Antivenin plants used for treatment of snakebites in Uganda: ethnobotanical reports and pharmacological evidences

Timothy Omara¹,²*, Sarah Kagoya³,⁴, Abraham Openy⁵, Tom Omute⁶, Stephen Ssebulime⁷, Kibet Mohamed Kiplagat⁸ and Ocident Bongomin⁹

Abstract
Snakebite envenomation is a serious public health concern in rural areas of Uganda. Snakebites are poorly documented in Uganda because most occur in rural settings where traditional therapists end up being the first-line defense for treatment. Ethnobotanical surveys in Uganda have reported that some plants are used to antagonize the activity of various snake venoms. This review was sought to identify antivenin plants in Uganda and some pharmacological evidence supporting their use. A literature survey done in multidisciplinary databases revealed that 77 plant species belonging to 65 genera and 42 families are used for the treatment of snakebites in Uganda. The majority of these species belong to family Fabaceae (31%), Euphorbiaceae (14%), Asteraceae (12%), Amaryllidaceae (10%) and Solanaceae (10%). The main growth habit of the species is shrubs (41%), trees (33%) and herbs (18%). Antivenin extracts are usually prepared from roots (54%) and leaves (23%) through decoctions, infusions, powders, and juices, and are administered orally (67%) or applied topically (17%). The most frequently encountered species were Allium cepa, Carica papaya, Securidaca longipedunculata, Harrisonia abyssinica, and Nicotiana tabacum. Species with global reports of tested antivenom activity included Allium cepa, Allium sativum, Basella alba, Capparis tomentosa, Carica papaya, Cassia occidentalis, Jatropha curcas, Vernonia cinereal, Bidens pilosa, Hoslundia opposita, Maytenus senegalensis, Securinega virosa, and Solanum incanum. There is need to identify and evaluate the antivenom compounds in the claimed plants.

Keywords: Antiophidic, Antivenin, Snakebite, Traditional medicine, Uganda

Introduction
Snake envenoming is a global health problem and a justification for morbimortality and various socio-economic losses. A recent conservative global estimate points that about 5.5 million snakebite cases are encountered every year causing about 2 million deaths [1, 2]. Up to 500,000 of these cases are reported in Africa [3–5]. In 2002, 108 cases of snakebites were reported in Gulu Regional Hospital (Uganda) though none of the victims died [6].

About 151 cases were reported in neighboring Kenya in 1994 with 19% of these from venomous snakes [7].

A recent study [8] in 118 health facilities throughout Uganda revealed that only 4% of the facilities stocked antivenin sera, thus most victims rarely seek medical care when bitten by snakes. A retrospective part of this study showed that in 140 surveyed facilities, 593 snakebite cases were recorded within six months with bites reported in the rainy seasons from April 2018 to June 2018 and then October 2018 to December 2018 [8]. Thus, fatalities in rural areas are due to lack of antidotes within the 24 h recommended [6, 9, 10] and antisera administration problems [11, 12].

Snakes are taxonomically carnivorous vertebrates of class Reptilia, order Squamata, sub-order Serpentes and families: Colubridae, Boidae, Elapidae, Pythonidae, Viperidae that characteristically kill their prey by constriction.
rather than envenomation [13, 14]. Most bites are due to circumstantial stepping on the snakes by unprotected or barefooted victims [6, 15], snake ecology [16] while others are initiated by malevolent and alcohol-intoxicated victims [17–19]. Over 3500 species of snakes have been classified and about 600 (15–17%) of these are venomous [1, 20]. East Africa is home to about 200 species of snakes and 145 of these from 45 genera and 7 families are found in Uganda [21]. Many are harmless or are a rarity though the puff adder (Bitis arietans), Gabon viper (Bitis gabonica), green or Jameson’s mamba (Dendroaspis jamesoni), black mamba (Dendroaspis polylepis), forest cobra (Naja melanoleuca), and black-necked spitting cobra (Naja naja nigricollis) are listed as venomous [10, 22].

Snake venom is secreted by snake oral glands and is injected subcutaneously or intravenously through the fangs into the victim on the hands, feet, arms, or legs [23]. Venoms are water-soluble, acidic, and have a specific gravity of about 1.03 [24]. The quantity, lethality, and composition of venoms vary with the age and species of the snake, time of the year, geographic location as well as the envenoming snake’s diet. A snake venom is a complex mixture of toxic proteins such as cardioxins, neurotoxins, metalloproteinases, nucleotidases, phospholipases A$_2$, serine proteinases, acetylcholinesterase nitrate, hyaluronidases, phosphomonoesterase and phosphodiesterase [25] which are injected to immobilize the victim [10, 26]. The toxins cause haemotoxicity–damage to blood vessels resulting in spontaneous systemic and muscle paralysis, myolysis, arrhythmias, cardiac, and renal failure [6].

At present, serum antivenom immunotherapy is the mainstay of treatment reported for snake envenomation [6, 10, 17, 26]. Antisera are either derived from horse serum after injecting it with sublethal doses of the venom (Antivenin Polyclonal) or sheep serum (Crotalidae Polyvalent Immune Fab) [19]. Though antivenom serum is lifesaving, it is associated with the development of immediate or delayed hypersensitivity (anaphylaxis or serum sickness) and does not prevent local tissue damage. The side effects are thought to be due to the action of non-immunoglobulin proteins present in high concentrations in antisera [27]. Worse still, there is a paucity of snake venom antiserum in rural Africa that even in the presence of money, it may not be readily available for purchase [6, 17]. This is in part attributed to the decline in antivenom production in Africa due to denationalization of the manufacturing industries by African countries [28], lack of ready market and low profits from the business. Thus, several attempts have been made to develop snake venom antagonists from other sources including plants, dogs, rabbits, cameldids, and avian eggs [12, 27, 29–33].

The use of plants in addressing medical challenges have been witnessed since antiquity and is regaining shape in the modern era due to their safety, effectiveness, cultural preferences, inexpensiveness, abundance, and availability. In Uganda, more than 230 species of angiosperms belonging to about 168 genera and 69 families are being utilized for treatment of erectile dysfunction, malnutrition, sickle cell anemia, hernia, venereal diseases (syphilis, HIV, and gonorrhoea), post-partum hemorrhage, snakebites, cancer, menorrhagia, threatened abortion, skin diseases, jaundice, and cough [34–60]. This study compiled information on antivenin plants reported in different districts of Uganda and presented some experimental evidence supporting their use in antivenom therapy.

**Methodology**

**Description of the study area**

Uganda is a landlocked country straddling the equator in Eastern Africa [61]. It is flanked by Lake Victoria, Tanzania, and Rwanda to the south, Kenya to the east, South Sudan to the North and Democratic Republic of Congo to the West (Fig. 1). The climate experienced is equatorial moderated by relatively high altitudes with a mean annual temperature of 20.5 °C. The country’s population is estimated to be 35.92 million with 5 main ethnic families: Nilotics (Acholi, Alur, Padhola, Lulya, and Jonam), Bantu (Baganda, Banyankole, Batoro, Bagwere, Bakiga, Bakiga, Banyarwanda, Bakonjo, Banyoro, and Bakiga), Hamities (mainly constituted by the Bahima), the Nilo-Hamities (Teso, Karamojong, Kakwa, Sebei, Labwor, and Tepeth) and the Sudanics (Lugwara, Madi, and Lendu) [62]. Health care services are inadequate [63], and access to allopathic drugs is limited in rural areas due to their prohibitive cost, poor transport network, chronic poverty and the general belief in efficacy of traditional medicine than western medicine [64].

**Literature search strategy**

Relevant original articles, books, thesis, dissertations, patents, and other reports written in English and other local languages on ethnobotany and pharmacological evidences on snakebites in Uganda were searched in Scopus [65], Web of Science [66], PubMed [67], Science Direct [68], Google Scholar [69], and Scientific Electronic Library Online (SciELO) [70] from July 2019 to September 2019. The key search words used were “snakebite,” “vegetal,” “traditional medicine,” “ethnobotany,” “alternative medicine,” “ethnopharmacology,” “antivenom,” “antiophidian,” “antitoxin,” “snake antidotes,” and “Uganda.” The botanical names of the plants were vetted in botanical databases: the Plant List [71], International Plant Names Index (IPNI) [72], NCBI taxonomy browser [73], and Tropicos [74]. Where a given
species was considered as distinct species in different reports, the nomenclature as per the botanical databases took precedence. The families, local names (Lango, Acholi, Ateso, Luganda, Lunyoro, Rukiga, and Lusoga), growth habit, part(s) used, conservation status, preparation and administration mode, status of antivenin activity investigation of the plants, and the districts where the plants were surveyed are reported (Table 1, Additional file 1).

