicaceae               |           |                 |                      |               |
| Gloriosa superba           | Radix     | N. nigrigollis  | SVH                  | [82]          |
| Combretaceae               |           |                 |                      |               |
| Combretum molle            | Folium    | N. nigrigollis  | SVH                  | [82]          |
| Guiera senegalensis        | Radix     | N. nigrigollis  | SVH                  | [82]          |
| Terminalia arjuna          | Bark      | N. n. karachiensis | PLA₂ | —     | [84]          |
| Plant family          | Plant name                     | Part used     | Snake venom     | Inhibited activities | Reference(s) |
|-----------------------|--------------------------------|---------------|-----------------|----------------------|---------------|
| Convolvulaceae        | Ipomoea rubens                 | Seed          | N. n. nigricollis | SVH                  | [82]          |
| Cucurbitaceae         | Citrullus colocynthis$^a$      | Fruit         | N. n. karachiensis | PLA$_2$            | [84]          |
|                       | Luffa cylindrica (syn. Luffa aegyptiaca) | Leaf         | N. nigricollis | Proteolytic          | [87]          |
|                       | Momordica charantia$^a$        | Fruit         | N. n. karachiensis | PLA$_2$            | [84]          |
| Ebenaceae             | Diospyros mespiliformis        | Cortex        | N. nigricollis | SVH                  | [82]          |
| Euphorbiaceae         | Alchornea laxiflora            | Cortex        | N. nigricollis | SVH                  | [82]          |
|                       | Cluita cordata                 | Radix         | N. nigricollis | SVH                  | [82]          |
|                       | Euphorbia hirta$^a$            | Whole plant   | N. naja         | PLA$_2$, proteolytic, SVH, Edema$^*$ | [88]          |
|                       | Jatropha curcas$^a$            | Leaf, root, stem | N. naja      | PLA$_2$            | [89]          |
|                       | Jatropha gossypifolia$^a$      | Leaf, root, stem | N. naja      | PLA$_2$            | [89]          |
|                       | Manihot foetida (syn. Jatropha foetida) | Leaf, stem | N. naja         | PLA$_2$            | [89]          |
| Fabaceae              | Abrus precatorius$^a$          | Radix         | N. nigricollis | SVH                  | [82]          |
|                       | Argyrolobium stipulacecum      | Radix         | N. nigricollis | SVH                  | [82]          |
|                       | Bauhinia thomningii            | Cortex, radix | N. nigricollis | SVH                  | [82]          |
|                       | Bauhinia variegata$^a$         | Root          | N. n. karachiensis | PLA$_2$           | [84]          |
|                       | Bobgunniad 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$^a$              | 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$^a$          | Folium, radix | N. nigricollis | SVH                  | [82]          |
| Gentianaceae          | Enicotema axillare (syn. Enicotema hyssopifolium)$^a$ | Whole plant | N. n. karachiensis | PLA$_2$           | [84]          |
| Hypericaceae          | Psorospermum corymbiferum      | Cortex, radix | N. nigricollis | SVH                  | [82]          |
| Lamiaceae             | Leucas aspera$^a$              | Leaf, root, whole plant | N. naja | PLA$_2$, proteolytic, SVH | [85, 94]        |
|                       | Leucas cephalotes (syn. Leucas capitata)$^a$ | Whole plant | N. n. karachiensis | PLA$_2$           | [84]          |
|                       | Leucas marticenensis           | ND            | N. nigricollis | SVH                  | [82]          |
|                       | Ocimum teneiflorum (syn. Ocimum sanctum)$^a$ | 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) |
|-----------------------------|-----------------|-------------|----------------------|---------------|
| *Teucrium kraussii*         | Aerial parts, cortex | *N. nigricollis* | SVH                  | —             | [82] |
| *Volkmeria 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* | PLA₂                 | —             | [95] |
| Malvaceae                   |                 |             |                      |               |
| *Althaea officinalis*       | Root            | *N. n. karachiensis* | PLA₂               | —             | [84] |
| *Dombeya quinquesta*        | 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* | PLA₂               | —             | [84] |
| *Pinus roxburghii*       | Oleoresin       | *N. n. karachiensis* | PLA₂               | —             | [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 spin-a-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* | PLA₂               | —             | [84] |
| *Zanthoxylum capense*       | Radix           | *N. nigricollis* | SVH                  | —             | [82] |
| Sapindaceae                 |                 |             |                      |               |
| *Paulinia pinnata*          | Folium          | *N. nigricollis* | SVH                  | —             | [82] |
| *Sapindus mukorossi*        | Fruit           | *N. n. karachiensis* | PLA₂               | —             | [84] |
Table 2: Continued.

