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Antivenin Plants Used for Treatment of Snakebites in Uganda: Ethnobotanical Reports and Pharmacological Evidences

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Abstract

Snakebite envenomation, cognized as a neglected tropical disease, is a dread public health concern with the most susceptible groups being herdsmen, the elderly, active farmers, hunters, fishers, firewood collectors, 10 to 14-year old working children and individuals with limited access to education and health care. Snakebites are fragmentarily documented in Uganda primarily because most occur in rural settings where traditional therapists end up being the first line defence for treatment. Ethnobotanical surveys in Uganda have unveiled that some plants are used to antagonize the activity of various snake venoms. This review was sought to compile the sporadic information on the vegetal species reported as antivenins in Uganda. Electronic data indicate that no study entirely reported on antivenin plants in Uganda. A total of 77 plant species belonging to 65 genera, distributed among 42 botanical families claimed as antiophidic in Uganda are used for treatment of snakebites. Majority of these species belong to family Fabaceae (30.9%), Euphorbiaceae (14.3%), Asteraceae (11.9%), Amaryllidaceae (9.5%) and Solanaceae (9.5%). The antiophidic species listed are shrubs (40.5%), trees (32.9%) and herbs (17.7%), usually found in the wild and uncultivated. Antivenin extracts are primarily prepared from roots and leaves, through decoctions, infusions, powders and juices and administered orally or topically. The most frequently encountered therapeutically important species are *Allium cepa* L., *Carica papaya* L., *Securidaca longipedunculata* Fres., *Harrisonia abyssinica* Oliv. and *Nicotiana tabacum* L. Baseline epidemiological data on snake envenomation and antivenin plants in Uganda remain incomplete due to inadequate research and diverse ethnic groups in the country. There is a dire need to isolate and characterize the bioactive compounds in the claimed plants to enable their adroit utilization in handling the plague of snake envenomation. More baseline data should be collected on snake ecology and human behaviour as well as antivenin plants in Uganda. Indigenous knowledge on the use of plant preparations in traditional medicine in Uganda is humongous, but if this is not quickly researched and appropriately documented, indications as to the usefulness of this vegetal treasure house will be lost in the not so distant future.

Keywords: Antiophidic, antivenin plants, envenomation, ethnobotany, ethnomedicine, phospholipase A_2, snakebite, traditional medicine, Uganda.

1.0 Introduction

Snake envenoming is an innocuous global wathe and a justification for morbimortality and socio-economic losses. A recent conservative estimate point that about 5.5 million snakebite cases are encountered every year, of which 2 million victims succumb to death (including fright deaths) while

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0.4 million get lifelong disability [1, 2]. Up to 500, 000 of these cases are reported annually in Africa [3-5] while a lion share of 4 million is reported in Asia (with 100,000 cases resulting into death) [6]. In 2002, 108 cases of snakebites were reported in Gulu Regional Hospital (Uganda) though none of the victims died [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 to June and then October to December [8].

In the neighbouring Kenya, an estimate of 151 snakebite cases per year was esimated in 1994, with only 19% of the cases being from venomous snakes [9]. Nonetheless, non-poisonous snakebites are equally unsafe, as these may be accompanied by bacteria such as *Clostridium* species and other anaerobes that are part of the oral microbiota of the snake [7]. In reality, most fatalities occur because of lack of commercial antidotes within the 24 hours recommended [7, 10, 11], as most cases are registered in remote areas, which have poor access to suboptimal health services, leave alone the preclusive costs involved in procuring the antidotes. Worse still, due to its storage difficulty and short expiry, the use of snake venom antiserum is restricted. It also has administration problems, the exact dosage being another current medical problem [12, 13].

Snakes are taxonomically carnivorous vertebrates of the class Reptilia, order Squamata, sub-order Serpentes and families : Colubridae**,** Boidae**,** Elapidae, Pythonidae**,** Viperidae that characteristically kill their prey with constriction rather than envenomation, though venomous snakes are prevalent in most continents of plant earth with the exception of Antarctica, Ireland, New Zealand and many small islands of the Atlantic and Central Pacific region [14, 15]. Most bites are due to circumstantial stepping on the snakes by unprotected or barefooted victims [7, 16], snake ecology [17], while a few others are initiated by malevolent victims [18, 19] and alcohol intoxications [20]. Over 3,500 species of snakes have been taxonomically reported [21]. Approximately 600 (15-17%) of these are venomous and 200 (5.7%) are regarded as medically significant [1, 21]. East Africa is a home to about 200 species of snakes of the over 400 species in Africa; 145 of these belonging to 45 genera and 7 families are found in Uganda [22]. Many are harmless or are a rarity, but the six most poisonous species in Uganda include 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*) (**Figure 1**) [11, 23]. Snake venom is secreted by the oral glands, which is a modification of the parotid salivary gland, situated on each side of the head below and behind the eye and encapsulated in a muscular sheath. The venom is usually injected or inoculated into the victim subcutaneously or intravenously via tubular or channelled (modified) teeth-the fangs on the hands, feet, arms or legs [24]. Venoms are water-soluble, acidic and have specific gravity of about 1.03 [25]. Cobra venoms are noted to be characteristically neurotoxic and exert their effect on the central nervous system, causing heart failure. However, the quantity, lethality, and composition of venoms vary considerably with the age and species of the snake, time of year, geographic location as well as the envenoming snake's diet. Another striking property is that venoms are highly stable, typically refractory to temperature changes, desiccation, and drugs.

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Figure 1. The six venomous snake species in Uganda. (a) *Bitis arietans*, (b) *Bitis gabonica*, (c) *Dendroaspis jamesoni*, (d) *Dendroaspis polylepis*, (e) *Naja melanoleuca* and (f) *Naja naja nigricollis* (Source: [23])

A snake venom is biochemically a complex mixture of pharmacologically active toxic proteins (enzymatic and non-enzymatic) such as L-amino acid oxidases (LAAOs), cardiotoxins, neurotoxins, snake venom metalloproteinases (SVMPs), nucleotidases, phospholipases A_2 (PLA_2s), snake venom serine proteinases (SVSPs), acetylcholinesterase (AChE) nitrate, snake venom hyaluronidases (SVHs), phosphomonoesterase and phosphodiesterase [26] which are chiefly injected to immobilize the victim [11, 27]. The toxins cause haemotoxicity-damage to blood vessels resulting in spontaneous systemic bleeding (petechiae, ecchymosis, haematemesis, haematuria), muscle paralysis, myolysis, haemolysis, arrhythmias, cardiac and renal failure from shock or haemoglobinuria [7].