Pertaining to pharmacological reports, the snake venom studied, phytochemicals, and positive results obtained using plants identified by this study (or species from the same genus) are reported. In some cases, some activities of the plant extracts such as antioxidant and radical scavenging activities are reported as these are some of mechanisms by which snake venoms are countered.

Results and discussion

Only full-text articles in English, Lango, Acholi, Ateso, Luganda, Lunyoro, Rukiga, and Lusoga were considered. A total of 15 articles (13 in English, 1 in Luganda, and 1 in Lusoga) with information on antivenin plants were retrieved, but two of these did not meet inclusion criteria because one was not a full-text article while the other had only one botanically unidentified antivenin plant. Thus, the following reports of interest specifically on the subject of antivenin plants in Uganda were retrieved (Table 1).

Traditional concept of snakebites in Uganda

From the electronic survey of data, it is indubitable that the local communities in Uganda have different perceptions about snakebites. The beliefs appear to be clan-related and include snakes “can protect” (among the Baganda) [18, 75] or “are dangerous and connected to witchcraft” in most communities [8]. By comparison, the Luo of Kenya associate snakes with witchcraft [76].

From the survey, 77 plant species from 65 genera belonging to 42 botanical families claimed as antiphidic in Uganda were retrieved (Table 1, Additional file 1). The most cited families were Fabaceae (31%), Euphorbiaceae (14%), Asteraceae (12%), Amaryllidaceae (10%), and Solanaceae (10%) (Fig. 2). Most families encountered in this study have reported antivenin potential in treating or avoiding snakebites in other countries across the globe. For example, Apocynaceae, Aristolochiaceae,
Table 1 Anti-venom plants used in rural communities of Uganda

| Plant family          | Latin botanical name                        | References |
|-----------------------|---------------------------------------------|------------|
| Acanthaceae           | Asystasia schimperi T. Anders.              | [42]       |
| Amaryllidaceae        | Allium cepa L.                              | [41, 42, 49]|
| Amaryllidaceae        | Allium sativum L.                           | [49]       |
| Amaryllidaceae        | Crinum kirkii                               | [41]       |
| Amaryllidaceae        | Scadoxus multiflorus (Martyn) Raf.          | [10, 42]   |
| Apocynaceae           | Carissa edulis                              | [50]       |
| Apocynaceae           | Thevetia peruviana (Pers.) Schumann         | [42]       |
| Aristolochiaceae      | Aristolochia tomentosa Sims.                | [50]       |
| Aristolochiaceae      | Aristolochia elegans Mast.                  | [42]       |
| Asclepiadaceae        | Cryptolepis sanguinolenta (Lindl.) Schltr  | [42]       |
| Asparagaceae          | Sansevieria dawei Stapf                     | [38]       |
| Asparagaceae          | Sansevieria trifasciata var. trifasciata    | [10]       |
| Asteraceae            | Bidens pilosa L.                            | [42]       |
| Asteraceae            | Cissuscepalum manni (Hook.f.) Milne-Redh.  | [35]       |
| Asteraceae            | Echinops amplexicaulis Oliv.                | [46]       |
| Asteraceae            | Microglossa pyrifolia (Lam) O. Kuntze       | [42]       |
| Asteraceae            | Vernonia cinerea (L.) Less                  | [41, 42]   |
| Basellaceae           | Basella alba L.                             | [39]       |
| Boraginaceae          | Trichodesma zeylanicum (L.) R.Br.           | [41]       |
| Cleomaceae            | Cleome gynandra L.                          | [35]       |
| Capparidaceae         | Capparis tormentosa Lam.                    | [42]       |
| Caricaceae            | Carica papaya L.                            | [41, 42, 50]|
| Celastraceae          | Maytensus senegalensis (Lam) Exell.         | [41]       |
| Combretaceae          | Combretum collinum Fresen                   | [41]       |
| Combretaceae          | Combretum molle ex G.don.                   | [41]       |
| Commelinaceae         | Murdannia simplex Vahl. Branan              | [35]       |
| Compositae            | Aspilia africana C.D Adams                  | [46]       |
| Convolvulaceae        | Hewittia sublobata L. Kuntze                | [49]       |
| Convolvulaceae        | Ipomoea batatas (L.) Lam.                   | [42]       |
| Dracacenae            | Dracaena steudneri Engl.                    | [49]       |
| Ebenaceae             | Euclea divinorum Hiern                      | [42]       |
| Euphorbiaceae         | Acalypha biparitata Muell. Arg.             | [42, 47]   |
| Euphorbiaceae         | Croton macrostachyus Hochst. ex. Delile     | [49]       |
| Euphorbiaceae         | Euphorbia tirucalli L.                      | [35]       |
| Euphorbiaceae         | Jatropha curcas L.                          | [42]       |
| Euphorbiaceae         | Ricinus communis L.                         | [35, 42]   |
| Euphorbiaceae         | Securinega virosa (Willd) Baill.            | [41]       |
| Fabaceae              | Acacia seyal Del. var. fistula (Schweinf.) Oliv. | [42] |
| Fabaceae              | Acacia species                              | [42]       |
| Fabaceae              | Albizia coriaria (Welw. ex) Oliver          | [42]       |
| Fabaceae              | Canavalia ensiformis L. D.C.                | [10]       |
| Fabaceae              | Indigofera arrecta Host. A. Rich.           | [42, 49]   |
| Fabaceae              | Indigofera garcineana Vatk                  | [42]       |
| Fabaceae              | Indigofera capitata Forsk.                  | [41]       |
Asteraceae, Convolvulaceae, Fabaceae, and Myricaceae were cited in Kenya [17] and Tanzania [77], Meliaceae in Ghana [78], Fabaceae in Rwanda [79], Asparagaceae, Leguminosae, and Menispermaceae in Sudan [80], Acanthaceae, Apocynaceae, Asteraceae, Capparaceae, Cariaceae, Combretaceae, Convulaceae, Ebenaceae, Eurphorbiaceae, Fabaceae, Malvaceae, Meliaceae, and Poaceae in Ethiopia [81] and Pakistan [82], Fabaceae, Aristolochiaceae, and Lamiaceae in Djibouti [83] and Nigeria [84], Melastomataceae and Menispermaceae in Cameroon [85]. Acanthaceae, Apocynaceae, Asteraceae, Euphorbiaceae, Fabaceae, Mora ceae, Rubiaceae, and Rutaceae were cited in India [86, 87], Bangladesh [88, 89], and Central America [90]. Fabaceae is always dominant in ethnobotanical reports because of the abundance of plant species from this family [88, 91–93].

The families reported were from different districts of Uganda (Fig. 3) representing different ethnic groups with diverse cultural beliefs and practices. About 40% of the plant species were reported in Kaliro (inhabited by the Basoga) followed by 21% from Lira (occupied by the Lango) and 11% from Mukono-Buikwe frontier occupied by the Baganda. In a similar cross-cultural comparison of antiophidic floras in the Republic of Kenya, Owuor and Kisangu [17] reported that two culturally and

