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Ethnobotanical survey and phytochemical screening of anti-snakebite plants used in Bissok District of Gabon

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Abstract. *Mengome, Mewono L, Mboma R, Engohang-Ndong J, Angone SA. 2021. Ethnobotanical survey and phytochemical screening of anti-snakebite plants used in Bissok District of Gabon. Biodiversitas 22: 3264-3275.* Snakebites remain a major health issue in tropical and subtropical regions in the world. The limited access of antivenom sera in remote areas of many countries forces populations to rely on plant-based remedies to manage snakebite-induced injury. In this study, we conducted an ethnobotanical survey of medicinal plants used for the management of snakebites in the district of Bissok (Northern Gabon). After collecting and verifying the authenticity of the plants, we further performed their phytochemical analysis. The procedure used in this study involved a structured questionnaire and direct interviews of local populations. Overall, data collected on-site included local names, the part of the plant used, the preparation, and the route of administration. The presence of some phytochemical compounds was determined according to standard methods. Overall, a total of 29 species of plants belonging to 20 different families were reported to be used to treat snakebites. The plants used were herbs (44.80%), trees (24.10%), shrubs (20.70%), liana (10.30%), and rhizomes (6.90%). They were mainly used as poultice or crush, and to a lesser extent as decoction and maceration. Regarding the route of administration, interviewees reported mainly external use on the site of the bite. Concerning the chemical composition, we found that the antivenom plants were rich in chemical compounds known to have antivenom, antipyretic and antimicrobial properties, e.g. alkaloids, terpenoids, flavonoids, steroids, coumarins, phenols, tannins gallic Our results open avenues to develop venom enzyme inhibitory assays.

Keywords: Medicinal plants, snake envenomation, phytochemicals, ethnobotany, phytochemical, Bissok District, Gabon

INTRODUCTION

According to the World Health Organization (WHO), snakebites are a neglected public health issue in many countries including those located in tropical and subtropical regions (de Moura et al. 2015; Dhananjaya et al. 2016). Snakebites are responsible for more deaths and disabilities than some tropical infectious diseases such as dengue fever, cholera, Japanese encephalitis, Chagas disease, and leishmaniasis (WHO 2017). Each year, about a million snakebites occur in Africa. However, the highest-burden is recorded in sub-Saharan Africa, causing between 100,000 and 500,000 envenoming cases and around 10,000 to 30,000 deaths (Chippaux 2011; Dhananjaya et al. 2016). Due to the importance of the threat, the World Health Organization (WHO) has re-added snakebite envenoming to the list of Neglected Tropical Disease (NTD) by the year 2017 (WHO 2017; Gómez-Betancur et al. 2019).

It is generally admitted that most snakebite cases are not reported. The above-mentioned data are likely underestimated (Chippaux 2011). In that respect, Chippaux (2011) and de Moura et al. (2015) claimed that the underreporting of snakebite-associated mortalities and disabilities may be explained by: insufficient access to antivenoms (healthcare centers), poorly trained healthcare personnel, and lack of appropriate epidemiological surveillance. In addition, it appears that the lack of antivenoms in most healthcare centers, mainly in rural areas, is a major drawback for the management of snakebites.

In sub-Saharan Africa and Gabon in particular, the use of medicinal plants is a reality and they are a common resource for dealing with snakebites (Omara 2020; Omara et al. 2020). Gabonese communities use traditional medicine for several reasons including economic, familiarity and knowledge of plants, attachment to their traditions, treatment of physical ailments, and in some instances belief in spiritual healing (Makita et al. 2011; Ngoua et al. 2019). Although the treatment for snakebites is effective, it is not readily available due to geographical areas, and anti-venom is usually administrated after local effects have already developed to some extent (Otero-Patiño et al. 2012). Research of alternative treatment from snake envenomation can be applied in the field to reduce the local and systemic actions induced by snake venoms.