At present, serum antivenom immunotherapy is the mainstay of treatment reported for snake envenomation [7, 11, 18, 27]. Antisera are either derived from horse serum after injecting the horse with sublethal doses of snake venom (Antivenin (Crotalidae) Polyvalent, ACP) or sheep serum (Crotalidae Polyvalent Immune Fab (Ovine) or CroFab™) [20]. Though antivenin is lifesaving, it carries some side effects such as development of immediate or delayed hypersensitivity (anaphylaxis or serum sickness). For efficacy, the antidote should be administered within 4-6 hours of the snakebite. The side effects of intravenous antivenoms are thought to be the aftermath of the action of non-immunoglobulin proteins present in higher concentrations in the antivenom [28]. Worse still, there is paucity of snake antivenom serum in rural Africa that even in the presence of money, it may not be readily available for purchase [7, 18]. This is in part, attributable to the decline in antivenom production in Africa due to denationalization of the manufacturing industries by African countries [29], lack of ready market and low profits from sale of snake venom antiserum. In this perspective, several attempts have been made to develop snake venom antagonists from other sources including plants, dogs, rabbits, camelids and avian eggs [13, 28, 30-34].

Exceptionally, the use of plants in folklore and 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, studies have revealed that over 230 species of angiosperms belonging to over 168 genera and 69 families are being utilized in herbal medicine [35-61] and some have been cited as potential antivenins for snakebites. Aside from the cited reports, a large portion of Uganda still remain unsurveyed ethnobotanically [62] because of the presence of many tribes with different cultural practices. This review compiled information on antivenin plant species reported in different districts of Uganda, parts used, conservation status, their

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mode of preparation and administration and presented some experimental evidences supporting their use.

2.0 Methodology

2.1 Description of the study area

Uganda, the pearl of Africa [63] is a landlocked country straddling the equator in Eastern Africa. 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 (**Figure 2**). The climate of Uganda is purely equatorial, moderated by relatively high altitudes with mean annual temperature of 16°C to 25°C.

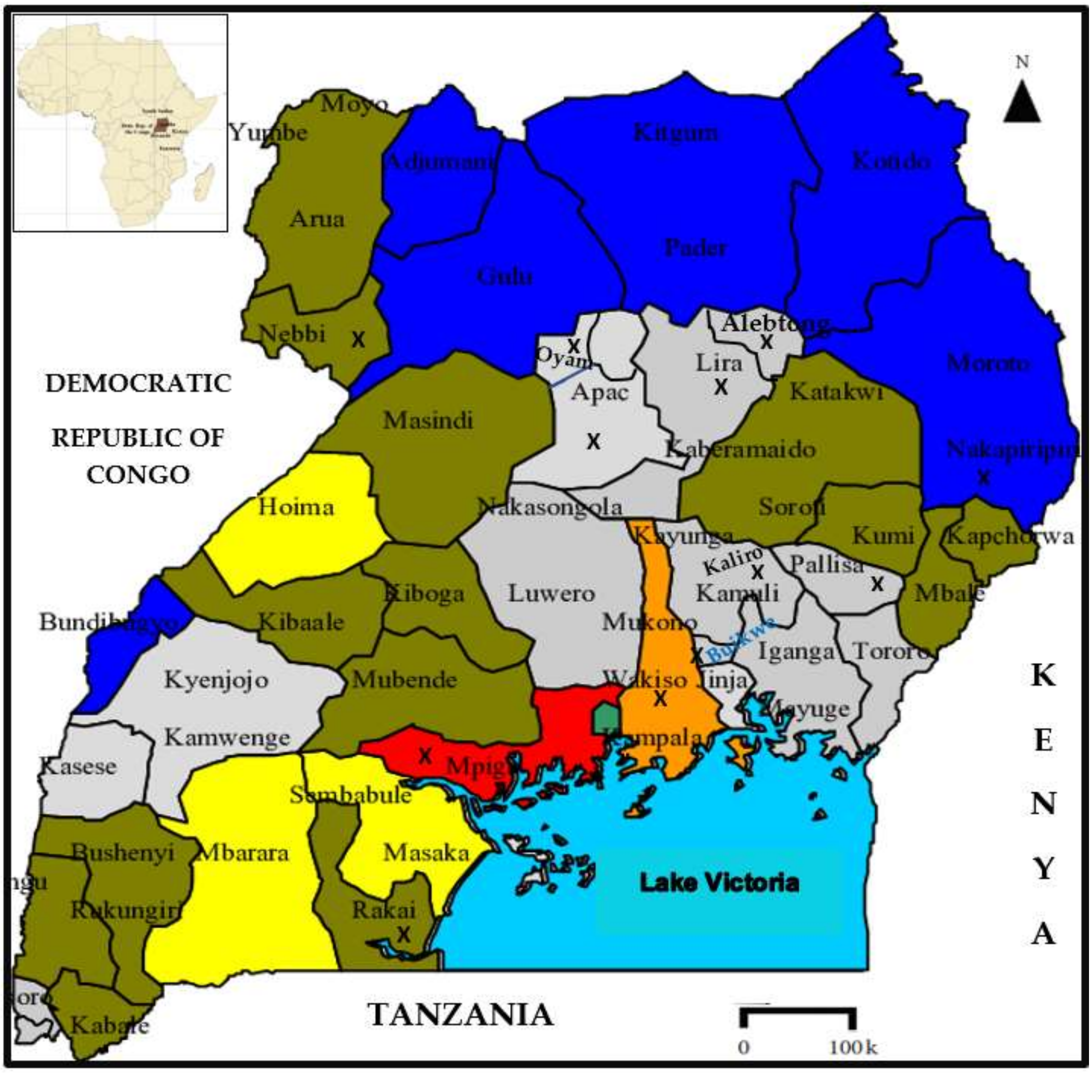

Figure 2. Map of Uganda showing the location of the districts with reports of ethnobotanical surveys (marked **X**). Inset is the location of Uganda on the African continent.

The country's population is conservatively estimated to be at 35.92 million (1.5 million of these are living with HIV/AIDs) with five main ethnic groups namely: The Nilotics (Lango, 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 which include the

Lugwara, Madi and Lendu [64]. Its land expanse covers a surface area of 93,064 square miles, with 82% of it agriculturally productive [65] . Non-degraded forest accounts for 6,500 km^2 (2.7%). The rest of the land cover is grassland (21.1%), scrub woodland (16.5%), water (20%), and bush (5.9%).