| Table 1 | Antivenin plants used in rural communities of Uganda (Continued) |
|-------------------------------------------------|-------------------------------------------------|
| Plant family | Latin botanical name | References |
| Fabaceae | *Pseudanthria hookeri* Wight and Arn. | [42, 48] |
| Fabaceae | *Senna occidentalis* (L.) Link | [42] |
| Fabaceae | *Senna septemtrionalis* (Viv.) L et B. | [39] |
| Fabaceae | *Senna siamea* (Lam.) Irwin and Barneby | [42] |
| Fabaceae | *Senna singueana* (Del.) Lock | [42] |
| Lamiaeae | *Hoslindia opposita* Vahl | [42] |
| Lamiaeae | *Plectranthus barbatus* | [37, 50] |
| Leguminosae | *Cassia occidentalis* L. | [35] |
| Liliaceae | *Anthericum carterianum* Bak | [41] |
| Loganiaceae | *Stychnos innocua* Del. | [41] |
| Malvaceae | *Urena lobata* L. | [42] |
| Melastomataceae | *Tristemma mauritianum* J.F. Gmel. | [41] |
| Meliaceae | *Ekebergia capensis* Sparrm | [44] |
| Meliaceae | *Trichilia ematica* Vahl | [38, 46] |
| Menispermaceae | *Cissampelos muchronata* A.Rich. | [41, 49] |
| Moraceae | *Ficus natalensis* Hochst. | [42] |
| Myricaceae | *Morella kandtiana* (Engl) Verdic and Polhill | [49] |
| Papilionaceae | *Ormocarpum trachycarpum* | [50] |
| Passifloraceae | *Adenia cissampeloides* (Hook) Harms | [42] |
| Poaceae | *Imperata cylindrica* (L.) P. Beauv | [42, 49] |
| Poaceae | *Sporobolus pyramidalis* P. Beauv. | [42] |
| Polygalaceae | *Securidaca longipedunculata* Fres. | [41, 42, 50] |
| Rosaceae | *Rubus rigidus* Sm | [49] |
| Rubiaceae | *Gardenia ternifolia* Schumach. and Thonn. | [42] |
| Rutaceae | *Citrus sinensis* (L.) Osb. | [42] |
| Rutaceae | *Fagaropsis angolensis* (Engl) Dale | [59] |
| Simaroubaceae | *Harrisonia abyssinica* Oliv. | [41, 42, 50] |
| Solanaceae | *Datura stramonium* L. | [41] |
| Solanaceae | *Nicotiana tabacum* L. | [42, 49, 59] |
| Solanaceae | *Solanum aculeatissimum* Jacq | [41, 46] |
| Solanaceae | *Solanum incanum* L. | [41, 42] |
| Umbellifereae | *Steganotaenia arateica* Hoscht | [41] |
| Verbenaceae | *Lantana camara* L. | [50] |
floristically distinct African groups (Kamba and Luo) had similar knowledge of snakebites but the antivenin plants utilized by the two ethnic groups were independently derived. The abundance of antivenin plants from Kaliro, Lira, and Mukono/Buikwe could be due to the presence of forest reserves in these districts. Kaliro, Namalemba, and Namukooge local forest reserves are found in Kaliro [94]. The district is also rich in water resources such as Lake Nakuwa, River Mpologoma, Nai-gombwa, and Lumbuye wetlands which provide rainfall for the growth of plants. Lira District has Lake Kwania, Okole, Moroto and Olweny wetland systems which support the growth of plants [95]. The district gazetted over 1000 hectares of land for forest conservation and this serves as a good source of plants for traditional medicine [96]. The Mukono-Buikwe frontier has Mabira forest reserve which has been protected since 1932 and contains a number of endangered plant species in Uganda [97]. The rainforest is a rain catchment for areas supplying River Nile and Ssezibwa River and has rainfall throughout the year thus plants flourish in this area [98].

**Growth habit, parts used, preparation, and administration of antivenin preparations**

Antivenin plants used in Uganda are majorly shrubs (41%), trees (33%) and herbs (18%) and the commonly
used plant parts are roots (54%) and leaves (23%) followed by whole plant (4%), bark (4%), and tuber (4%) (Figs. 4 and 5). The regular use of roots and leaves in antivenin preparations is a characteristic feature of traditional antivenin therapy [17, 81, 86, 99, 100], no wonder some of these plants are named “snakeroot” in some rural communities [101]. Comparatively, embryonal plant parts such as fruits, seeds, buds, bulbs, and flowers which have reputation for accumulating certain compounds are less frequently used, concordant with reports from other countries [17, 81]. Majority of the plants reported grow in the wild (82%), 14% are cultivated while 4% are semi-wild (occurs in the wild but can also be cultivated). The commonest mode of preparation is as decoctions and infusion. The plants are collected from fallow land, cultivated fields or home gardens when needed. Traditional medicine practitioners either collect herbal plants personally or hire collectors. All traditional medical practitioners cultivate some medicinal plants especially fast growing ones around their homes and shrines in order to have them within easy access when needed. The antidotes are administered orally (67%) or applied at the point of snakebite (17%).

In this survey, it was noted that few plant species are used against snakebites simultaneously in different districts. This could probably be attributed to the abundant distribution of the analog active substances among species especially those of family Fabaceae. Some of the plants listed are also used for wading off or discouraging snakes from reaching human and livestock abodes. In most instances, the plants possess a strong smell that causes discomfort and disorientation to snakes when they slither over them. In exceptional cases as with tobacco, the plant (dried whole plant or leaves) are burnt to produce unpleasant odor that discourages snakes (Table 2). The Lango of Northern Uganda burn bicycle, motorcycle, and vehicle tyres to discourage snakes.

Other ethnomedicinal uses and toxicity of the reported antivenin plants

Almost all the plants recapitulated in this review are employed for the treatment of various ailments. For example, *Bidens pilosa* L. has been reported to be useful in the treatment of more than 40 disorders including inflammation, immunological disorders, digestive disorders, infectious diseases, cancer, metabolic syndrome, and wounds among others [103–106]. *Albizia coriaria* (Welw. ex) Oliver is used in the management of syphilis, postpartum haemorrhage, sore throats, menorrhagia, threatened abortion, skin diseases, jaundice, cough, sore eyes, and as a general tonic [35]. Such plants tend to be used in different communities for treating snakebites and can be a justification of their pharmacological efficacy [107].

On the other hand, some of the antivenin plants cited exhibit marked toxicity. A striking example is *Jatropha curcas* L. leaf and latex which contain a purgative oil (irritant curcanoleic acid and croton oil), curcin (toxalbumin), and diterpene of tigliane skeleton classified as phorbol esters [108]. Curcin has protein translation inhibitory (N-glycosidase) activity whereas phorbol esters are amphiphillic molecules that can bind phospholipid membrane receptors [109]. This observation explains why some antivenin preparations in Uganda are applied topically or ingested in small amounts. Fortuitously, topical application is a better approach for reducing the local action of venoms at the bitten site.

![Fig. 4 Growth habit of the antivenin plants used in rural communities of Uganda](image-url)
Knowledge dynamics of antivenin plants in Uganda

Knowledge of traditional medicine and medicinal plants are usually acquired and passed on orally from the elders to the young [34]. This is comparable to reports from other African countries [17, 78]. Knowledge is gained through trainings, divine call, and in some instances, the plant to be used can be asked for from the dead [42, 59]. Because of civilization, efforts to pass on traditional medical knowledge to children is impeded by lack of interest and the fact that most children spend their youthful years in school [17, 34, 60]. Most Ugandans know that their current social conditions such as poverty, sleeping in mud houses and activities such as cultivation, hunting, and herding cattle increase their chances of getting bitten by a snake. Snakebites are always taken as exigencies with economic implications due to the expenses involved in transporting the victims for treatment, the care needed, enforced borrowing, amputation of necrosed legs, and arms as well as loss of time [8].

Treatment of snakebites

Treatment of snakebites in Uganda involves various procedures that vary from culture to culture and religion to religion, for example, Pentecostal Assemblies of God (PAG) believe prayers can treat snakebites. Use of tourniquets to tie the injured part above the affected area to prevent the venom from spreading to heart, the lungs, kidney, and other delicate parts of the body has been prescribed as a supportive first aid in Northern Uganda [6]. This is usually done at five-minute intervals to avoid the weakening of the local tissues.