Medicinal plants are a common source of active drugs for treating a wide range of diseases all over the world. Most of these medicinal plants are consumed as food or used for their rich phytochemical compounds that are known to have both preventive and curative effects on consumers for the treatment of various diseases (Prohp and Onoagbe 2012; Shabbir et al. 2014). According to the World Health Organization, Traditional Medical Program has provided evidence that ethnomedical information can lead to valuable drug discovery (Susana et al. 2019). Since the dawn of time, several active compounds have been discovered from plants on the basis of ethnobotanical information. Presently, the World Health Organization estimated that 80% of the population in some Asian and African countries use medicinal plants as an alternative form of primary healthcare. Regarding the management of snakebite in rural areas of the world, several plant species and plant part are commonly used (WHO 2019). In Nigeria for instance, *Mucuna pruriens* (L.) DC. was used for prophylactic for snakebite (Gómez-Betancur et al. 2019), while Akindele et al. (2020) reported that methanolic extracts of *Annona senegalensis* Pers. were able to reduce *Naja nigricollis*' venom-induced both mortality and hyperthermia in rats. This study aims to report an ethnobotanical survey and phytochemical compounds obtained in aqueous extracts of medicinal plants used to treat snakebites in Bissok, a District located in northern Gabon.

MATERIALS AND METHODS

Materials and reagents

Botanical materials were obtained by informants when the species were not very far from the house. Field guides were used to help in locating the district of Bissok and offerring translation services. Chemical solvents and all other reagents were obtained from Sigma-Aldrich (Sigma-Aldrich GmbH, Stemhein, Germany) or Merck (France).

Study area

The survey was carried out in Bissok District, Woleu-Ntem Province, the northern province of Gabon, a country located in central Africa. This province covers an area of 38,465 km², meaning 14.4% of the national territory. It is bordered on the western side by Equatorial Guinea, on the north by Cameroon, on the east by the Republic of Congo Brazzaville, on the south by the provinces of Ogooué-Ivindo, Moyen-Ogooué, and Estuaire (Figure 1). Access to health centers is extremely limited for populations of Woleu-Ntem because on one hand roads are overall in very bad conditions in almost all seasons of the year which makes them impassable and on the other hand when existing, health centers are very poorly equipped and lack anti-serum to treat snakebites, such as Gabon viper (*Bitis gabonica*); Mamba de Jameson (*Dendroaspis jamesoni*); mamba vert (*Dendroaspis viridis*); Cobra aquatique (*Naja annulate*).

Figure 1. A map showing the location of the study area in Bissok District, Woleu-Ntem Province, Gabon. Adapted from an original version published by Geology.com (https://geology.com/world/gabon-satellite-imageshtml)

Field interviews

We conducted a survey of plants used to treat snakebites by connoisseurs and by traditional healers in the district of Bissok (N:1°16'0"; E:11°35'0") which is an area predominantly occupied by the Fang ethnic group. The survey was conducted between June 2014 and August 2016. In this district, populations relied extensively on subsistence agriculture and hunting. Interviews were based on a direct questionnaire on the plants used by the populations to treat snakebites. Interviewees belong to the following ethnic groups: Fang, Pygmy, Kota, and Punu. While Fang and Pygmies are native to the area, the Kota and Punu seem to have arrived through marriage to a Fang or Pygmy (Wily 2012). Practically, people were asked information about the use of plants including the local name, the parts of the plant used, methods of preparation, and routes of administration.

Plants collections

Plants were identified by botanists of the National Herbarium of Gabon (NHG). We completed identification with other support such as Checklist of Gabonese Vascular plants (Sosef et al. 2006) and web sources such as the Plant List (http://www.theplantlist.org/) and the Plants of the World Online (http://www.plantsoftheworldonline.org/). Both the scientific names and corresponding voucher numbers were attributed.

Preparation of the antivenom plant extracts

After botanical identification of plants, samples were dried using a dehumidifier (Bioblock Scientific LMS Cooled Incubator) at 35°C for one week. Further, they were cut into small pieces and reduced to fine powders using an electric grinder.

Ten (10) g of powdered samples were mixed with 100 ml of distilled water. The mixture was then heated in a water bath at 100°C for 1 hour. Samples were then allowed to cool at room temperature, after which decoctions were filtered using a 33 mm diameter sterile syringe Millipore filter with 0.45 µm pore size (Millipore, Bebford, MA), dried, and used for further tests.