Uganda is divided into ten agro-ecological zones: Southern highlands, Southern drylands, Lake Victoria crescent, Eastern, Mid Northern, Lake Albert crescent, West Nile, Western highlands, South East and Karamoja drylands with 80% of the population who are agriculturalists living in rural areas [65-67]. In the presence of fertile soils and regular rainfall, environmental degradation, lack of good farming skills, and shortage of quality livestock hamper farmers' attempts to escape chronic poverty and makes many of the rural population subsistence farmers. Agriculture employ 80% of the population, contributing about 24 % to the Gross Domestic Product [64]. Health care services are inadequate to address the various sicknesses such as malaria (the leading cause of mortality), HIV/AIDS related diseases (diarrhea and respiratory infections-tuberculosis), measles, polio, diarrhoea, cough and skin infections [68]. Though a number of pharmaceutical industries have been set up, synthetic drugs are still not readily available in rural areas due to their prohibitive costs, poor transport network and chronic poverty. In fact, the sturdy resistance offered by pathogens to synthetic drugs is almost throwing Uganda into a post-antibiotic era [69] with the result that many (close to 80%) depend on herbal pharmacopoeias and the traditional herbalists for daily health care [68, 70].

2.2 Literature search strategy

Relevant literature pertaining to snakes, snakebites and medicinal plants in Uganda were selected from Scopus [71], Web of Science [72], PubMed [73], Science Direct [74], Google Scholar [75] and Scientific Electronic Library Online (SciELO) [76], from July 2019 to September 2019. These are the popular multidisciplinary platforms of modern researchers. EndNote® (version X7) was chosen as the bibliographic software for instant citation and bibliographic formatting .

2.3 Selection of articles for review

The study database included original articles published in peer-reviewed journals, as well as books, thesis, dissertations, patents, and other reports covering antiophidic plants, dated until September 2019. All publishing years were considered. Articles particularly pertaining to either snake bites or medicinal plants or snakes in Uganda were given priority. Because of this, references contained within the returned results were assessed concerning inclusion in this study, and further searches were carried out at the Google search engine [77] using more general search terms, to broaden the search, as follows: words "plant" **or** "plants" **or** "plant extract" **or** "vegetal" **or** "vegetal species" **or** "vegetal extract" **or** "traditional medicine" **or** "alternative medicine" **or** "complementary therapy" **or** "natural medicine" **or** "ethnopharmacology" **or** "ethnobotany" **or** "herbal medicine" **or** "herb" **or** "herbs" **or** "decoction" **or** "infusion" **or** "macerate" **and** "snake venom" **or** "snake" **or** "snakes" **or** "snakebite" **or** "snakebites" **or** "antivenom" **or** "antivenoms" **or** "antivenom" **or** "anti-venoms" **or** "antivenin" **or** "antivenins" **or** "anti-venin" **or** "anti-venins" **or** "antiophidian" **or** "antiophidic" **or** "snake envenomation" **or** "antitoxin" **or** "antitoxins" **or** "snake antidote" **or** "snake antidotes" **or** "snake venom neutralization" **or** "snake venom inhibition" **or** "snake toxins inhibition" **or** "snake toxins neutralization" **or** "viper" **or** "viperidae" **or** "crotalinae" **or** "viperinae" **or** "elapidae" **or** "mamba" **or** "cobra" **or** "naja" **or** "bitis" **or** "vipera", ''envenomation'', ''Uganda'' were used.

3.0 Results and Discussion

Only results in the ''article'' category, in English, Lango, Acholi, Ateso, Luganda, Lunyoro (Rukiga) and Lusoga, were considered. The sciencometric search gave relatively few results, mostly in English, indicating that investigation of medicinal plants and snakebites in Uganda have been done by a few investigations. After the multidisciplinary database and Google search engine result assessments, the following reports of interest specifically on the subject of antivenins in Uganda were retrieved (**Table 1**).

The botanical names of antivenin plants listed were vetted in at least two botanical databases: The Plant List [78], International Plant Names Index (IPNI) [79], NCBI taxonomy browser [80] or Tropicos [81]. Where a given species was considered as distinct species in different reports, the nomenclature as per the botanical databases above took precedence in the review, highlighting the synonyms employed in the original reports in parentheses. The botanical families used, the plant local names (Lango, Acholi, Ateso, Luganda, Lunyoro (Rukiga) and Lusoga), the life form, part(s) used, conservation status, preparation and administration mode, status of antivenin activity investigation of the plants and the districts where the antiophidic plants were reported are recapitulated (**Additional file 1)**. Pertaining to pharmacological evidence, the snake species studied as per global reports, the active phytochemicals reported and tested (with median lethal doses, LD_{50} where applicable) and that presented positive results in the plant species (or same genus) identified by the ethnobotanical surveys 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.

3.1 Traditional concept of snakebites in Uganda

From the electronic survey of data, it is indubitable that local communities in Uganda have a traditional concept of snakebites. In point of fact, beliefs about snakes play a pivotal role in the health behaviour of communities as well. The beliefs appear to be clan-related, and include some such as snakes ''can protect'' or ''are dangerous'' to clans and are associated with superstition and witchcraft [8]. Some species of snakes for example, are avoided when found because killing them is believed to cause headache to the concerned (**Omara, 2019, personal communication**). On Musumbwa island, Rakai district on Lake Victoria, islanders believe that black cobras are signs of good luck (spirits), and their presence in a house should not be of concern as they do not bite anyone [19, 82]. In Doho rice scheme, Butaleja district of Uganda, snakes are usually found preying on rats that eat spilt rice grains and do not harm farmers in the scheme unless when they are attacked [19]. By comparison, the Luo people of the neighbouring Kenya tend to associate presence of snakes with witchcraft [83].

Most Ugandans know that their current social conditions such as poverty, sleeping in houses made of mud and reeds, and occupations (cultivation, hunting, herding cattle) increase the chances of getting bitten by a snake. Snakebites are always taken as exigencies and the economic implications are considered as being high due to the costs for transport to the health facilities, the care needed by victims, enforced borrowing, loss of legs and arms, and the loss of income and time [8].

3.2 Antivenin plants, parts used, preparation and administration methods in rural communities of Uganda

The use of plants for treatment of snakebites is not novel in rural communities [18, 84-90] and cases handled using antivenin plants rarely record victims succumbing to death [18, 86, 91, 92]. As per the data gathered by this review, 77 plant species from 65 genera and belonging to 42 botanical families