Among the Baganda (Central Uganda), the use of black stones (carbonized absorptive animal bone) and Haemanthus multiflorus bulb have been reported (Fig. 6) [10]. A black stone is placed on incisions made around

### Table 2: Plants used in Ugandan rural communities for repelling of snakes

| Family         | Botanical name | Growth habit | Part used     | Mode of use to prevent snakes                          | References |
|----------------|----------------|--------------|---------------|---------------------------------------------------------|------------|
| Amaryllidaceae | Allium cepa L  | Herb         | Bulb          | Decoction made and sprinkled around the house. Snakes are discouraged by the sharp onion smell. | [10]       |
| Amaryllidaceae | Allium sativum L | Herb         | Bulb          | Decoction made and sprinkled around the house. Snakes do not are discouraged by the sharp onion smell. | [10]       |
| Asteraceae     | Tagetes minuta | Herb         | Leaves        | Plants have bitter tastes and strong smells that cause discomfort and disorientation to snakes when they slither over them. | [10]       |
| Euphorbiaceae  | Ricinus communis | Herb         | Leaves/ whole plant | Plant have strong smell that cause discomfort and disorientation to snakes when they slither over them. | [10]       |
| Poaceae        | Cymbopogon citrus | Grass        | Leaves        | Decoction made and sprinkled around the house. Snakes do not like the citrus smell from the leaves | [10]       |
| Solanaceae     | Nicotiana tabacum L | Shrub      | Leaves        | Planted around the house, leaves burnt                | [10, 102]  |
the bitten area until it sticks. It is administered to reassured victims and left for 20-30 minutes for it to “suck out” the poison. The stone is reported to be 30% effective and can be reused if boiled in hot water after use and can be used alongside other medical treatments [10]. For Haemanthus multiflorus, the bulb is chewed by the victim or it is crushed and put on the bite.

In Northern Uganda, the use of 500 Uganda shilling copper coins and black stones have been reported [6]. The copper coins are placed on the bite until it gets stuck and it is left to fall off on its own. In some communities like Lango of Northern Uganda, antivenin therapy involves oral administration of egg yolk and albumin similar to the therapy reported among the Luo of Kenya [17]. Overall, traditional antivenin therapy in Uganda involves administration of plant preparations to the victims [35].

**Antivenin activity of plants and pharmacological evidence**

Pharmacological studies have revealed that some plants used in traditional medicine are able to antagonize the activity of various crude venoms and purified toxins [110–112]. Antigen-antibody interaction is the proposed mechanism through which the activity of venoms is countered by antivenins. Reported mechanisms of venom inactivation include precipitation or inactivation of the toxic venom proteins [113], inactivation, or enzyme inhibition [114], chelation [115], adjuvant action [116], antioxidant activity or a synergistic interaction of these mechanisms. Enzyme inhibition and protein precipitation are by far the most conventionally accepted mechanisms [117]. To start with, plant metabolites such as flavonoids, polyphenols, saponins, tannins, terpenoids, xanthenes, quinonoids, steroids, and alkaloids have been reported to snuggly bind to toxic proteins of snake venoms, thereby offsetting their deleterious effects. Another explained scientific possibility is the competitive blocking of the target receptors [118]. For example, atropine (an alkaloid reported in family Solanaceae) is reported to inhibit the activity of green and dark mamba (Dendroaspis angusticeps and D. polylepis) venoms by blocking cholinergic nerve terminals usually attacked by the venoms. Aristolochic acid I (8-methoxy-6-nitro-pyrene-thro(3,4-d),3-dioxyo 5-carboxylic acid), an alkaloid present in Aristolochia species acts in the same way.

Another mechanism of snake venom inactivation involves inhibition of the active enzymes such as phospholipase A₂, metalloproteases, and hyaluronidases by polyphenolic compounds such as tannins. In this scenario, the metabolites interact with the venom enzymes by non-specific binding proteins [119] through hydrogen bonding with hydroxyl groups in the protein molecules generating chemically stable complexes [120]. For example, in a study experimented with aristolochic acid I and PLA₂ isolated from Viper russelli venom, molecular interactions between the two were reported to be between their hydroxyl groups which formed two hydrogen bonds with Granulocyte Marker Monoclonal Antibody (His48) and myotoxins I (Asp49) of the venom [121]. Aristolochic acid I is also an inhibitor of hyaluronidase of Naja naja venom [122]. Other examples of these are outlined in Table 3. Chelation on the other hand is reported to be effective for antivenin plant extracts with molecules (compounds) capable of binding to divalent metal ions necessary for some enzymatic activities. For the cause that chemical coordination of metal ions is indispensable for normal hydrolytic activities of phospholipases and metalloproteases, secondary metabolites capable of disrupting the enzyme-metal ion bondage inhibits enzymatic progression [166]. In antioxidation mechanism, plant metabolites (flavonoids, terpenoids, tannins, polyphenols, vitamins A, C, E, and minerals such as selenium) prevent, stop or reduce oxidative damage due to phospholipase A₂ activity by selectively binding to the active sites or modifying the conserved residues that are inevitable for phospholipase A₂ catalytic action [119].