| Plant name         | Part used | Snake venom | Inhibited activities | Reference(s) |
|--------------------|-----------|-------------|----------------------|---------------|
| Solanaceae         |           |             |                      |               |
| Nicotiana rustica  | Leaf      | N. nigrinellis | Proteolytic          | —             | [87] |
| Schwenckia americana | Folium   | N. nigrinellis | SVH                  | —             | [82] |
| Thymelaeaceae      |           |             |                      |               |
| Gnidia anthyloides | Radix     | N. nigrinellis | SVH                  | —             | [82] |
| Gnidia kraussiana  | Radix     | N. nigrinellis | SVH                  | —             | [82] |
| Gnidia splendens   | Radix     | N. nigrinellis | SVH                  | —             | [82] |
| Verbenaceae        |           |             |                      |               |
| Lantana trifolia   | Cortex    | N. nigrinellis | SVH                  | —             | [82] |
| Vitaceae           |           |             |                      |               |
| Cissus populnea    | Stem      | N. nigrinellis | 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 antiphidic 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 gossypifolia (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 PLA2 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) |
|-------------------------------------|-------------------|-------------|----------------------|---------------|
| **Acanthaceae**                     |                   |             |                      |               |
| Justicia pectoralis               | Leaf              | B. jararaca | —                    | [33]          |
| **Amaranthaceae**                  |                   |             |                      |               |
| Blutaparon portulacoides           | Aerial parts      | B. jararacussu | —                  | [109]         |
| **Anacardiaceae**                  |                   |             |                      |               |
| Anacardium excelsum                | Leaf, twig        | B. asper    | PLA₂                | [111]         |
| **Annonaceae**                     |                   |             |                      |               |
| Ephedrantus columbianus            | Leaf, twig        | B. asper    | PLA₂                | [111]         |
| **Apocynaceae**                    |                   |             |                      |               |
| Allamanda cathartica              | Branch, leaf, stem| B. atrox   | —                    | [124]         |
| Fernaldia pandurata (syn. Mandevilla velutina) | Leaf, stem, subterranean system | B. alternatus, B. jararacussu, B. moojeni, B. pirajai | PLA₂ | Edema⁺⁺⁺, hemorrhage⁺⁺⁺, myotoxicity⁺⁺⁺ | [125] |
| Tabernaemontana catharinensis      | Root bark         | B. jararacussu | Myotoxicity        | Myotoxicity** | [126] |
| **Araeaceae**                      |                   |             |                      |               |
| Dracantium croattii               | Rhizome           | B. asper    | —                    | [127]         |
| Philodendron megalophyllum         | Liana, vine       | B. atrox, B. jararaca | PLA₂ | Edema⁺⁺⁺, hemorrhage⁺⁺⁺ | [33, 128] |
| Philodendron tripartitum           | Branch, leaf      | B. atrox    | —                    | [124]         |
| **Asteraceae**                     |                   |             |                      |               |
| Chaptalian nutans                 | Leaf              | B. asper    | —                    | [129]         |
| Eclipta prostrata (syn. Eclipta alba) | Aerial parts  | B. jararaca, B. jararacussu | Myotoxicity | Myotoxicity | [130] |
| **Aseae**                          |                   |             |                      |               |
| Mikania glomerata                 | Leaf              | B. jararaca | —                    | [131, 132]    |
| Neuoalaena lobata                 | Branch, leaf, stem| B. atrox   | —                    | [124]         |
| Pseudelephantopus spicatus         | Whole plant       | B. atrox    | —                    | [124]         |
| **Bignoniaceae**                  |                   |             |                      |               |
| Fridericia chica (syn. Arrabidaea chica) | Leaf      | B. atrox    | —                    | [133]         |
| *Tabeuia aurea*                    | Stem bark         | B. neuwiedi | H₂O₂ production by peritoneal macrophages | Edema, hemorrhage⁺⁺⁺, myonecrosis⁺⁺⁺, peritonitis | [110] |
| *Tabeuia rosea*                    | Stem bark         | B. asper, B. atrox | PLA₂ | Edema⁺⁺⁺, Hemorrhage⁺⁺⁺ | [124, 127, 134] |
| **Bixaceae**                       |                   |             |                      |               |
| Bixa orellana                      | Branch, leaf      | B. asper, B. atrox | PLA₂ | Edema⁺⁺⁺, hemorrhage⁺⁺⁺ | [124, 127, 134] |
| *Bixa orellana*                    |                  |             |                      |               |
| Cordia verbenacea                  | Leaf              | B. jararacussu | —                  | [135]         |
| Clusiaaceae                        |                   |             |                      |               |
| Clusia fluminensis                 | Fruit             | B. jararaca | Proteolytic         | Hemorrhage**  | [136] |
| **Combretaceae**                   |                   |             |                      |               |
| Combretum leprosum                 | Root              | B. jararaca, B. jararacussu | Collagenase, myotoxicity, PLA₂, proteolytic | Edema, hemorrhage⁺⁺⁺, myotoxicity⁺⁺⁺ | [99] |
Table 3: Continued.