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claimed as antiophidic were retrieved. A summary of these vegetal species is presented in **Table 1.** The most cited families were Fabaceae (30.9%), Euphorbiaceae (14.3%), Asteraceae (11.9%), Amaryllidaceae (9.5%) and Solanaceae (9.5%) (**Table 1**, **Figure 3**). Most botanical families encountered in this study have reported antivenin potential in treating or avoiding snakebites in other countries across the globe. For example, Apocynaceae, Aristolochiaceae, Asteraceae, Convolvulaceae, Fabaceae and Myricaceae families were cited in Kenya [18] and Tanzania [93], Meliaceae in Ghana [94], Fabaceae in Rwanda [95] , Asparagaceae, Leguminosae, Menispermaceae in Sudan [96], Acanthaceae, Apocynaceae, Asteraceae, Capparaceae, Cariaceae, Combretaceae, Convulaceae, Ebenaceae, Eurphorbiaceae, Fabaceae, Malvaceae, Meliaceae, Poaceae in Ethiopia [97] and Pakistan [98], Fabaceae, Aristolochiaceae and Lamiaceae in Djibouti [99] and Nigeria [100], Melastomataceae and Menispermaceae in Cameroon [101]. Acanthaceae, Apocynaceae, Asteraceae, Euphorbiaceae, Fabaceae, Moraceae, Rubiaceae and Rutaceae were cited in India [102, 103], Bangladesh [90, 91] and Central America [104]. Fabaceae is, for the most part, the dominant family in ethnobotanical reports presumably owing to global prevalence of the species from this family [90, 105-107]. These families were from different districts of Uganda (**Additional file 1, Figure 4**), representing different agroecological zones and ethnic groups with diverse cultural beliefs and practices. About 39.8% of the plant species were reported in Kaliro (South East agroecological zone) followed by 21.4% from Lira (Mid Northern) (**Figure 4).** In a similar cross-cultural comparison of antiophidic floras in Republic of Kenya, Owuor and Kisangu [18] reported that two culturally and floristically distinct African groups (the Kamba and Luo) had similar knowledge of snakebite conditions and etiological perceptions but the antivenin plants utilized by the two ethnic groups were approvingly independently derived.

Antivenin plants used in Uganda are majorly shrubs (40.5%), trees (32.9%) and herbs (17.7%) and the commonly used plant parts are roots (53.8%) and leaves (23.1%), followed by whole plant (4.4%), bark (4.4%) and tuber (4.4%) (**Figure 5, Figure 6**). The regular use of roots and leaves in antivenin preparations is a characteristic feature of traditional antivenin therapy [18, 97, 102, 108, 109], no wonder some of these plants are named ‘‘snakeroot’’ in some rural communities [110]. 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 the reports from other countries [18, 97]. Verily, majority of the antisnake venom shrubs and trees grow in the wild (81.6%), 14.4% are cultivated while 4% are semi-wild (occurs in the wild but can also be cultivated) (**Additional file 1**). 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 usually applied at the point of snakebite (topically) or ingested orally (**Additional file 1**).

In this survey, it was noted that few plant species are used against snakebites simultaneously in different districts and agro-ecological zones (**Figure 4, Additional file 1**). This could probably be attributed to the abundant distribution of the analogue active substances among species, especially belonging to family Fabaceae. Some of the plants listed are also used for wading off or discouraging snakes from reaching human and livestock abodes (**Table 2**). In most instances, the plants possess strong smell that cause discomfort and disorientation to snakes when they slither over them. In a few cases, as with tobacco, the plant (particularly dried whole plant or leaves) are burnt to produce strong unpleasant odour that discourage snakes. Among the Lango of Northern Uganda, burning of bicycle, motorcycle and vehicle tyres are also done to prevent snakes (**Omara, 2019, personal communication**).

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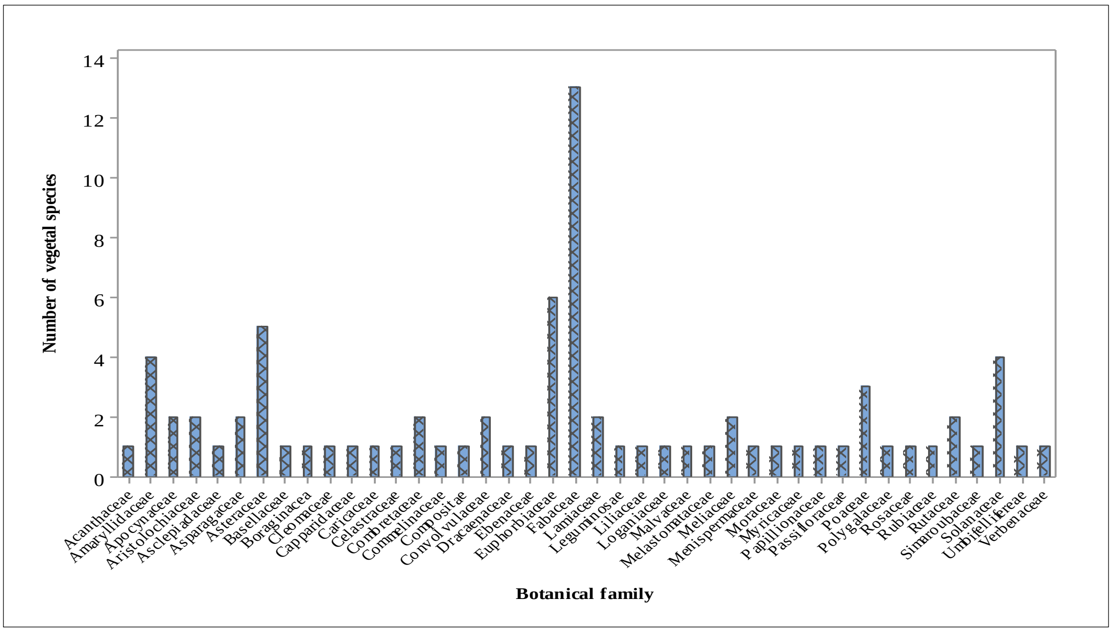

Figure 3. Families from which vegetal antivenins are obtained in Uganda

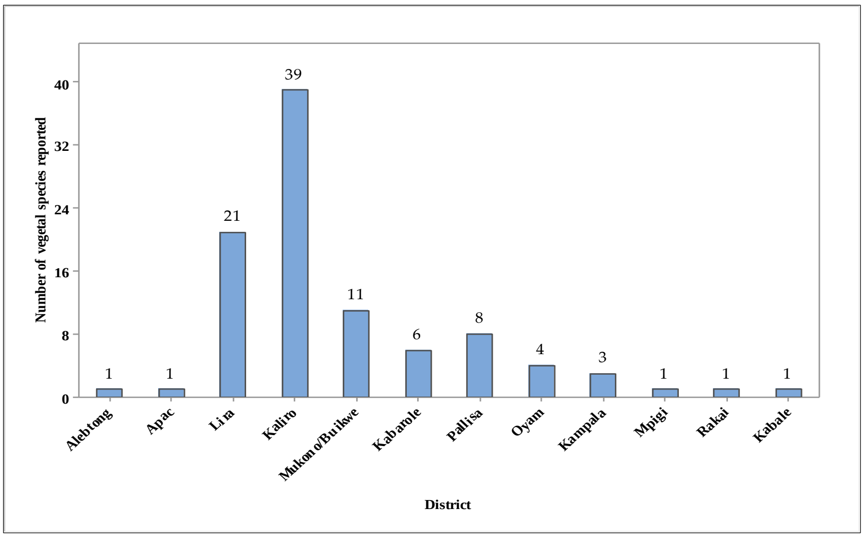

Figure 4. Distribution of the different species of antivenin plants in Ugandan districts as per ethnobotanical reports