The efficacy of plant extracts in antivenom action tends to be related to the solvent used for the extraction of the bioactive compounds. A study [152] reported that
| Plant          | Part used | Solvent used | Antivenin activity (comments)                                                                 | Active chemical constituents                                                                 | Authors                                                                 |
|---------------|-----------|--------------|-----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|------------------------------------------------------------------------|
| *Allium cepa* | Bulb      | Methanol     | Cardioprotective activity (14.8 ± 1.65 units/l; p > 0.5) on creatine kinase isoenzyme levels to neutralize snake venoms. Concentrations (< 160 µg/ml) stabilized human red blood corpuscles membrane (antithrombotic) against *N. naja karachiensis* venom, though elevated concentrations were cytotoxic. Provided 50% protection from *N. naja karachiensis* phospholipase A (PLA₂) in terms of an increase in pH of an egg yolk suspension. Neutralized the anticoagulant effect induced by weak PLA₂ enzymes in *N. naja karachiensis* venom (76% inhibition, coagulation time of 106 ± 0.57 s). Quercetin is a potent inhibitor of lipoprotein lipase. | Quercetin, sulfurous volatile oils, oleanolic acid, protocatechuric acid | [123–127]                                                            |
| *Allium sativum* | Bulb     | Methanol     | Hepatoprotective activity (p > 0.5, 49 ± 0.01 and 82.5 ± 18.55 units/l of aspartate aminotransferase and alanine aminotransferase against 52.5 ± 3.51 and 69.5 ± 18.55 units/l for standard antiserum) assessed in rabbits. Provided 50% protection from *N. naja karachiensis* PLA₂ in terms of an increase in pH of an egg yolk suspension. Provided 50% protection from *N. naja karachiensis* PLA₂ in terms of an increase in pH of an egg yolk suspension. Neutralized the anticoagulant effect induced by weak phospholipase A enzymes in *N. naja karachiensis* venom (40% inhibition, coagulation time of 115 ± 1.52 s). Quercetin, scordinines A, B allicin, thiosulfinates, 2 mercapto-L-cysteines, anthocyanins, alliinase, polysaccharides, sativin I, sativin II, glycosides of kaempferol | | [123, 125, 126] |
| *Asystasia* spp (A. gangetica L) | Leaves | Methanol     | 1000 mg/kg provided 80% protection against *N. melanoluca* venom (PLA₂) | Flavonoids, saponins and tannins                                                           | [128]                                                               |
| *Aristolochia* spp (A. indica, A. odoratissima) | Leaves | Methanol, Ethanol, Water, pentane | PLA₂ and hyaluronidase enzymes from *N. naja* and *V. russelli* venoms inhibited. Strong gelatinolytic, collagenase, peroxidase, and nuclease activities, i-amino acid oxidase and protease inhibitory potencies. Protected mice against lethal effects of *Bothrops atrox* venom at higher doses of 8 and 16 mg/kg | Aristolochic acid I, lignan (-)-cubebin | [129–131] |
| *Basella alba* L. | Fruit  | Methanol     | Radical scavenging activity against 1,1-diphenyl 2-picryl-hydrazyl (DPPH) experimented in mice. | Flavonoids, phenolics, betacyanins, Lupeol, β-sitosterol                                       | [132–134] |
| *Capparis tomentosa* Lam. | Root | Water, petroleum ether | The antioxidant activity by DPPH was 35.50 ± 0.02%, by phosphomolybdate assay was 41.22 ± 0.17 mg/kg ascorbic acid equivalent, and the reducing power increased with increase in concentration up to a maximum at 800 µg/ml in alloxanized male mice (aqueous extracts). | N-benzylphenylnalanylalinol acetate, 24-ethylcholestan-5-en-3-ol, L-stachydrine, 3-hydroxy-3-methyl-4-methoxyxindole | [135, 136] |
| *Carica papaya* L. | Leaves | Water, ethanol | Hepatoprotective against carbon tetrachloride induced hepatotoxicity in mice. | Saponins, cardiac glycosides, alkaloids, phenolic acids, chlorogenic acid, flavonoids and coumarin compounds | [137–140] |
| *Carissa* spp (C. spinarum L.) | Leaves | Methanol     | Acetylcholinesterase, PLA₂, hyaluronidase, phosphornooesterase, phosphodiesterase,5-nucleotidase enzymes from *Bungarus caeruleus* and *V. russelli* venoms inhibited by 100 µg/ml of the extract. | Steroids, flavonoids, tannins, saponins, alkaloids, ursolic acid | [141, 142] |
| *Cassia occidentalis* L. | Leaves, roots | Ethanol | Stimulated angiogenesis, inhibited epidermal hyperplasia, and minimized local effects caused by *Boothrops moojeni* venom. | Anthraquinones                                                                             | [143, 144] |
| *Citrus* spp. (C. limon L. Burm. F) | Root, ripe fruits | Methanol | Neutralized the anticoagulant effect induced by weak PLA₂ enzymes in *N. naja karachiensis* venom (64% inhibition, coagulation time of 109 ± 1.00 s). In vitro inhibitory ability against the lethal effect of *Lachesis muta* venom with effective dose 50% of 710 µg extract per mouse | d-x-pinene camphene, d-limonene, linalool, ichangin 4-β-glucopyranoside, nomicilic acid, 4-β-glucopyranoside | [126, 145, 146] |
| Plant       | Part used | Solvent used | Antivenin activity (comments)                                                                 | Active chemical constituents                                    | Authors                  |
|------------|-----------|--------------|---------------------------------------------------------------------------------------------|-------------------------------------------------------------------|--------------------------|
| Cleome spp  | Bulb      | Methanol, ethyl acetate | Significant anti-inflammatory activity against cara-geenin-, histamine-, dextran-induced rat paw edema compared to Diclofenac sodium (20 mg/kg) standard | Flavonoid glycosides, querection 3-O-(2′-acetyl)-glucoside, phenolics | [147, 148] |
|            |           |              |                                                                                             |                                                                    |                          |
| Crinum spp  | Bulb      | Methanol     | Extract of 1000 mg/kg protected 50% of mice; injection of a pre-incubated mixture of the same extract dose and venom gave 100% protection against E. ocellatus venom (10 mg/kg). Administration of extract at 250 mg/kg, 30 min before the injection of E. ocellatus venom (10 mg/kg) prolonged (p < 0.05) death time of poisoned mice. Extract of 500 mg/kg provided 50% protection against Betans venom (9.5 mg/kg) while pre-incubation of a mixture of the same dose of venom and extract prior to injection provided 33.3% protection. Plasma creatine kinase concentrations in poisoned mice reduced with injection 1000 mg/kg of extract pre-incubated with 5 mg/kg of E. ocellatus or 7 mg/kg B. arietans venoms. The extract blocked hemorrhagic activity of a standard hemorrhagic dose (2.8 mg/ml) of E. ocellatus venom at 1.7, 3.3, and 6.7 mg/ml. | Phenolic compounds, tannins, alkaloids, cardiac glycosides          | [148, 149] |
|            |           |              |                                                                                             |                                                                    |                          |
| Indigofera spp. | Leaves | Methanol, ethanol, water | Extracts reduced bleeding and clotting times of N. nigricollis envenomed rats. Ethanol and aqueous extracts of I. capitata were more effective at a dose of 300 mg/kg with lowest clotting time of 174 ± 3.67 s and 1000 mg/kg with lowest bleeding time of 228 ± 3.00 s. I. conferta at a dose of 1000 mg/kg had the lowest clotting time of 173 ± 5.61 s (ethanol extract) and 234 ± 7.64 s for aqueous extract). Edema forming activity was inhibited by ethanol and aqueous extracts, effective at higher doses of 300 mg/kg (ethanol extract) and 1000 mg/kg (aqueous extract) with the lowest edema forming activity of 108.80 ± 1.90 and 102.00 ± 1.90 (%mm) respectively by I. capitata and at dose of 250 mg/kg, 500 mg/kg, and 1000 mg/kg of aqueous extract with the lowest edema forming activities of 100.8 ± 1.89, 100.20 ± 1.90 and 100.60 ± 1.90 (%mm) by I. conferta | Flavonoids, phenolic compounds, steroids, triterpenes, anthraquinone, alkaloids | [150] |
| (I. pulchra Wild.) |          | Methanol     | Extract inhibited anticoagulant, hemolytic and PLA2 activities of N. nigricollis venom  |                                                                    |                          |
| Jatropha carcus L. | Leaf latex | Methanol | Inhibits hemolytic activity of PLA2 from N. naja venom                                         | Terpenoids, alkaloids, phenolics, flavonoids, saponins               | [152] |
| Vernonia cinerea (L.) Less. | Whole plant | Methanol | Antioxidant activity by DPPH free radical scavenging assay. Ethyl acetate fraction exhibited 63.3% DPPH radical scavenging activity at 100 μg/ml.                                                         | Phenolics, flavonoids                                             | [153] |
| Sansevieria spp. | Rhizome, root | Methanol | LD50 of 352.5 ug/kg. The extract, n-hexane, ethyl acetate, and butanol fractions significantly protected mice from N. naja nigricollis venom-induced mortality                                                                 | Terpenoids, flavonoids, saponins                                   | [154] |
| (S. libérica ger. and labr) |              |              |                                                                                             |                                                                    |                          |
| Albizia spp. | Root/bark Water | 1000 mg/kg, N. kauothia venom, provided 50% protection from N. naja karachiensis PLA2 in terms of an increase in pH of an egg yolk suspension | Carbohydrates, proteins, alkaloids, flavonoids, tannins, echinocystic acid, amino acids | [109, 123, 125, 154] |
| (A. lebeck L. (Benth) bark) |              |              |                                                                                             |                                                                    |                          |
| Euphorbia species (E. hirta) | Whole plant | Methanol | LD50 not specified, against N. naja venom                                                                 | Quercetin-3-O-alpha-rhamnoside, terpenoids, alkaloids, steroids, tannins, flavonoids, phenolic compounds | [155, 156] |
| Bidens pilosa L. | Leaves, whole water, hexane | 1000 mg/kg, N. kauothia venom, provided 50% protection from N. naja karachiensis PLA2 in terms of an increase in pH of an egg yolk suspension | Carbohydrates, proteins, alkaloids, flavonoids, tannins, echinocystic acid, amino acids | [109, 123, 125, 154] |
| |              |              |                                                                                             |                                                                    |                          |

**Table 3** Antivenin activities of some plants used for snakebite treatment in Uganda as per global reports (Continued)**
methylene extracts of *Jatropha curcas* L. were more effective than the aqueous and chloroform fractions in inhibiting phospholipase A2 activity. The authors attributed this to the possible presence of divalent ions (Calcium (II), Strontium (II), and Barium (II) ions) or quercetin-like compounds which are reported to augment the activity of phospholipase A2 through induction of conformational changes in its substrate-binding sites [167, 168]. Table 3 summarizes some of the solvents employed by studies done on antivenom activity of some plants reported in this survey. It is worth noting that methanol appears to be the solvent of choice probably because of its ability to dissolve both polar and non-polar compounds [169, 170].

Testing for the efficacy of plants as antivenins has been perfected using mice as the test specimens. Experimentally, the extracts are tested against the lethal dose of the venom that causes death of 50% of the subjects (LD50). Tests are done either in vivo or in vitro on specific toxic activities of venoms. So far, the inhibitory activity of most extracts has been tested against phospholipase A2, one of the toxic constituents of snake venoms [111].

### Conclusions and recommendations

Uganda has over 125 districts hence less than 1% of the country have been surveyed for antivenin plants. The inventory of plants utilized by Ugandan communities present considerable potential for the treatment of snake envenomation. The present review therefore opens the lead for isolation and elucidation of the chemical structures of the antivenom compounds from the claimed plants that could be harnessed in combined therapy with commercial antiserum. There is a need for concerted efforts by scholars, traditional healers, local authorities, and the state to address the ongoing African snakebite crisis and meet World Health Organizations’ great interest in documenting the various medicinal plants utilized by different tribes worldwide.

### Supplementary information

**Supplementary information** accompanies this paper at https://doi.org/10.1186/s41182-019-0187-0.

**Additional file 1.** Family, local name, botanical name, growth habit, conservation status, part used, method of preparation and route of administration of antivenin plants used in different districts of Uganda.