| Plant name | Part used | Snake venom | Inhibited activities | In vitro | In vivo | Reference(s) |
|------------|-----------|-------------|----------------------|----------|---------|--------------|
| **Connaraceae** | | | | | | |
| *Connarus favosus* | Bark | *B. atrox, B. jararaca* | PLA₂, proteolytic | Edema*, hemorrhage*** | [33, 115, 128] |
| **Costaceae** | | | | | | |
| *Costus lasius* | ND | *B. atrox* | PLA₂ | — | [134] |
| *Costus spicatus* | Leaf | *B. atrox* | — | Edema*, hyperalgesia* | [137] |
| **Crassulaceae** | | | | | | |
| *Bryophyllum pinnatum* (syn. *Kalanchoe pinnata*) | Leaf | *B. jararaca* | PLA₂ | Edema, hemorrhage | [138] |
| *Kalanchoe laciniata* (syn. *Kalanchoe brasiliensis*) | Leaf | *B. jararaca* | PLA₂ | Edema, hemorrhage*** | [33, 138] |
| **Dicranaceae** | | | | | | |
| *Dicranum frigidum* | Whole plant | *B. asper* | PLA₂ | — | [111] |
| **Dilleniaceae** | | | | | | |
| *Davilla elliptica* | Leaf | *B. jararaca* | — | Hemorrhage* | [139] |
| **Euphorbiaceae** | | | | | | |
| *Croton urucurana* | Stem bark | *B. jararaca* | — | Hemorrhage* | [140] |
| *Hevea nitida* | Leaf, twig | *B. asper* | PLA₂ | — | [111] |
| *Jatropha gossypifolia* | Leaf | *B. erythromelas, B. jararaca* | PLA₂, proteolytic, SVH | Edema, hemorrhage, myotoxicity | [96, 119] |
| *Jatropha mollissima* | Leaf | *B. erythromelas, B. jararaca* | — | | [141] |
| **Fabaceae** | | | | | | |
| *Abarema cochliacarpos* | Stem bark | *B. leucurus* | — | | [101] |
| *Brownia ariza* | Bark, leaf | *B. asper* | PLA₂, proteolytic | — | [142] |
| *Brownia rosa-de-monte* | Leaf, stem bark | *B. asper, B. atrox* | PLA₂, proteolytic | Edema***, hemorrhage*** | [124, 127, 134, 143] |
| *Cassia fistula* | Seed | *B. jararaca* | — | Hemorrhage* | [33] |
| *Dipteryx alata* | Bark | *B. jararacussu, B. alternatus, B. asper, B. atrox, B. jararaca, B. mojeni, B. neuwiedi, B. pirajai* | Myotoxicity | — | [144] |
| *Pentaclethra macroloba* | Bark | *B. jararacussu, B. mojeni, B. neuwiedi, B. pirajai* | PLA₂ | Edema*, hemorrhage*, myotoxicity* | [145] |
| *Plathymenia reticulata* | Bark | *B. atrox, B. jararaca* | PLA₂ | Edema*, hemorrhage* | [33, 128] |
| *Schizolobium parahyba* | Leaf | *B. alternatus, B. mojeni, B. pauloensis* | PLA₂ | Hemorrhage*, myotoxicity*** | [146, 147] |
| *Senna dariensis* | Whole plant | *B. atrox* | PLA₂ | Hemorrhage* | [124, 134] |
| **Heliconiaceae** | Rhizome | *B. asper, B. atrox* | PLA₂, proteolytic | Edema***, hemorrhage*** | [124, 127, 134, 148] |
| *Heliconia curtispatha* | Rhizome | *B. asper* | PLA₂, proteolytic | — | [148] |
| *Heliconia latispata* | Rhizome | *B. asper* | PLA₂, proteolytic | — | [148] |
| *Heliconia wagneriana* | Rhizome | *B. asper* | PLA₂, proteolytic | — | [148] |
Table 3: Continued.