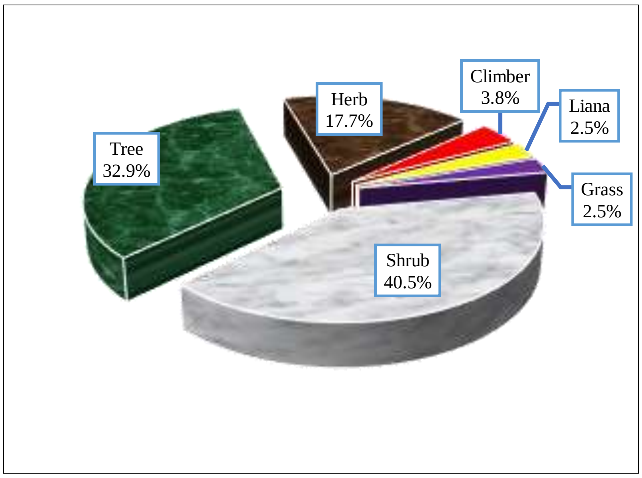

Figure 5. Life forms of the antivenin plants used by rural communities of Uganda

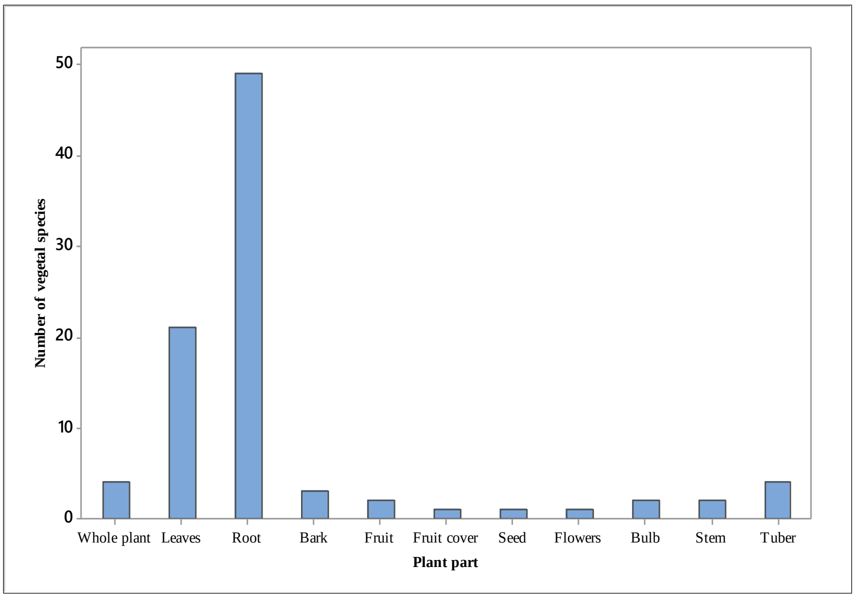

Figure 6. Different parts of antivenin plants used by the rural communities of Uganda

Almost all the plants recapitulated in this review are employed for the treatment of various maladies. For example, *Bidens pilosa* L., either as a whole plant or different parts, 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, wounds among others [111-114]. Such multifaceted plants tend to be used in different communities for treating snakebites and can be a justification of their pharmacological efficacy [115]. On the other hand, some of the antivenin plants cited tend to exhibit toxicity. A striking example is *Jatropha carcus* L., particularly the leaves and latex that are reported to contain a purgative oil (irritant curcanoleic acid and croton oil), curcin (toxalbumin) and diterpene of tigliane skeleton classified as phorbol esters [116]. Curcin has protein translation inhibitory activity or *N*-glycosidase activity whereas phorbol esters are amphiphillic molecules, with the ability to bind phospholipid membrane receptors [117]. This observation explains, in part, why some antivenin preparations in Uganda are applied topically. More so, topical application can provide better reduction of local action of venom proteins at the bitten site.

3.3 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 [35]. This is comparable to reports from other African countries [18, 94]. Some of the knowledge are gained through trainings as well as divine call. In some instances, the knowledge of which plant to be used can be asked for from the dead [43, 60]. Because of civilization, sometimes efforts to pass on this knowledge to children is impeded by dearth of interest and the salient fact that most children spend their youthful years in school [18, 35, 61].

3.4 Treatment of snakebites

Before a victim is rushed to the hospital for treatment, a quick first aid should be administered to prevent the venom from exceeding to the heart or other delicate parts of the body like the kidney. Some of the first aid treatments are given in **Table 3.** It is a general rule at thumb that the victim needs to be taken away to avoid any more snake bites and monitored to notice whether there is a change in voice. Victims with a hoarse voice implies the respiratory system have been affected [11]. First aid in the field or at home is important and should include procedures such as splinting the bitten limb, wound dressing with a firm bandage, reassurance and immediate transport to a medical facility where supportive therapy and antivenom are available [7, 20]. Procedures such as application of a loose tourniquet proximal to the bite, incision and suction of the fang marks and excision of the fang marks are controversial, may be helpful in skilled hands but are not advisable. If the snake is killed it should be identified. If it is non-poisonous, reassuring the patients is important. For less seriously ill victims, general supportive treatment is sufficient. Other proposed first aid measures for delaying the spread of venoms and scientific studies that support or refute them span beyond the scope of this review but have been recapitulated elsewhere [118].

In some communities like Lango of Northern Uganda, some therapy involves oral administration of egg yolk and albumin before treatment (Omara, 2019, personal communication). This has been too reported among the Luo of Kenya by Owuor and Kasangi [18], though pharmacological efficacy of these egg components warrant investigation. It can be thought that the proteins in the egg counteract the effects of the toxic proteins in the venoms.

3.5 Antivenin activity of plants and pharmacological evidences

Pharmacological studies have revealed that some plants used in traditional medicine are able to antagonize the activity of various crude venoms and purified toxins [88, 119, 120]. 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 [121], inactivation or enzyme inhibition [122], chelation [123], adjuvant action [124], antioxidant activity or a synergistic interaction of these mechanisms. Enzyme inhibition and protein precipitation are by far the most conventionally accepted mechanisms [125].

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 competitive blocking of the target receptors [126]. For example, atropine (an alkaloid reported in botanical family Solanaceae) is reported to inhibit activity of green and dark mambas (*Drendroaspis angusticeps* and *D. polylepsis*) venoms by blocking cholinergic nerve terminals (active sites) usually attacked by the venoms. Aristolochic acid I (8-methoxy-6-nitro-phenanthro(3,4-d)1,3-dioxole 5-carboxylic acid), an alkaloid present in *Aristolochia* species acts in the same way.