**Abbreviations**

DPPH: 1,1-diphenyl 2-picrylhydroxyl; DPPH-1,1: Diphenyl 2-picrylhydroxyl; LD50: Median lethal dose; N. naja: Naja naja; PL A2: Phospholipase A2; spp: Species; V. russelli: Viper russelli

**Acknowledgements**

TO, KMK, and OB are grateful to the World Bank and the Inter-University Council of East Africa (IUCEA) for the scholarship awarded to them through the Africa Centre of Excellence II in Phytochemicals, Textiles and Renewable Energy (ACE II PTRE) at Moi University, Kenya, that prompted this ethnomedical communication. The authors commend preceding authors for their fruitful quest for knowledge on medicinal plants utilized by rural communities of Uganda.

**Authors’ contributions**

TO, SK, and OB designed the study. AO, TO, SS, and KMK performed the literature search. TO, AO, TO, KMK, and OB analyzed the collected data. TO, SK, TO, SS, and OB verified the plant names in botanical databases, Lusoga, Lango, Luganda, and Acholi, respectively. TO, SK, AO, TO, and OB wrote the first draft of the manuscript. All authors revised and approved the final manuscript.

**Funding**

This research received no external funding.

**Availability of data and materials**

This is a review article and no raw experimental data was collected. All data generated or analyzed during this study are included in this published article.

**Ethics approval and consent to participate**

Not applicable.
Consent for publication
Not applicable

Competing interests
The authors declare that they have no competing interests.

Author details
1. Department of Chemistry and Biochemistry, School of Biological and Physical Sciences, Moi University, Uasin Gishu County, Kesses, P.O.Box 3900-30100, Eldoret, Kenya. 2. Department of Paediatric and Child Health, Faculty of Medicine, Gulu University, P.O.Box 166, Gulu, Uganda. 3. Department of Biochemistry, Faculty of Health Sciences, Lira University, P.O.Box 1035, Lira, Uganda. 4. Directorate of Government Analytical Laboratory, Ministry of Internal Affairs, P.O.Box 2174, Kampala, Uganda. 5. Department of Manufacturing, Industrial and Textile Engineering, School of Engineering, Moi University, Uasin Gishu County, Kesses, P.O.Box 3900-30100, Eldoret, Kenya.

Received: 21 October 2019 Accepted: 26 November 2019

Published online: 11 February 2020

References
1. WHO. Guidelines for the production, control and regulation of snake antivenom immunoglobulins. Geneva: World Health Organization; 2010. https://www.who.int/immunization/technical_updates/antivenom_WHO_Guidelines_D1.pdf. Accessed 29 Sept 2019.
2. Gutierrez JM, Rojas E, Quezada L, Leon G, Nunez J, Laing GD, et al. Medicinal plants used in the treatment and prevention of malaria in Cegere community. J Ethnopharmacol. 2011;136:236–44.
3. Gallego R, Waterman B, Kiesige M. Snakebite management: experiences from Gulu Regional Hospital, Uganda. East Cent Afr J Surg. 2004;9(1–2). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1250224/
4. Snow RW, Bronzan R, Roques T, Nyamawi C, Murphy S, Marsh K. The prevalence and morbidity of snake bite and treatment seeking behavior among a rural Kenyan population. Annals Trop Med Parasitol. 1994;88:665–71.
5. Fact sheet snakebite incidents, response & antivenom supply (Uganda). 2018. https://aidsstream.org/files/documents/Fact-Sheet-Uganda-Research-Snakebite-20190128010145.pdf.
6. Gutierrez JM, Rojas E, Quezada L, Leon G, Nunez J, Laing GD, et al. Pan-African poyospecific antivenom produced by caprylic acid purification of viper (Echis carinatus): epidemiological studies in Nigeria and a review of the world literature. Acta Trop. 1976;33:307–41.
7. Thebaud RDG, Warrell DA, Griffiths E. Report of a WHO workshop on the standardization and control of antivenoms. Toxicon. 2003;41:541–57.
8. Wangodi R, Waterman B, Kiesige M. Snakebite management: experiences from Gulu Regional Hospital, Uganda. East Cent Afr J Surg. 2004;9(1–2). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1250224/
9. Ahmad R, Rajendran K, Jaiswal D, Singh HP, Mishra A, Chanda D, et al. Anti-viper venom activity of different extracts of Pouzolzia indica against Russell viper venom. Int J Chem Tech Res. 2010;2:744–51.
10. Gomes JAS, Felix-Silva J, Fernandes JM, Amaral JG, Lopes TP, Tabosa do Erito ES, et al. Aqueous leaf extract of Jatropha mollissima (Pohl) ball decreases local effects induced by Bothropic venom. BioMed Res Int. 2016. https://doi.org/10.1155/2016/6101742.
11. Anandram D, Calderon, et al. Biodiversity as a source of bioactive compounds against snakebite. Biotechn (NY). 1990;8:934–8.
12. Asuzu IU, Harvey AL. The antitoxin venom activities of Parkia biglobosa (Mimosaceae) stem bark extract. Toxicon. 2003;42:2753–8.
13. Austin MD, Dart RC. North American snake envenomation: diagnosis, treatment, and management. Emerg Med Clin N Am. 2014;32(2):433–43.
14. Daily Monitor. Using nature to get rid of snakes and their venom. 2019. https://www.monitor.co.ug/News/National/No-drugs-treat-snakebite-victims/688334-496070-ppq9rnlz/index.html.
15. Dreisbach RH, Robertson WO. Reptiles: snakes. In: A handbook of poisoning. 12th ed. Los Altos: a LANGE Medical Book; 1987.
16. Musah Y, Ameade EPK, Attuquayefio DK, Holbech LH. Epidemiology, ecology and human perceptions of snakebites in a savanna community of northern Ghana. PLoS Neg Trop Dis. 2019;13:8.
17. Owusu BO, Kisangau DP. Kenyan medicinal plants used as antivenin: a comparison of plant usage. Ethnobot Etnomed. 2006;27.
18. New Vision. Sleeping with snakes at Musambwa. 2018. https://www.newvision.co.ug/new_vision/news/1197460/sleeping-snakes-musambwa.
19. Gold BS, Barish RA, Dart RC. North American snake envenomation: diagnosis, treatment, and management. Emerg Med Clin N Am. 2014;32:433–43.
20. Figueiredo A, McKevey AD, Grimmer LL, Bell CD, Laiavons P. A species-level phylogeny of extant snakes with description of a new colubrid subfamily and genus. PLoS ONE. 2016;11:9.
21. New Vison. Many snake victims buried alive. 2013. https://www.newvision.co.ug/new_vision/news/1314577/snakebite-victims-buried-alive Accessed 23 July 2019.
22. Daily Monitor. No drug to treat snakebite victims. 2019. https://www.monitor.co.ug/News/National/No-drugs-treat-snakebite-victims/688334-496070-ppq9rnlz/index.html.
23. Guimaraes CLS, Moreira-Dill LS, Fernandes RS, Costa TR, Hage-Melwin LS. Calderon, et al. Biodiversity as a source of bioactive compounds against snakebites. Current Med Chem. 2014;21:2952–79.
24. Goswami PK, Sarratt M, Srivastava R. Snake venom, anti-snake venom & potential of snake venom. Int J Pharm Pharmaceut Sci. 2014;6(4).-7.
25. Kung TS, Georgieva D, Genov N, Murakami MT, Sinha M, Kumar RP, et al. Enzymatic toxins from snake venom: structural characterization and mechanism of catalysis. FEBS J. 2011;278:4544–76.
26. Janardhan B, V. S, Mirajkar KK, More SS. In vitro screening and evaluation o Janardhan B, Shirkhan VM, Mirajkar KK, More SS. In vitro screening and evaluation of antivenom phytochemicals from Azanza tetaacantha Lam. leaves against Bungarus caeruleus and Vipera russellii. J Venom Anim Toxins Ind Trop Dis. 2014;2012.
27. Devi CM, Bai MV, Lal AV, Umashankar PR, Krishnan LK. An improved method for isolation of anti-viper venom antibodies from chicken egg yolk. J Biochem Biophys Method. 2002;51:129–38.
28. Thekaekar RDG, Warrell DA. Crisis in antivenin supply for Africa. Lancet. 2000;356:2104.
29. Harrison RA, Hasson SS, Harsen M, Laing GD, Conrath K, Theakston RD. Neutralisation of venom-induced haemorrhage by IgG from camels and llamas immunised with viper venom and also by endogenous, non-IgG components in camelid sera. Toxicon. 2006;47:364–8.
30. Thallay BS, Carroll SB. Rattle snake and scorpion antivenoms from the egg yolks of immunised hens. Biotech (NY). 1990;8:934–8.
31. Asuzu IU, Harvey AL. The antitoxin venom activities of Parkia biglobosa (Mimosaceae) stem bark extract. Toxicon. 2003;42:2753–8.
32. Ahmed R, Rajendran K, Jaiswal D, Singh HP, Mishra A, Chanda D, et al. Anti-viper venom activity of different extracts of Pouzolzia indica against Russell viper venom. Int J Chem Tech Res. 2010;2:744–51.
33. Gomes JAS, Felix-Silva J, Fernandes JM, Amaral JG, Lopes TP, Tabosa do Erito ES, et al. Aqueous leaf extract of Jatropha mollissima (Pohl) ball decreases local effects induced by Bothropic venom. BioMed Res Int. 2016. https://doi.org/10.1155/2016/6101742.
34. Anwar G, Charlotte IEA, Klooster V, Byamukama R, Willcox M, Mulamuni PA, et al. Medicinal plants used in the treatment and prevention of malaria in Cegere sub-county. Northern Uganda. Ethnobot Res Appl. 2016;14:505–16.
35. Namukobe K, Kasenene JM, Kiremire BT, Byamukama R, Kamatenesi-Mugisha M, Krief S, et al. Traditional plants used for medicinal purposes in local communities around the northern sector of Kibale National Park. Uganda. J Ethnopharmacol. 2011;136:236–45.
36. Stangeland T, Aale EPE, Katuura E, Lye KA. Plants used to treat malaria in Nyakayojo sub-county. Western Uganda. J Ethnopharmacol. 2011;137:154–66.
37. Adia MM, Anwar G, Byamukama R, Kamatenesi-Mugisha M, Sekagya Y, Kakudidi EK, et al. Medicinal plants used in malaria treatment by Prometa herbalists in Uganda. J Ethnopharmacol. 2014;155:580–8.
38. Okello J, Siegawa P. Medicinal plants used by communities of Ngai Subcounty, Apac district. Northern Uganda. Afr J Ecol. 2007;45:76–83.
39. Hamill FA, Apio S, Mubiru NK, Mosango M, Bukanya-Ziraba R, Maganyi OW, et al. Traditional herbal drugs of Southern Uganda. J Ethnopharmacol. 2000;70:281–300.
preparatory study, draft of final report to Ministry of Health, Archive, Ministry of Health: Uganda, 1996.