| Plant name                      | Part used          | Snake venom       | Inhibited activities | Reference(s)  |
|--------------------------------|--------------------|-------------------|----------------------|---------------|
| Hymenophyllaceae               |                    |                   |                      |               |
| Trichomanes elegans<sup>2</sup>| Whole plant        | B. asper, B. atrox| PLA<sub>2</sub>       | Edema<sup>***</sup>, hemorrhage<sup>*</sup> [124, 127, 134] |
| Hypericaceae                   |                    |                   |                      |               |
| Hypericum brasiliense          | Whole plant        | B. jararaca       | Proteolytic          | Edema<sup>·</sup>, hemorrhage<sup>·</sup> [149] |
| Icacinaceae                    |                    |                   |                      |               |
| Casimirella ampla (syn.        | Root               | B. atrox, B.      | Myotoxicity, PLA2,   | Edema<sup>***</sup>, hemorrhage<sup>·</sup>, myotoxicity<sup>·</sup> [102] |
| Humirianthera ampla)           |                    | jararacussu       | proteolytic          |               |
| Lamioaceae                     |                    |                   |                      |               |
| Marsypianthes chamædræs<sup>5</sup> | Inflorescence,    | B. atrox          | PLA<sub>2</sub>       | Peritonitis [108] |
| Peltodon radicans              | Flower, leaf, stem | B. atrox          | —                    | Edema         [150] |
| Lauraceae                      |                    |                   |                      |               |
| Aniba parviflora (syn. Aniba  | Bark, leaf         | B. atrox, B.      | PLA<sub>2</sub>       | Edema<sup>·</sup>, hemorrhage<sup>·</sup> [33, 128] |
| fragrans)<sup>2</sup>          |                    | jararacussu       | proteolytic          |               |
| Loasaceae                      |                    |                   |                      |               |
| Nasa speciosa (syn. Loasa      | Leaf               | B. asper          | —                    | Edema         [129] |
| speciosa)                      |                    |                   |                      |               |
| Loganiaceae                    |                    |                   |                      |               |
| Strychnos pseudoquina          | Leaf               | B. jararaca       | —                    | Hemorrhage<sup>·</sup> [139] |
| Strychnos xinguensis<sup>5</sup>| ND                 | B. atrox          | PLA<sub>2</sub>       | —             [134] |
| Loranthaceae                   |                    |                   |                      |               |
| Struthanthus orbicularis<sup>5</sup>| Branch, leaf      | B. asper, B.      | PLA<sub>2</sub>       | Edema<sup>**</sup>, hemorrhage<sup>·</sup> [124, 127, 134] |
| Magnoliaceae                   |                    |                   |                      |               |
| Magnolia espinalii (syn.       | Leaf, twig         | B. asper          | PLA<sub>2</sub>       | —             [111] |
| Talauma espinalii)             |                    |                   |                      |               |
| Magnolia guatapensis (syn.     | Leaf, twig         | B. asper          | PLA<sub>2</sub>       | —             [111] |
| Dugandiodendron guatapense)    |                    |                   |                      |               |
| Magnolia hernandezii (syn.     | Leaf, twig         | B. asper          | PLA<sub>2</sub>       | —             [111] |
| Talauma hernandezii)           |                    |                   |                      |               |
| Magnolia yarumalensis (syn.    | Leaf, twig         | B. asper          | PLA<sub>2</sub>       | —             [111] |
| Dugandiodendron yarumalense)   |                    |                   |                      |               |
| Malpighiaceae                  |                    |                   |                      |               |
| Byrsonima crassa               | Leaf               | B. jararaca       | —                    | Hemorrhage<sup>·</sup> [111] |
| Malvaceae                      |                    |                   |                      |               |
| Pachira glabra (syn. Bombacopsis glabra) | Root bark | B. pauloensis     | —                    | Hemorrhage     [151] |
| Melastomataceae                |                    |                   |                      |               |
| Bellucia dichotoma<sup>5</sup> | Bark               | B. atrox, B.      | PLA<sub>2</sub>       | Edema<sup>***</sup>, hemorrhage<sup>·</sup> [33, 98, 128, 152] |
| Mouriri pusa                   | Leaf               | B. jararaca       | —                    | Hemorrhage<sup>·</sup> [139] |
| Meliaceae                      |                    |                   |                      |               |
| Carapa guianensis              | Leaf, twig         | B. asper          | PLA<sub>2</sub>       | —             [111] |