The phytochemical screening of the anti-snake venom plant extracts

The prepared aqueous extracts were screened for their qualitative chemical composition using standard methods described elsewhere (Mengome et al. 2010; Badjin et al. 2016b). The identification of the following groups was considered: alkaloids, sterols, triterpenes, coumarins, flavonoids, tannins, polyphenols, carotenoids, reducing sugars, carbohydrates, and saponosides. According to the precipitate or color intensity in each sample and test, the following evaluations were given: (i) +++: represents very high, (ii) ++: indicates moderate, (iii) +: indicates little/traces, and (iv) –: indicates absent (Gul et al. 2017; Suleiman and Ateeg 2020).

Data analysis

Raw data were entered in Microsoft Excel and analyzed using simple descriptive statistics. This was followed by the computation of frequency of use, family abundance, and the determination of preparation procedure and route of administration.

For each medicinal plant a Use Index (UI%) was calculated to give a ranking of the importance of the use of medicinal species. The Use Index is based on information collected and the UI% is calculated from the following formula:

$$UI = \left(\frac{na}{NA}\right) \times 100$$

Where: "na" is the number of interviewees who cited a given species of plant as useful and "NA" is the total number of people interviewed (Randriamiharisoa et al. 2015; Bajin et al. 2016a).

RESULTS AND DISCUSSION

Ethnobotanical survey

Information on the plants used to treat snakebites in the Bissok District in northern Gabon is summarized in Table 1. In 18 villages of the district, 51 people belonging to two social groups were interviewed, i.e. healers and professionals of the traditional use of plants. Four different ethnic groups were interviewed among whom were the Fang people constituting 58.8% followed by Pygmies (17.6%), Kota (13.7%), and Punu (9.8%).

A total of 29 plants from 20 families and 29 genera were reported to be used in the treatment of snakebites and were further classified in alphabetical order according to their families. Local names or common names are provided in Fang language because it is the most common language spoken throughout the surveyed region. Further, in Table 1, these plants are shown to be used alone or in combination.

Among the 20 families, the most commonly mentioned were Asteraceae with six species. The Apocynaceae, Piperaceae, Rubiaceae, and Zingiberaceae families had each two species while all other families listed in Table 1 were represented by only one species. We further sought to determine which plants were mostly cited by interviewees. The highest index was found for *Emilia coccinea* (Sims) G.Don (62.7%), followed by *Adenia reticulata* (De Wild. & T.Durand) Engl., *Cyanthillium cinereum* (L.) H.Rob., and *Mangifera indica* L (all having 52.9% of respondents), and *Drymaria cordata* (L.) Willd. ex Schult.(50.9%). Twelve plants had between 35% and 50% respondents such as *Alstonia congensis* Engl.; *Eclipta prostrata* (L.) L. (35.3%), *Carica papaya* L.; *Plectranthus bojeri* (Benth.) Hedge (37.2%), *Piper umbellatum* L., *Jateorhiza macrantha* (Hook.f.) Exell & Mendonça; *Manihot esculenta* Crantz (39.2%), *Dacryodes edulis* (G.Don) H.J.Lam and *Oldenlandia herbacea* DC. (43.1%), *Zanthoxylum gilletii* (De Wild.) P.G.Waterman (45.1%), *Anthocleista vogelii* Planch. (47.1%), and *Costus ligularis* Baker (49%).

Analysis of ethnobotanical data

It appears that 44.8% of plants reported to be used for treating snakebites were herbaceous plants. Trees and shrubs accounted for 24.1% and 20.7% of plants used while lianas and rhizomes represented respectively 10.3% and 6.9% of all mentioned plants (Figure 2).

Furthermore, the survey revealed that the use of leaves and that of the whole plant were the most commonly used parts of the plant, with 51.7% and 24.1% respectively reported by respondents. The use of stems, roots, and rhizomes was only marginal (Figure 3). Gabon Poultice and crush were the most occurring mode of preparation of plants (25% and 21% respectively) (Figure 4).