40. Okullo JB, Omujal F, Biriginya C, Isibukulu P, Malinga M, Bizuru E, et al. Ethno-medical uses of selected indigenous fruit trees from the Lake Victoria basin districts in Uganda. J Med Plants Stud. 2014;2:78–88.

41. Oyeyemi C, Bukenya Ziraba R, Omagor N, Opio A. Medicinal plants of Erute county, Lira district, Uganda with particular reference to their conservation. Afr J Ecol. 2010;48:285–98.

42. Tabut JRS, Lye LA, Dhillon SS. Traditional herbal drugs of Bulamogi, Uganda: plants, use and administration. J Ethnopharmacol. 2003;88:19–44.

43. Lamoide M, Tabut JRS, Obua C, Kukunda-Byobona C, Lanyero Y, Byakaka-Kibwika P, et al. Medicinal plants used by traditional medicine practitioners for the treatment of HIV/AIDS and related conditions in Uganda. J Ethnopharmacol. 2008. https://doi.org/10.1016/j.jep.2010.04.004.

44. Opio DR, Andama E, Kureh GT. Ethnobotanical survey of antimalarial plants in areas of Abukama, Angeta, Ocukokori and Oumarri of Alebtong district in Northern Uganda. Eur J Med Plant. 2017;21:1–14.

45. Katura E, Waako P, Owgwal-Okeng J, Bukenya-Ziraba R. Traditional treatment of malaria in Mbarara district. Western Uganda. Afr J Ecol. 2007;45:48–51.

46. Kamatenesi MM, Acipa A, Oyeyemi-Origa H. Medicinal plants of Otway and Ngi Sub counties in Oyam district. Northern Uganda. J Ethnobiol Etnomed. 2011;7:77.

47. Nambejja C, Tugume P, Nyakoojo C, Kamatenesi-Mugisha M. Medicinal plant species used in the treatment of skin diseases in Kataba subcounty, Wakiso district, Uganda. Ethnobot Res Appl. 2019;18:1–17.

48. Segawa P, Kaseneje JM. Plants for malaria treatment in Southern Uganda: Traditional use, preference and ecological viability. J Ethnobiol. 2007;27:110–31.

49. Tugume P, Kakudidi EK, Buyinza M, Namukolo J, Kamatenesi M, Mucunguzi P, et al. Ethnobotanical survey of medicinal plant species used by communities around Mabura Central Forest Reserve, Uganda. J Ethnobiol Etnomed. 2016;125.

50. Kodji P, Mwangi ME, Kiplagat CP, Karuki TS. Ethnobotanical survey of antimalarial medicinal plants used in Butere county. Eastern Uganda. Eur J Med Plant. 2017;21:1–22.

51. Oyeyemi-Origa H, Kakudidi EK, Katende AB, Bukenya-Ziraba R. Utilization of medicinal plants in Bundibugyo district, Uganda. In: Kinyua A, Kofi-Tsekpo WM, Dangana LB, editors. Conservation and utilization of indigenous medicinal plants and wild relatives of food crops. Nairobi: UNESCO; 1997. p. 75–80.

52. Tabut JRS, Kukunda CB, Waako WJ. Medicinal plants used by traditional medicine practitioners in the treatment of tuberculosis and related ailments in Uganda. J Ethnobiol Etnomed. 2010;17:130–6.

53. Tabut JRS, Dhillon SS, Lye KA. Traditional medicine in Bulamogi County, Uganda. Its practitioners, users & viability. J Ethnobiol. 2003;85:119–29.

54. Kakudidi EK, Bukenya-Ziraba R, Kaseneje JM. The medical plants in and around Kibale National Park in western Uganda. Lidia. 2004;1:99–104.

55. Kibuuka MS, Anywar G. Medicinal plant species used in the management of helminths by traditional medicine practitioners in central Uganda. Ethnobot Res Appl. 2015;14:289–98.

56. Katura E, Kalabala E, Lubega A. Uterotonic potential of selected plants used by Ugandan local communities in the treatment of malaria. Eur J Med Plant. 2018;24:1–12.

57. Tabut JRS, Kukunda CB, Kwesesi D, Kasito OMU. Herbal medicine used in the districts of Nakapiripirit, Pallisa, Kanungu and Mukono in Uganda. J Ethnobiol Etnomed. 2012;8:35.

58. Kalumansi P, Kamatenesi Mugisha M, Anywar G. Medicinal plants used in paediatric health care in Namungale sub county, Iganga district, Uganda. Nova J Med Biol Sci. 2014;2:1–11.

59. Lacroix D, Prado S, Kamoga D, Kasenene J, Namukobe J, Krief S, et al. Medicinal plant species used by the people in the Region of Randa. J Ethnobiol Ethnomed. 2011;7:3.

60. Shah A, Sarvat R, Shoaib A, Ayodele AE, Nadeem M, Qureshi TM, et al. An ethnobotanical survey of medicinal plants used for the treatment of snakebite and scorpion sting among the people of Narval valley, Manwalli district, Punjab, Pakistan. Appl Ecol Environ Res. 2016;18:111–43.

61. Hassan-Abdallah A, Merito A, Hassan S, Abouabaker D, Djama M, Assaf Z, et al. Medicinal plants and their uses by the people in the Region of Randa. Djiibouti. J Ethnobiol Ethnomed. 2013;148:701–13.

62. Abd E-G. Traditional medicinal plants of Nigeria: an overview. Agric Biol J N Am. 2016;7:220–47.

63. Ndad NR, Egie AE, Bechim EET, Asaha S, Yengo T, Chia EL, et al. Ethnobotanical study of commonly used medicinal plants of the Takamanda Rainforest South West Cameroon. Afr J Plant Sci. 2013;7:21–34.