| Cedrela odorata                 | Leaf, twig         | B. asper          | PLA<sub>2</sub>       | —             [111] |
| Swietenia humilis              | Leaf, twig         | B. asper          | PLA<sub>2</sub>       | —             [111] |
| Swietenia macrophylla          | Leaf, twig         | B. asper          | PLA<sub>2</sub>       | —             [111] |
| Swietenia mahagoni             | Leaf, twig         | B. asper          | PLA<sub>2</sub>       | —             [111] |
| Plant name               | Part used            | Snake venom | Inhibited activities | Reference(s) |
|-------------------------|----------------------|-------------|----------------------|--------------|
| Menispermaceae          |                      |             |                      |              |
| *Cissampelos pareira*   | Leaf                 | *B. asper*  | —                    | [153]        |
| Moraceae                |                      |             |                      |              |
| *Brosimum guianense*    | Leaf                 | *B. atrox*  | —                    | [154]        |
| *Castilla elastica*     | Branch, leaf, stem   | *B. atrox*  | —                    | [124]        |
| *Ficus nymphaefolia*    | Branch, leaf, stem   | *B. asper*  | —                    | [124, 127]   |
| Musaceae                |                      |             |                      |              |
| *Musa × paradisiaca*    | Exudate              | *B. jararacussu* | PLA2, proteolytic     | [155]        |
| Myrtaceae               |                      |             |                      |              |
| *Myrcia guianensis*     | Leaf                 | *B. jararaca* | PLA2                 | [156]        |
| Passifloraceae          |                      |             |                      |              |
| *Passiflora quadrangularis* | Branch, leaf   | *B. atrox*  | —                    | [124]        |
| Piperaeae               |                      |             |                      |              |
| *Piper arboreaum*       | Branch, leaf         | *B. atrox*  | PLA2                 | [124, 134]   |
| *Piper pulchrum*        | Leaf, branch, stem   | *B. atrox*  | —                    | [124]        |
| Polypodiaceae           |                      |             |                      |              |
| *Pleoptilus percuta*    | Branch, leaf, stem, whole plant | *B. asper, B. atrox* | PLA2, proteolytic | [124, 127, 134] |
| Rubiaceae               |                      |             |                      |              |
| *Gonzalagunia panamensis* | Branch, leaf, stem | *B. asper, B. atrox* | PLA2         | [124, 127, 134] |
| *Randia aculeata*       | Fruit                | *B. asper*  | —                    | [78]         |
| *Uncaria tomentosa*     | Root                 | *B. asper*  | —                    | [129]        |
| Rutaceae                |                      |             |                      |              |
| *Citrus limon*          | Ripe fruit           | *B. asper, B. atrox* | —                | [124, 127]   |
| *Murraya paniculata*    | Leaf, twig           | *B. asper*  | —                    | [111]        |
| Salicaceae              |                      |             |                      |              |
| *Casearia grandiflora*  | Leaf                 | *B. moojeni, B. neuwiedi* | PLA2 | Myotoxicity*       | [157]        |
| *Casearia sylvestris*   | Leaf                 | *B. asper, B. jararacussu, B. moojeni, B. neuwiedi, B. pirajai* | PLA2 | Myonecrosis, neuromuscular blockade | Edema", hemorrhage", myotoxicity" | [158–160] |
| Sapindaceae             |                      |             |                      |              |
| *Billia hippocastanum*  | Leaf, twig           | *B. asper*  | PLA2                 | [111]        |
| *Cupania americana*     | Leaf, twig           | *B. asper*  | PLA2                 | [111]        |
| *Sapindus saponaria*    | *In vitro* cultivated callus, leaf, twig | *B. asper, B. jararacussu, B. moojeni* | PLA2 | Hemorrhage*       | [111, 161]   |
| *Serjania erecta*       | Aerial parts         | *B. jararacussu* | PLA2 | Edema", hemorrhage", myotoxicity" | [162]         |
cardiototoxicity, 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. nigrigollis* SVHs, PLA₂, 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 nigrigollis* and *Bitis arietans* employing in vitro and ex vivo models [123]. However, although plant extracts have shown 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 significant 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 3: Continued.

| Plant name          | Part used     | Snake venom | Inhibited activities | Reference(s) |
|---------------------|---------------|-------------|----------------------|--------------|
| **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 alpina* ‡ | Leaf, rhizome | *B. asper, B. atrox* | PLA₂, proteolytic Edema**, hemorrhage | [107, 127, 134, 165, 166] |

ND = information not described in the work; PLA₂ = snake venom phospholipase A₂; H₂O₂ = 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).