Another mechanism of snake venom inactivation entails inhibition of the active enzymes such as PLA_2, metalloproteases and hyaluronidases by polyphenolic compounds such as tannins. In this scenario, the metabolites interact with the venom enzymes by non-specific binding proteins [127], through hydrogen bonding with hydroxyl groups in the protein molecules, generating chemically stable complexes [128]. For example, in a study experimented with aristolochic acid I and PLA_2 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 [129]. Aristolochic acid I is also an inhibitor of hyaluronidase of *Naja naja* venom [130]. Other examples of these are outlined in **Table 4**.

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 PLA_2s and metalloproteases, secondary metabolites capable of disrupting the enzyme-metal ion bondage inhibits enzymatic progression [131]. 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 PLA_2 activity by selectively binding to the active sites or modifying the conserved residues that are inevitable for PLA_2 catalytic action [127].

The efficacy of plant extracts in antivenom action tends to be related with the solvent used for extraction of the bioactive compounds. For example, a study [132] reported that methanolic extracts of *Jatropa curcas* L. were more effective than the aqueous and chloroform fractions in inhibiting PLA_2 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 PLA_2 through induction of conformational changes in its active and substrate binding sites [133, 134]. **Table 4** summarizes some of the solvents employed by studies done on antivenom activity of some plants (or members of their genus) reported in this survey. It is worth noting that methanol appears the solvent of choice, because of its ability to dissolve both polar and non-polar compounds.

Wontedly, testing for the efficacy of plants as antivenins have been perfected using mice as the test specimens. Experimentally, the extracts are tested against lethal dose of the venom that cause death of 50% of the subjects (LD_{50}). 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 A_2 (PLA_2), one of the toxic constituents of snake venoms [119].

Conclusively, the subject of antivenins from plants will require obsessive efforts. Given the obvious untoward failures of antivenom serum therapy, such as its inability to effectively neutralize venom induced haemorrhage, myonecrosis and nephrotoxicity, this area requires immediate and devoted attention. In the case of Uganda, there is still a lot undone as very few studies such as that of Byamukama *et al.* [135] and Ocheng *et al.*[136] have subtly elucidated the phytochemical composition of some of the medicinal plants with antiophidic potential reported in this study. The present review, therefore, opens the lead for isolation and elucidation of the chemical structures of the specific venom inhibitory compounds from the claimed folklore plants that could be harnessed in combined therapy with antiserum, which could reduce snakebite deaths as well create income for the local communities.

Conclusion

Uganda has over 125 districts, thus less than 1% of the country have been ethnobotanically surveyed for antivenin plants. Most antiophidic plants used in Uganda are from families : Fabaceae, Euphorbiaceae, Asteraceae, Amaryllidaceae and Solanaceae. The most therapeutically important antivenin plants include *Allium cepa* L., *Trichilia ematica* Vahl, *Scadoxus multiflorus, Vernonia cinerea* (L) Less, *Acalypha bipartita* Muell. Arg., *Ricinus communis* L., *Indigofera arrecta* Host. A. Rich., *Pseudarthria hookeri* Wight & Arn., *Cissampelos muchronata* A.Rich., *Imperata cylindrica* (L.) P. Beauv, *Securidaca longipedunculata* Fres., *Harrisonia abyssinica* Oliv., *Nicotiana tabacum*, *Solanum aculeatissimum* Jacq and *Solanum incanum* L. From the electronic survey, it can be concluded that the inventory of plants utilized by Ugandan communities present a considerable potential for treatment of snake envenomation and wading off snakes from human settlements. More ethnobotanical surveys should be done in uncovered districts of Uganda. There is 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 of documenting the various plants medicinal plants utilized by different tribes worldwide.

Availability of data and materials

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

Supplementary material

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

Competing interests

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Authors' contributions

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

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Table 1. Antivenin plants used in rural communities of Uganda

Plant family	Latin Botanical name	Reference
Acanthaceae	*Asystasia schimperi* T. Anders.	[43]
Amaryllidaceae	*Allium cepa* L.	[42, 43, 50]
Amaryllidaceae	*Allium sativum* L.	[50]
Amaryllidaceae	*Crinum kirkii*	[42]
Amaryllidaceae	*Scadoxus multiflorus* (Martyn) Raf. (*Haemanthus multiflorus*)	[11, 43]
Apocynaceae	*Carrisa edulis*	[51]
Apocynaceae	*Thevetia peruviana* (Pers.) Schumann	[43]
Aristolochiaceae	*Aristolochia tomentosa* Sims.	[51]
Aristolochiaceae	*Aristolochia elegans* Mast.	[43]
Asclepiadaceae	*Cryptolepis sanguinolenta* (Lindl.) Schltr	[43]
Asparagaceae	*Sansevieria dawei* Stapf (*Sansevieria* species)	[39]
Asparagaceae	Sansevieria *trifasciata* var. trifasciata	[11]
Asteraceae	*Bidens pilosa* L.	[43]
Asteraceae	*Crassocephalum mannii* (Hook.f.) Milne-Redh.	[36]
Asteraceae	*Echinops amplexicaulis* Oliv.	[47]
Asteraceae	*Microglossa pyrifolia* (Lam.) O. Kuntze	[43]
Asteraceae	*Vernonia cinerea* (L) Less	[42, 43]
Basellaceae	*Basella alba* L.	[40]
Boraginacea	*Trichodesma zeylanicum* (L.) R.Br.	[42]
Cleomaceae	*Cleome gynandra* L.	[36]
Capparidaceae	*Capparis tomentosa* Lam.	[43]
Caricaceae	*Carica papaya* L.	[42, 43, 51]
Celastraceae	*Maytensus senegalensis* (Lam) Exell.	[42]
Combretaceae	*Combretum collinum* Fresen	[42]
Combretaceae	*Combretum molle* ex G.don. (*Combretum molle* G.don.)	[42]
Commelinaceae	*Murdannia simplex* Vahl. Branan	[36]
Compositae	*Aspilia africana* C.D Adams	[47]
Convolvulaceae	*Hewittia sublobata* L. Kuntze	[50]
Convolvulaceae	*Ipomoea batatas* (L.) Lam.	[43]
Dracaenaceae	*Dracaena steudneri* Engl.	[50]
Ebenaceae	*Euclea divinorum* Hiern	[43]
Euphorbiaceae	*Acalypha bipartita* Muell. Arg.	[43, 48]
Euphorbiaceae	*Croton macrostachyus* Hochst. ex. Delile	[50]
Euphorbiaceae	*Euphorbia tirucalli* L.	[36]
Euphorbiaceae	*Jatropha curcas* L.	[43]
Euphorbiaceae	*Ricinus communis* L.	[36, 43]
Euphorbiaceae	*Securinega virosa* (Willd) Baill.	[42]
Fabaceae	*Acacia seyal* Del. var. *fistula* (Schweinf.) Oliv.	[43]
Fabaceae	*Acacia* species	[43]
Fabaceae	*Albizia coriaria* (Welw. ex) Oliver	[43]
Fabaceae	*Canavalia ensiformis* L. D.C	[11]
Fabaceae	*Indigofera arrecta* Host. A. Rich.	[43, 50]
Fabaceae	*Indigofera garckeana* Vatk	[43]
Fabaceae	*Indigofera capitata* Forsk. (*Indigofera spicata* Forsk.)	[42]
Fabaceae	*Pseudarthria hookeri* Wight & Arn.	[43, 49]
Fabaceae	*Senna occidentalis* (L.) Link	[43]
Fabaceae	*Senna septemtrionalis* (Viv.) I. et B.	[40]
Fabaceae	*Senna siamea* (Lam.) Irwin & Barneby	[43]
Fabaceae	*Senna singueana* (Del.) Lock	[43]
Lamiaceae	*Hoslundia opposita* Vahl	[43]