Phytochemical profile of the aqueous extracts

The phytochemical screening of aqueous extract of medicinal plants reported in this study is summarized in Table 2. Fifteen types of chemical compounds were screened including flavonoids (Fla), tannins gallic (Tang) or tannins catechic (Tanc), quinones (Qun), phenols (Phe), sterols (Ste), triterpenes (Trit), carotenoids (Car), total sugars (Sug), reducing sugar (Res), desoxysugar (Deso), Cardiotonic sugar (Cars), mucilage (Muc), saponosides (Sap), and organs (Org). In addition, alkaloids were screened using the Draggendorff test for AlkD and the Mayer test for AlkM. Overall, 208 assays were performed to screen the targeted chemical compounds. Out of the 208 tests carried, 143 tests were positive while 65 were negative.

A close look at the chemical analysis of samples shows that plants reported by respondents could be divided into five categories according to chemical diversity and chemical abundance found in the extract as shown in Figure 5. The first category of plants includes *Mangifera indica* and *Emilia coccinea* which both contained 13 bioactive chemical groups with a relative abundance of 81.3% of chemicals found in the extract. The second category includes *Anthocleista vogelii* and *Cissus quadrangularis* containing 12 bioactive chemical groups with a relative abundance of 75%. The third category includes five species (*Dacryodes edulis*, *Drymaria cordata*, *Manihot esculenta*, *Piper umbellatum*, and *Lantana camara*) and contained 11 bioactive chemical groups with a relative abundance of 68.8%. *Alstonia congensis* and *Peperomia pellucida* made the fourth category of plants with 10 types of bioactive chemicals and 62.5% of relative abundance. Finally, the fifth category included *Ageratum conyzoides* and *Zanthoxylum gilletii* which both contained nine bioactive chemical groups with 56.3% of relative abundance.

Furthermore, the relative abundance of phytochemicals was analyzed in plant organs used to treat snakebites. Thus, Figure 6 indicates barks which use was mentioned for 55 positive profiles, containing about 38.5% of bioactive chemicals while whole plants (43 positive profiles), and leaves (33 positive profiles) contained respectively 31.5% and 23.1% of bioactive compounds. Finally, liana in 12 plants mentioned and assayed contained only 8.4% of bioactive chemicals.

When looking into the relative abundance of each type of chemical compound (Figure 7), it appears that nine compound types are particularly dominant, including alkaloids (88.5%), flavonoids (92.3%), phenols (100%), triterpenes (76.9%), total sugars (100%), reducing sugars (84.6%), deoxy sugars (84.6%), cardiac glycoside (100%) and mucilage (76.9%).

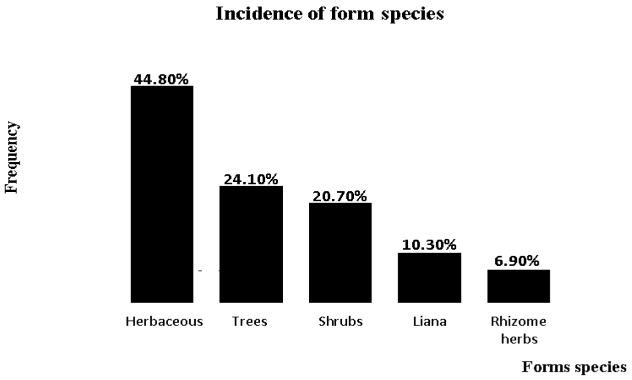

Figure 2. Forms of medicinal plants species used in the management of snake envenomation in canton Bissok of the northern Gabon

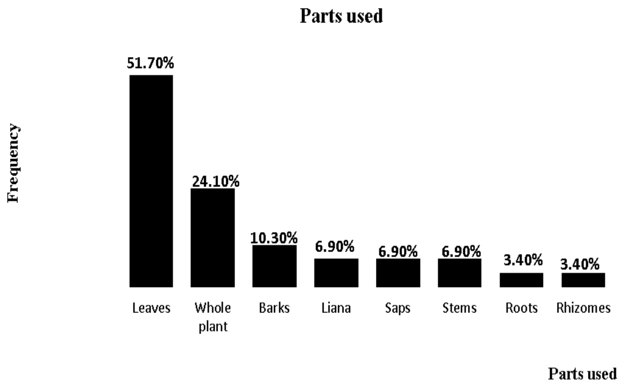

Figure 3. Plant parts used in the management of snake envenomation in canton Bissok of the northern