| Plant name                      | Part used | Snake venom | Inhibited activities | In vitro | In vivo | Reference(s) |
|--------------------------------|-----------|-------------|----------------------|----------|---------|--------------|
| **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]         |
| **Ebenaceae**                  |           |             |                      |          |         |              |
| *Diospyros mespiliformis*      | Cortex    | *B. arietans* | PLA$_2$, proteolytic, SVH | —     | —       | [82]         |
| **Euphorbiaceae**              |           |             |                      |          |         |              |
| *Alchornea laxiflora*          | Cortex    | *B. arietans* | PLA$_2$, proteolytic, SVH | —     | —       | [82]         |
| **Fabaceae**                   |           |             |                      |          |         |              |
| *Baithinia thomningii*         | Cortex, radix | *B. arietans* | PLA$_2$, proteolytic, SVH | —     | —       | [82]         |
| *Bolbunnia madagascariensis*   | Folium, radix | *B. arietans* | PLA$_2$, proteolytic, SVH | —     | —       | [82]         |
| (syn. Swartzia madagascariensis) |           |             |                      |          |         |              |
| *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**               |           |             |                      |          |         |              |
| *Molinieria capitulata* (syn. Curculigo recurvata) | Folium | *B. arietans* | SVH | — | — | [82] |
Table 4: Continued.

| Plant name | Part used     | Snake venom | Inhibited activities | Reference(s) |
|------------|---------------|-------------|----------------------|--------------|
|            |               |             | In vitro             |              |
| **Lamiaceae** |               |             | In vivo              |              |
| 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* | PLA2, 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* | PLA2, proteolytic, SVH | — | [82] |
| Grewia mollis | Cortex, folium, radix | *B. arietans* | PLA2, proteolytic, SVH | — | [82] |
| Sterculia setigera | Cortex | *B. arietans* | PLA2, SVH | — | [82] |
| Waltheria indica | Radix | *B. arietans* | PLA2, proteolytic, SVH | — | [82] |
| **Menispermaceae** |               |             |                      |              |
| Cissampelos mucronata | Herbal | *B. arietans* | Proteolytic, PLA2 | — | [82] |
| **Moraceae** |               |             |                      |              |
| Ficus platyphylla | Folium | *B. arietans* | PLA2, SVH | — | [82] |
| **Olacaceae** |               |             |                      |              |
| Ximenia americana | Folium | *B. arietans* | PLA2, proteolytic, SVH | — | [82] |
| **Phyllanthaceae** |               |             |                      |              |
| Flueggea virosa (syn. Securinega virosa) | Radix | *B. arietans* | PLA2, proteolytic, SVH | — | [82] |
| **Primulaceae** |               |             |                      |              |
| Maesa lanceolata* | Cortex | *B. arietans* | PLA2, proteolytic, SVH | — | [82] |
| **Rhamnaceae** |               |             |                      |              |
| Ziziphus mucronata | Radix | *B. arietans* | PLA2, proteolytic, SVH | — | [82] |
| Ziziphus spinosa-christi | Cortex | *B. arietans* | PLA2, proteolytic, SVH | — | [82] |
| **Rubiaceae** |               |             |                      |              |
| Crossopteryx febrifuga | Cortex | *B. arietans* | PLA2, SVH | — | [82] |
| Pentanisia prunelloides | Radix | *B. arietans* | PLA2, proteolytic, SVH | — | [82] |
| Pentas zanzibarica | Folium | *B. arietans* | PLA2 | — | [82] |
| **Rutaceae** |               |             |                      |              |
| Zanthoxylum capense | Radix | *B. arietans* | PLA2, proteolytic | — | [82] |
| **Sapindaceae** |               |             |                      |              |
| Paullinia pinnata | Folium, radix | *B. arietans* | PLA2, proteolytic, SVH | — | [82] |
| **Solanaceae** |               |             |                      |              |
| Schwennckia americana | Folium | *B. arietans* | SVH | — | [82] |
| **Verbenaceae** |               |             |                      |              |
| Lantana trifolia | Cortex | *B. arietans* | PLA2, SVH | — | [82] |
| **Vitaceae** |               |             |                      |              |
| Cissus populinia | Stem | *B. arietans* | SVH | — | [82] |

PLA2 = snake venom phospholipase A2; SVH = snake venom hyaluronidase. *Vegetal species with related folk use as antiophidian 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 antiophidian 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 confusing, 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 olsfiersii, 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 antiophidian 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
| Plant name               | Part used      | Snake venom | Inhibited activities                  | Reference(s) |
|-------------------------|----------------|-------------|----------------------------------------|---------------|
| Anacardium occidentale  | Bark           | D. russelli | PLA₂, proteolytic, SVH Edema, hemorrhage, myotoxicity | [170]         |
| Mangifera indica        | Stem bark      | D. russelli | PLA₂, LAAO, SVH, proteolytic Edema, hemorrhage, myotoxicity | [171]         |