Lamiaceae	*Plectranthus barbatus*	[38, 51]
Leguminosae	*Cassia occidentalis* L.	[36]
Liliaceae	*Anthericum cameroneii* Bak	[42]
Loganiaceae	*Strychnos innocua* Del.	[42]
Malvaceae	*Urena lobata* L.	[43]
Melastomataceae	*Tristemma mauritianum* J.F. Gmel.	[42]
Meliaceae	*Ekebergia capensis* Sparrm (*Ekebergia capensis* Sperrm)	[45]
Meliaceae	*Trichilia ematica* Vahl	[39, 47]
Menispermaceae	*Cissampelos muchronata* A.Rich.	[42, 50]
Moraceae	*Ficus natalensis* Hochst.	[43]
Myricaceae	*Morella kandtiana* (Engl.) Verdic & Polhill	[50]
Papillionaceae	*Ormocarpum trachycarpum*	[51]
Passifloraceae	*Adenia cissampeloides* (Hook.) Harms	[43]
Poaceae	*Imperata cylindrica* (L.) P. Beauv	[43, 50]
Poaceae	*Sporobolus pyramidalis* P. Beauv.	[43]
Polygalaceae	*Securidaca longipedunculata* Fres.	[42, 43, 51]
Rosaceae	*Rubus rigidus* Sm	[50]
Rubiaceae	*Gardenia ternifolia* Schumach. & Thonn.	[43]
Rutaceae	*Citrus sinensis* (L.) Osb.	[43]
Rutaceae	*Fagaropsis angolensis* (Engl.) Dale	[60]
Simaroubaceae	*Harrisonia abyssinica* Oliv.	[42, 43, 51]
Solanaceae	*Datura stramonium* L.	[42]
Solanaceae	*Nicotiana tabacum* L.	[43, 50, 60]
Solanaceae	*Solanum aculeatissimum* Jacq	[42, 47]
Solanaceae	*Solanum incanum* L.	[42, 43]
Umbifellifereae	*Steganotaenia araelicea* Hoscht	[42]
Verbenaceae	*Lantana camara* L.	[51]

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

Family	Botanical name	Life form (vegetation)	Part used	Mode of use to prevent snakes	References
Euphorbiaceae	*Ricinus communis*	Herb	Leaves/whole plant	Plant have strong smell that cause discomfort and disorientation to snakes when they slither over them.	[11]
Asteraceae	*Tagetes minuta*	Herb	Leaves	Plants have bitter tastes and strong smells that cause discomfort and disorientation to snakes when they slither over them.	[11]
Poaceae	*Cymbopogon citrus*	Grass	Leaves	Decoction made and sprinkled around the house. Snakes do not like the citrus smell from the leaves	[11]
Amaryllidaceae	*Allium sativum* L.	Herb	Bulb	Decoction made and sprinkled around the house. Snakes do not like the citrus smell from the leaves	[11]
Amaryllidaceae	*Allium cepa* L	Herb	Bulb	Decoction made and sprinkled around the house. Snakes do not like the citrus smell from the leaves	[11]
Solanaceae	*Nicotiana tabacum* L.	Shrub	Leaves	Planted around the house, leaves burnt	[11, 137]

Table 3. First aid treatments given to victims of snakebites in Ugandan rural communities

First aid measure	Mode of administration	Investigation of efficacy	Reference(s)
Tourniquets	Injured part tied with a piece of cloth/bandage above the affected area to prevent the venom from spreading to heart, the lungs, kidney and other delicate parts of the body. Done in an interval of five minutes to avoid weakening of the tissues.	Investigated	[7, 11]
Coins (500 Ugandan shilling copper coins, **Figure 7(a)**	Put on the wound until it gets stack on the wound	Investigated	[7]
Haemanthus multiflorus, **Figure 7(b)**	Chewed orally by victim/put on the bite. Should be used with care as it is itself poisonous in large quantities	Investigated	[7, 11]
Blackstone (carbonised absorptive animal bone), **Figure 7(c)**	Administered to calm patients, placed on cleaned incisions made around the bite area until it sticks by itself. It is left for 20-30 minutes, 30% effective and can be reused if boiled in hot water for 10 minutes after use, washed in soapy and clear water, dried well and stored in a dry airtight container	Investigated, can be used alongside medicinal antivenom plants	[11]

(a) (b) (c)

Figure 7. Some of the items used for first aid treatment of snake bites in Uganda : (a) 500 Uganda shillings copper coin, side displayed is usually placed on the bite , (b) *Haemanthus multiflorus* bulb, (c) Black stone.

Table 4. Antivenin activities of plants used for snakebite treatment in Uganda and their active phytochemical constituents

Plant	Part used	Solvent used	Antivenin activity (Comments)	Active chemical constituents	Authors
Allium cepa L.	Bulb	Methanol	Cardioprotective activity (14.8 ± 1.65 units/litre; $P > 0.5$) on creatine kinase isoenzyme levels to neutralize snake bite envenomation in experimental rabbits. Concentrations (< 160 µg / mL) stabilized human red blood corpuscles membrane(antihemolytic) against *N. naja karachiensis* venom , though elevated concentrations were cytotoxic. Provided 50% protection from *N. naja karachiensis* phospholipase A (PLA_2) in terms of an increase in pH of an egg yolk suspension. Neutralized the anticoagulant effect induced by weak PLA_2 enzymes in *N. naja karachiensis* venom (76% inhibition, coagulation time of 106±0.57 s). Quercetin is a potent inhibitor of lipoxygenase	Quercitin, sulfurous volatile oils, oleanolic acid, protocatechuric acid	[138-142]