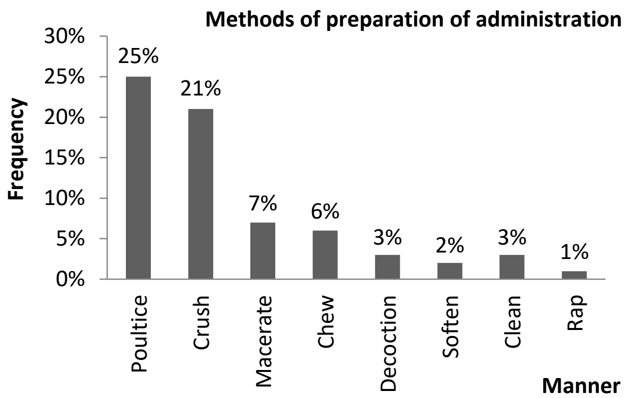

Figure 4. Methods of preparation and administration of the medicinal plants used in the management of snake envenomation in canton Bissok of the northern Gabon

Table 1. Plant species used in the management of snakebites in Bissok District (Northern of Gabon). Plants are listed according to family/scientific name/voucher, local name, parts used, methods of preparation, manners of use, and routes of administration

Family/scientific name/voucher	Local or common name (Fang)	Part used	Method of preparation	Routes of administration	Incidence	Use Index (UI)
Acanthaceae	Nyar-élòc	Whole plant	Macerate the plant and mix with *Emilia coccinea*	Oral	12	23.5%
Brillantaisia owariensis P. Beauv. 4006			Crush all fresh herbal and place them in poultice on the snakebite	External		
Anacardiaceae	Andok ntangha	Barks	Chew barks and drink the juice	Oral	27	52.9%
Mangifera indica L. 1588			Crush barks and place them in poultice on the snakebite	External		
Apocynaceae	Ekuk	Barks	Macerate barks or leaves, boil, and drink at room temperature	Oral	18	35.3%
Alstonia congensis Engl. 1093		Leaves	Crush fresh barks and place them in poultice on the bite	External		
Rauwolfia vomitoria Alfez 15766	Oyomtsüè, oyomtè	Roots	Crush fresh roots and place them in poultice on the snakebite	External	12	23.5%
Asteraceae	Mekwa me kong	Whole plant	Crush fresh herbal and applied on the snakebite	External	12	23.5%
Ageratum conyzoides L.1017						
Bidens pilosa L. 2934	Anyông-élòc	Leaves	Boil in water to make an infusion and drink it hot	Oral	5	9.8%
Eclipta prostrata L. 2299	Envongha	Whole plant	Macerate in water and drink	Oral	18	35.3%
			Crush fresh whole plants and place them in poultice on the snakebite	External		
Emilia coccinea (Sims) G.Don 1065	Alò-mvu	Whole plant	Macerate the whole plant and drink to annihilate the effects of the snake venom	Oral	32	62.7%
			Crush fresh whole plants and place them in poultice on the snakebite	External		
Cyanthillium cinereum (L.) H.Rob. 3134	Ayapana sauvage	Leaves	Softened the leaves on the fire, crush them and mix with leaves of *Plectranthus bojeri* and *Adenia reticulata* then place the mixture in poultice on the snakebite	External	27	52.9%
Baccharoides guineensis (Benth.) H.Rob. 2952	Vernonia	Leaves	Crushed fresh leaves are mixed with leaves of *Costus ligularis*, then apply the mixture in poultice on the snakebite	External	13	25.5%
Burseraceae	Osas	Barks	Chew fresh barks and swallow the juice	Oral	22	43.1%
Dacryodes edulis (G.Don) H. J. Lam. 1114			Crushed the barks and place them in poultice on the snakebite	External		
Caricaceae	Alòla, fôfôl	Leaves	Crush fresh leaves, mix it with the sap, and place the mixture in poultice on the		19	37.2%
Carica papaya L. 1365		Sap	snakebite	External		
Caryophyllaceae	Mouron blanc	Leaves	Crush fresh leaves and place them in poultice on the snakebite		26	50.9%
Drymaria cordata Wild. ex Schult 5629				External		
Clusiaceae / Guttiferae	Okès	Sap	Apply the sap to the wound caused by a snakebite	External	15	29.4%
Garcinia mannii Oliv. 212						
Euphorbiaceae	Mboe	Leaves	Crush fresh leaves or stem to release the sap and apply on the snakebite	External		
Manihot esculenta Grantz 11412		Stem			20	39.2%
Lamiaceae	Inùke	Leaves	Crush fresh leaves, mix with crushed leaves of *Cyanthillum cinereum* and *Adenia reticulata* and place them in poultice on the snakebite	External	19	37.2%
Plectranthus bojeri (Benth.) Hedge 978						
Loganiaceae	Ayinebe	Leaves	Clean fresh young leaves and place them in poultice on the snakebite	External	24	47.1%
Anthocleista vogelii Planch. 811						