64. Upasani SV, Beldar VG, Tattiya AU, Upasani MS, Suresh SJ, Patil DS. Ethnomedical plants used for snakebite in India: a brief overview. Integ Med Res. 2017;6:114–30.

65. Kumar SJU, Chaitanya KMJ, Semotiuk AJ, Krishna V. Indigenous knowledge of medicinal plants used by ethnic communities of South India. Ethnobot Res Appl. 2019;18:10017.

66. Shah A, Sarvat R, Shoaib A, Ayodele AE, Nadeem M, Qureshi TM, et al. An ethnobotanical survey of medicinal plants used for the treatment of snakebite and scorpion sting among the people of Narval valley, Manwalli district, Punjab, Pakistan. Appl Ecol Environ Res. 2016;18:111–43.

67. Hassan-Abdallah A, Merito A, Hassan S, Abouabaker D, Djama M, Assaf Z, et al. Medicinal plants and their uses by the people in the Region of Randa. Djiibouti. J Ethnobiol Ethnomed. 2013;148:701–13.

68. Upasani SV, Beldar VG, Tattiya AU, Upasani MS, Suresh SJ, Patil DS. Ethnomedical plants used for snakebite in India: a brief overview. Integ Med Res. 2017;6:114–30.

69. Alkhalifa A, Alhajeri R, Alrayes R, Alshehri R, Alshamsan A, Alshamsan S. A randomized ethnomedical survey of snakebite treatment in southwestern parts of Bangladesh. J Tradit Complement Med. 2019;9:1–14.

70. Kadir MF, Sayeed MSB, Shams T, Mia MMK. Ethnobotanical survey of antidiabetic plants and their active constituents. Int J Adv Med Life Sci. 2017;6:114–60.

71. Nambejja C, Tugume P, Nyakoojo C, Kamatenesi-Mugisha M, Kambbenya R, et al. Medicinal plants used in the treatment of malaria in the Namasakwa sub-county, Iganga district, shops plant sector review: pharmaceuticals promoting programme.
142. Janardhan B, Shrikant VH, Mirikar KS, More SS. In vitro anti-snake venom properties of Carissa spinarum Linn leaf extracts. J Herbs Spices Med Plant. 2015;21:283–93.

143. Mathuram V, Brahmadhayalessavan A. Chemical constituents of carissa spinarum and their antibacterial activity. J Indian Chem Soc. 1998;75:262–4.

144. Delmut MB, Leila MLP, Paula JR, Concioaco EC, Santos AS, Pfrimer IA. Cassia occidentalis: Effect on skin wound healing in mice induced by Bootrops moojeni venom. J Pharm Technol Drug Res. 2013;2:1–6.

145. Yadava RN, Satnami DK. Chemical constituents from Cassia occidentalis Linn. Indian J Chem. 2011;50B:1112–8.

146. Uggulu I. Traditional ethnobotanical knowledge about medicinal plants used for external therapies in Alasehir, Turkey. Int J Med Aromat Plants. 2011;1:101–6.

147. Núñez V, Otero R, Barona J, Fonneraga R, Jiménez S, Osorio RG, et al. Inhibition of the toxic effects of Lachesis muta, Crotalus durissus cumanensis and Micrurus mirapitus snake venoms by plant extracts. Pharm Biol. 2004;42:49–54.

148. Parimala B, Boominathan R, Mandel SC. Evaluation of anti-inflammatory activity of Cleome viscosa. Indian J Nat Prod. 2003;19:8–12.

149. Abubakar UD, Walde FT. Phytochemical screening and elemental analysis of the Crinum jagus bulb. J Chem Soc Nigeria. 2017;42:53–5.

150. Ode OJ, Asuzu IU. The anti-snake venom activities of the methanolic extract of the bulb of Crinum jagus (Amaryllidaceae). Toxicon. 2006;48:331–42.

151. Kadiin S. Comparative, antibacterial, anti-venom and phytochemical studies of Indigofera capitata Kotschy and Indigofera conferta Gillett in albino rats. PhD thesis. Nigeria: Ahmadu Bello University; 2016.

152. Musa AM, Sule MI, Haruna AK, Ilyas M, Ilya I, Yaro AH, et al. Preliminary gastrointestinal studies of methanol extract of Indigofera pulchra wild in rodents. Niger J Pharm Sci. 2008;7:86–92.

153. Sonibare MA, Aremu OT, Okorie FN. Antioxidant and antimicrobial activities of solvent fractions of Vernonia cinerea (L). Less leaf extract. Afr Health Sci. 2016;16:529–39.

154. Chiou YL, Shinne R, Wan PH, Long SC. Quercetin modulates activities of the Crinum jagus bulb. J Chem Soc Nigeria. 2017;42:53–5.

155. Akah AP, Nwagu TS, Oforkansi MN. Evaluation of the anti-snake venom activity of leaf extract of Sansevieria liberica ger& labr (Agavaceae) in mice. Int J Sci. 2019;8:60–8.

156. Byamukama R, Barbarea G, Namukobe J, Heydenreich M, Kiremire BT. Antioxidant activity of crude and methanol extracts of Carisssa spinarum Linn leaf extracts. J Herbs Spices Med Plant. 2015;21:283–93.

157. Gopi K, Anbarasu K, Renu K, Jayanthi S, Vishwanath BS, Jayaraman G. Bioactive compounds in the stem bark of Albizia coriaria (Welw. ex Oliver). Int J Biol Chem Sci. 2015;9:397–401.

158. Kadiri S. Comparative, antibacterial, anti-venom and phytochemical studies of Indigofera capitata Kotschy and Indigofera conferta Gillett in albino rats. PhD thesis. Nigeria: Ahmadu Bello University; 2016.

159. Ugulu I. Traditional ethnobotanical knowledge about medicinal plants used for external therapies in Alasehir, Turkey. Int J Med Aromat Plants. 2011;1:101–6.

160. Chian J, Yau E, Ho S. Antioxidant and antimicrobial activities of solvent fractions of Vernonia cinerea (L). Less leaf extract. Afr Health Sci. 2016;16:529–39.

161. Chiou YL, Shinne R, Wan PH, Long SC. Quercetin modulates activities of the Crinum jagus bulb. J Chem Soc Nigeria. 2017;42:53–5.

162. Ode OJ, Asuzu IU. The anti-snake venom activities of the methanolic extract of the bulb of Crinum jagus (Amaryllidaceae). Toxicon. 2006;48:331–42.

163. Kadiin S. Comparative, antibacterial, anti-venom and phytochemical studies of Indigofera capitata Kotschy and Indigofera conferta Gillett in albino rats. PhD thesis. Nigeria: Ahmadu Bello University; 2016.

164. Musa AM, Sule MI, Haruna AK, Ilyas M, Ilya I, Yaro AH, et al. Preliminary gastrointestinal studies of methanol extract of Indigofera pulchra wild in rodents. Niger J Pharm Sci. 2008;7:86–92.

165. Sonibare MA, Aremu OT, Okorie FN. Antioxidant and antimicrobial activities of solvent fractions of Vernonia cinerea (L). Less leaf extract. Afr Health Sci. 2016;16:529–39.

166. Chian J, Yau E, Ho S. Antioxidant and antimicrobial activities of solvent fractions of Vernonia cinerea (L). Less leaf extract. Afr Health Sci. 2016;16:529–39.

167. Assefa A, Urga K, Guta A, Melaku D, Mekonen W, Melesse M, et al. Spasmolytic activity of the aqueous root extract of Solanum incanum. J Ethnopharmacol. 2000;24:259–63.

168. Reddi KVNR, Rajesh SS, Narendra K, Jangala S, Reddy PCO, Satya AK, et al. In vitro anti-venom potential of various Jatropha extracts on neutralizing cytotoxic effect induced by phospholipase A2 of crude venom from Indian cobra (Naja naja). Bangladesh J Pharmocol. 2014;2:22–8.

169. Jang MS, Fletcher JE, Smith LA. Factors influencing the hemolysis of human erythrocytes by Crotalus durissus terrificus from Naja naja kanutha and Naja naja atra venoms and a phospholipase A2 with cardiotoxin-like activities from Bungarus fasciatus venom. Toxicon. 1989;27:247–57.

170. Encyclopaedia Britannica. Methanol. https://www.britannica.com/science/methanol.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.