| Apocynaceae             |                |             |                                        |               |
| Hemidesmus indicus     | Root           | D. russelli | —                                      |               |
| Tylophora indica       | Leaf, root     | D. russelli | PLA₂ Hemorrhage                        | [85]          |
| Aristolochiaceae       |                |             |                                        |               |
| Aristolochia bracteolata | Leaf, root   | D. russelli | PLA₂ Hemorrhage                        | [85]          |
| Aristolochia indica    | Root           | D. russelli | LAAO, proteolytic —                    | [173]         |
| Asteraceae              |                |             |                                        |               |
| Pluchea indica         | Root           | D. russelli | —                                      | [172]         |
| Euphorbiaceae          |                |             |                                        |               |
| Acalypha indica        | Leaf           | D. r. russelli | —                                      | [174]         |
| Fabaceae               |                |             |                                        |               |
| Butea monosperma       | Stem bark      | D. russelli | SVH Hemorrhage                         | [175]         |
| Mimosa pudica          | Root           | D. russelli | LAAO, proteolytic —                    | [91]          |
| Tamarindus indica      | Seed           | D. r. siamensis, D. russelli | LAAO, PLA₂, SVH, proteolytic Edema, hemorrhage, myotoxicity | [176, 177] |
| Lamiaceae              |                |             |                                        |               |
| Leucas aspera          | Leaf, root     | D. russelli | PLA₂ Hemorrhage                        | [85]          |
| Vitex negundo         | Root           | D. russelli | —                                      | [178]         |
| Loganiaceae            |                |             |                                        |               |
| Strychnos nux-vomica   | Seed           | D. russelli | PLA₂ Hemorrhage                        | [95]          |
| Moraceae               |                |             |                                        |               |
| Morus alba             | Leaf           | D. russelli | Proteolytic, SVH Edema, hemorrhage, myotoxicity | [179]         |
| Phyllanthaceae         |                |             |                                        |               |
| Phyllanthus emblica (syn. Emblica officinalis) | Root | D. russelli | —                                      | [178]         |
| Piperaceae             |                |             |                                        |               |
| Piper longum           | Fruit          | D. russelli | Hemorrhage                             | [104]         |
| Rubiaceae              |                |             |                                        |               |
| Ophiuorrhiza mungos    | Root           | D. russelli | Hemorrhage                             | [180]         |
| Salvadoraceae          |                |             |                                        |               |
| Azima tetragonantha    | Leaf           | D. russelli | SVH —                                  | [181]         |
| Vitaceae               |                |             |                                        |               |
| Vitis vinifera         | Seed           | D. russelli | Proteolytic, SVH Edema, hemorrhage, myonecrosis | [182]         |

LAAO = L-amino acid oxidase; PLA₂ = snake venom phospholipase A₂; SVH = snake venom hyaluronidase. *Vegetal species with related folk use as antiophidian 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) |
|----------------------------------|-----------|-------------|----------------------|--------------|
| Apocynaceae                       |           |             |                      |              |
| *Fernaldia pandurata* (syn. *Mandevilla velatina*) | Root      | *L. muta*   | Proteolytic, PLÀ₂, Hemorrhage* | [188]        |
| Asteraceae                        |           |             |                      |              |
| *Eclipta prostrata* (syn. *Eclipta alba*) | Aerial parts, root | *L. muta* | Myotoxicity, proteolytic, PLÀ₂, Hemorrhage*, myotoxicity | [130, 188] |
| *Mikania glomerata*              | Root      | *L. muta*   | Proteolytic, PLÀ₂    | [188]        |
| Erythroxylaceae                   |           |             |                      |              |
| *Erythroxylum ovalifolium*        | Stem      | *L. muta*   | Proteolytic, PLÀ₂, Edema***, hemorrhage*** | [189]        |
| *Erythroxylum subsessile*         | Stem      | *L. muta*   | Proteolytic, PLÀ₂, Edema***, hemorrhage*** | [189]        |
| Euphorbiaceae                     |           |             |                      |              |
| *Jatropha elliptica*              | Root, stem| *L. muta*   | Proteolytic, PLÀ₂, Hemorrhage* | [188]        |
| Fabaceae                          |           |             |                      |              |
| *Pentaclethra macroloba*          | Bark      | *L. muta*   | —                    | Hemorrhage*  | [145] |
| *Stryphnodendron adstringens* (syn. *Stryphnodendron barbatinm*) | Root      | *L. muta*   | Proteolytic, PLÀ₂, Hemorrhage* | [188]        |