Melastomaceae *Dissotis multiflora* Triana 69	Otouglame	Leaves	Crush fresh leaves and mix with the *Costus ligularis* juice. The mixture is used as a poultice on the snakebite	External	10	19.6%
Menispermaceae *Jateorhiza macrantha* (Hook. f.) Exell & Mendonça 4422	Ntu-mevine, nkòl-ngü	Liana	Place the crushed liana in poultice on the snakebite	External	20	39.2%
Passifloraceae *Adenia reticulata* (De Wild. et Th. Durand) Engl. 920	Ndòndòlœ	Whole plant	The whole plant is hand-rubbed, and its juice is mixed with crushed leaves of *Plectranthus bojeri* and *Cyanthillum cinereal*. Drink the macerate of the whole plant The mixture is then spread on the snakebite	Oral External	27	52.9%
Piperaceae *Piper umbellatum* L. 2339	Abò-me-nzang	Leaves	Boil leaves in water then drink the infusion warm Softened fresh leaves by crushing them and apply them in poultice on the snakebite	Oral External	20	39.2%
Piperomiar pellucida 927	Caisson de palmier	Whole plant	Chew the whole plant and swallow Crush the whole plant and apply in poultice on the snakebite	Oral External	15	29.4%
Rubiaceae *Oldenlandia herbacea* (L.) Roxb 1571	Mille grains	Whole plant	Crush the whole plant, put it in water then drink and chew the plant Crush the whole plant and apply it in poultice on the snakebite	Oral External	22	43.1%
Otomeria volubilis (K.Schum.) Verdc 608	Dème-nze	Leaves	Crush leaves and apply the juice on the snakebite	External	16	31.3%
Rutaceae *Zanthoxylum gilletii* (De Wild.) P.G. Waterman 2551	Nlo-mvoghe	Leaves	Triturated leaves are macerated in the juice of *Costus ligularis* and the mixture is applied to the snakebite	External	23	45.1%
Verbenaceae *Lantana camara* L. 818	Asèp-ntangha	Leaves	Crush leaves and apply as a poultice on the snakebite	External	12	23.5%
Vitaceae *Cissus quadrangularis* L. 125	Fó-ndzic	Liana	The raping of the liana is used as a poultice on the snakebite Drink the macerate of the liana	External Oral	17	33.3%
Zingiberaceae *Costus ligularis* Bak. 264	Myan	Leaves, stem	The juice of the whole plant is said to be a snake repellent	External	25	49%
Zingiber officinale Roscoe 159	Okam-si	Rhizome	Chew and crush rhizomes and apply them as a poultice on the snakebite	Oral External	15	29.4%

Table 2. Phytochemical screening of some species of plants used to treat snakebites in Gabon