Plant	Part used	Solvent used	Antivenin activity (Comments)	Active chemical constituents	Authors
Allium sativum L.	Bulb	Methanol	Hepatoprotective activity (*P*> 0.5; 49 ± 5.01 and 82.5 ± 18.55 units/litre of aspartate aminotransferase and alanine aminotransferase against 52.5±3.51 and 69.5±18.55 units/litre for standard antiserum) assessed in rabbits. Provided 50% protection from *N. naja karachiensis* PLA_2 in terms of an increase in pH of an egg yolk suspension. Provided 50% protection from *N. naja karachiensis* PLA_2 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	[138, 140, 141]
Asystasia spp (*A. gangetica* L)	Leaves	Methanol	1000 mg/kg provided 80% protection against *N. melanoleuca* venom (PLA_2)	Flavonoids, saponins and tannins	[143]
Aristolochia spp (*A. indica*, *A. odoratissima*)	Leaves	Methanol, Ethanol, Water, pentane	PLA_2 and hyaluronidase enzymes from *N. naja* and *V. russelli* venoms inhibited. Strong gelatinolytic, collagenase, peroxidase and nuclease activities, L-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	[144-146]
Basella alba L.	Fruit	Methanol	Radical scavenging activity against 1,1-diphenyl 2-picrylhydroxyl (DHPP) experimented in mice.	Flavonoids, phenolics, betacyanins, Lupeol, β sitosterol	[147-149]
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-benzoylphenylalanylaninol acetate, 24-ethylcholestan-5-en-3-ol, L-stachydrine, 3-hydroxy-3-methyl-4-methoxyoxindole	[150, 151]
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	[152-155]
Carissa spp (*C. spinarum* L.)	Leaves	Methanol	Acetylcholinesterase, PLA_2, hyaluronidase, phosphomonoesterase, 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	[156, 157]
Cassia occidentalis L.	Leaves, roots	Ethanol	Stimulated angiogenesis, inhibited epidermal hyperplasia, acted positively on wound healing progress and minimized local effects caused by *Bootrops moojeni* venom.	Anthraquinones	[158, 159]
Citrus spp. (*C. limon* L. Burm. F)	Root , ripe fruits	Methanol	Neutralized the anticoagulant effect induced by weak PLA_2 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	d-x-pinene camphene, d-limonene, linalool, ichangin 4-β-glucopyranoside, nomilinic acid, 4-β-glucopyranoside	[141, 160, 161]

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Plant	Part used	Solvent used	Antivenin activity (Comments)	Active chemical constituents	Authors
			effective dose 50% of 710 µg extract per mouse		
Cleome spp (*C. viscosa*)		Methanol, ethyl acetate	Significant anti-inflammatory activity against carageenin-, histamine-, dextran-induced rat paw edema compared to Diclofenac sodium (20 mg/kg) standard	Flavonoid glycosides, querection 3-0-(2″-acetyl)-glucoside, phenolics	[162, 163]
Crinum spp (*C. jagus*)	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 haemorrhagic activity of a standard haemorrhagic 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	[163, 164]
Indigofera spp. (*I. capitata* Kotschy, *I. conferta* Gillett)		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 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 lowest clotting time of 173 ± 5.61 s (ethanol extract) and 234 ± 7.64 s for aqueous extract). Oedema 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 lowest oedema 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 oedema 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	[165]
(*I. pulchra* Willd.)	Methanol		Extract inhibited anticoagulant, hemolytic and PLA_2 activities of *N. nigricollis* venom	Tannins, flavonoids, saponins and steroids	[163, 166]
Jatropa carcus L.	Leaf latex	Methanol	Inhibits haemolytic activity of PLA_2 from *N. naja* venom	Terpenoids, alkaloids, phenolics, flavonoids, saponins	[132]
(*J. mollissima* (Pohl) Bail)	Leaves	Water	Reduced local effects induced by *Bothropic erythromelas* venom	Flavonoids (isoschaftoside, schaftoside, isoorientin, orientin, vitexin, isovitexin)	[34]

Plant	Part used	Solvent used	Antivenin activity (Comments)	Active chemical constituents	Authors
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	[167]
Sansevieria spp (*S.* liberica ger.& labr)	Rhizome, root	Methanol	LD_{50} of 353.5 ug/kg. The extract, n-hexane, ethyl acetate and butanol fractions significantly protected mice from *N. naja nigricollis* venom-induced mortality	Terpenoids, flavonoids, saponins	[168]
Albizia spp (*A. lebbeck* L. (Benth) bark)	Root/bark	Water	1000 mg/kg, *N. kauothia* venom, provided 50% protection from *N. naja karachiensis* PLA_2 in terms of an increase in pH of an egg yolk suspension	Carbohydrates, proteins, alkaloids, flavanoids, tannins, echinocystic acid, amino acids	[117, 135, 138, 140]
Euphorbia species (*E. hirta)*	Whole plant	Methanol	LD_{50} not specified, against *N. naja*) venom	Quercetin-3-O-alpha-rhamnoside, terpenoids, alkaloids, steroids, tannins, flavonoids, phenolic compounds	[169, 170]
Bidens pilosa L.	Leaves, whole part		Effective against *Dendroaspis jamesoni* and *Echis ocellatus* venom	Linalool, Cadinene, β-Caryophyllene, β-Cubebene, Cedrene, Humulene, Selina-3,7(11)-diene, Thujopsene, (−)-Globulol, Elixene, 2-Hexen-1-ol, 2-Hexenal	[136, 171]
Hoslundia opposita Vahl	Root, leaves	Methanol, Water	DPPH radical scavenging activity of 32.3 ± 1.9 µg/ml compared to standard L-ascorbic acid with activity of 21.1± 1.1 µg/ml.	α-Cadinol, Ethyl linolenate, Palmitic acid	[136, 172]
Maytensus senegalensis	Root	Methanol, chloroform	Anti-inflammatory activity, inhibited ear edema induced by croton oil in mice	Maytenoic acid, lupenone, β −amyrin	[173]
Securinega virosa	Leaves	hexane, ethyl acetate, methanol	N-hexane extract provided protection against lethal dose of *Naja nigricollis* venom (significant at 20mg/kg , $p<0.05$)	Alkaloids, phenols, saponins and triterpenes/steroids	[174, 175]
Solanum incanum L.	Root	Water	Inhibited the response to acetylcholine in a concentration-dependent manner like atropine. The extract inhibited charcoal travel in mice intestine by 36.28, 51.45, 52.93 and 38.53% in doses of 50, 100, 200 and 400 mg/kg body weight respectively	Quercetin, Isoquercitrin, Kaempferol, β-Sitosterol, Luteolin 7-O-b-D-glucopyranoside, sodium, potassium, chromium, vitamins B &C	[176-179]

Notes: DPPH-1,1- diphenyl 2-picrylhydroxyl, LD_{50}-Median lethal dose, *N. -naja,* PLA_2-phospholipase A, spp-species, *V. russelli - Viper russelli*

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