| Melastomataceae                   |           |             |                      |              |
| *Miconia albicans*               | Stem      | *L. muta*   | Proteolytic, PLÀ₂, Hemorrhage* | [188]        |
| *Miconia fallax*                 | Stem      | *L. muta*   | Proteolytic, PLÀ₂, Hemorrhage* | [188]        |
| *Miconia sellowiana*             | ND        | *L. muta*   | Proteolytic, PLÀ₂, Hemorrhage* | [188]        |
| *Tibouchina stenocarpa*           | Root      | *L. muta*   | Proteolytic, PLÀ₂, Hemorrhage* | [188]        |
| Salicaceae                        |           |             |                      |              |
| *Casearia sylvestris*             | Root      | *L. muta*   | Proteolytic          | Hemorrhage*  | [188] |
| Sapotaceae                        |           |             |                      |              |
| *Manilkara subserticea*           | Leaf, stem| *L. muta*   | Proteolytic, PLÀ₂, Edema**, hemorrhage** | [100]        |

ND = information not described in the work; PLÀ₂ = snake venom phospholipase A₂. *Vegetal species with related folk use as antiphidic 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 antiphidic 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 antiphidic 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 edemagenic 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) |
|-----------------------------|----------------------------------|-------------|----------------------|---------------|
| Apocynaceae                 |                                  |             |                      |               |
| *Fernaldia pandurata* (syn. *Mandevilla velatina*) | Leaf, stem, subterranean system | *C. d. terrificus* | PLA$_2$ Edema*, myotoxicity* | [125] |
| *Mandevilla ilustris*       | Subterranean system              | *C. d. terrificus* | PLA$_2$ — | [190] |
| Asteraceae                  |                                  |             |                      |               |
| *Eclipta prostrata* (syn. *Eclipta alba*)$^g$ | Aerial parts | *C. d. terrificus* | Myotoxicity Myotoxicity* | [11] |
| Bignoniaceae                |                                  |             |                      |               |
| *Fridericia chica* (syn. *Arrabidaea chica*) | Leaf | *C. d. ruruima* | — Edema | [133] |
| Fabaceae                    |                                  |             |                      |               |
| *Pentaclethra macroloba*$^a$ | Bark                             | *C. atrox* | — Hemorrhage* | [145] |
| *Schizolobium parahyba*     | Leaf                             | *C. d. terrificus* | PLA$_2$ Edema* | [146, 147] |
| Musaceae                    |                                  |             |                      |               |
| *Musa × paradisiaca*$^a$    | Exudate                          | *C. d. terrificus* | PLA$_2$ — | [155] |
| Rubiaceae                   |                                  |             |                      |               |
| *Randia aculeata*$^a$       | Fruit                            | *C. simus* | — Myotoxicity | [78] |
| Sapindaceae                 |                                  |             |                      |               |
| *Sapindus saponaria*        | *In vitro* cultivated callus     | *C. d. terrificus* | PLA$_2$ — | [161] |

PLA$_2$ = snake venom phospholipase A$_2$. $^a$Vegetal species with related folk use as antiophidic agents, as showed in Table 1. $^g$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.

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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)               |
|---------------------|-----------|---------------------------|-------------------------------------------|----------------------------|
| Amaryllidaceae       | Bulb      | *Echis ocellatus*         | Hemorrhage, Myotoxicity**                | [167, 191]                |
| *Asteraceae*         | Aerial parts | *Montivipera xanthina*    | —                                         | [192]                      |
| *Artemisia absinthium* | Leaf     | *Philodryas olfersii*     | Inflammation, myotoxicity                 | [193]                      |
| *Fabaceae*           | Seed      | *Echis carinatus*         | Proteolytic, SVH                         | [194]                      |
| *Mimosa pudica*      | Root      | *Bungarus caeruleus*      | PLA2, proteolytic, SVH                    | [91, 92]                   |
| *Parkia biglobosa*   | Stem bark | *Echis ocellatus*         | Cytotoxicity against muscle cells, hemorrhage | [93]                       |
| *Pentaclethra macroloba* | Bark   | *Calloselasma rhodostoma* | —                                         | [145]                      |
| *Senna auriculata* (syn. *Cassia auriculata*) | Leaf | *Echis carinatus*         | PLA2, proteolytic, SVH                    | [195]                      |
| *Malvaceae*          | Whole plant | *Echis carinatus*         | Cytotoxicity against muscle cells, hemorrhage | [196, 197]                |
| *Salvadoraceae*      | Leaf      | *Bungarus caeruleus*      | PLA2                                      | [181]                      |
| *Vitaceae*           | Seed      | *Echis carinatus*         | Proteolytic, SVH                         | [198]                      |

PLA2 = snake venom phospholipase A2; 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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