Family/ scientific name/voucher	AlkD	AlkM	Fla	Tang	Tanc	Qun	Phe	Ste	Trit	Car	Sug	Res	Deso	Cars	Muc	Sap	Org	R+
Anacardiaceae/*Mangifera indica* L./1588	+++	+	+++	-	+++	+++	+++	-	+++	+	+	+++	+++	+++	++	-	B	13 (81.3%)
Apocynaceae/*Alstonia congensis* Engl./1093	+++	+++	+++	+	-	+	+	-	+++	-	+++	+++	-	+++	-	-	B	10 (62.5%)
Asteraceae/*Ageratum conyzoides* L./1017	+++	++	+++	-	-	-	+++	++	-	-	++	-	++	++	+	-	Wp	9 (56.3%)
Asteraceae/*Emilia coccinea* (Sims) G.Don/1065	+++	+++	+++	+++	-	+++	+++	-	+++	+++	+++	+++	+++	+++	++	-	Wp	13 (81.3%)
Burseraceae/*Dacryodes edulis* (G.Don) H. J.Lam./1114	+++	+++	+	+	-	-	+++	-	-	+++	+++	+++	+++	+++	+++	-	B	11 (68.8%)
Caryophyllaceae/*Drymaria cordata* Wild. ex Schult/5629	+++	+++	-	++	-	-	++	-	++	+	+++	+++	++	++	++	-	Wp	11 (68.8%)
Euphorbiaceae/*Manihot esculenta* Grantz/11412	+++	+++	+++	+++	-	+++	+++	-	+++	-	++++	+++	-	+++	++	-	L	11 (68.8%)
Loganiaceae/*Anthocleista vogelii* Planch./811	+++	+++	+++	+++	-	-	+++	-	++	+	+++	+++	+	++	++	-	B	12 (75%)
Piperaceae/*Piper umbrellatum* L./2339	-	++	+++	+	-	-	+	-	++	-	+++	+++	+	++	++	+	L	11 (68.8%)
Piperaceae/*Piperomia pellucida/*927	+++	+++	+++	+++	-	-	+++	-	-	-	+++	-	+++	+++	+++	+	Wp	10 (62.5%)
Rutaceae/*Zanthoxylum gilletii* (De Wild.) P.G.Waterman/2551	+++	-	+++	+++	-	-	++	-	++	-	+++	+++	++	++	-	-	B	9 (56.3%)
Verbenaceae/*Lantana camara* L./818	+++	++	++	++	-	-	++	-	++	-	+++	+++	++	++	++	-	L	11 (68.8%)
Vitaceae/*Cissus quadrangularis* L./125	+	-	+	+++	-	+	+++	-	++	+	+++	+++	+	++	+	-	Li	12 (75%)

Note: AlkD: Alkaloids according to Dragendorff test, AlkM: Alkaloids according to Mayer test, Fla: Flavonoids, Tang: Tannins gallic, Tanc: Tannins catechic, Qun: Quinones, Phe: Phenols, Ste: Steroids, Trit: Triterpenes, Car: Carotenoids, Sug: Total sugars, Res: Reducing sugars, Deso: Desoxysugars, Cars: Cardiotonic sugars, Muc: Mucilages, Sap: Saponosids, B: Barks, Wp: Whole plant, L: Leaves, Li: Liana, Org: organs, (+): positive result, (-): negative result, R+: Percentage of positive results. +++ represents very high, ++ indicates moderate, + indicates little/traces, and – no presence

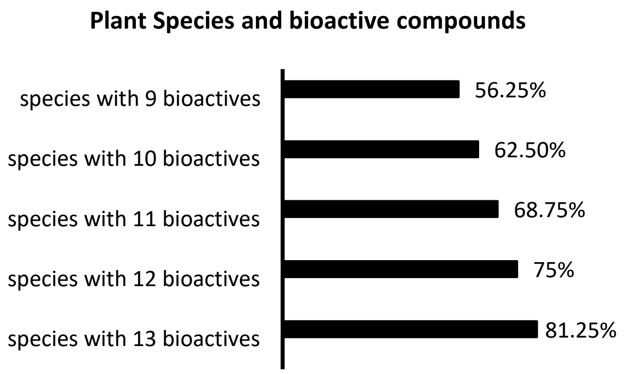

Figure 5. Plants were grouped into five categories according to the diversity and relative abundance of chemical compounds screened

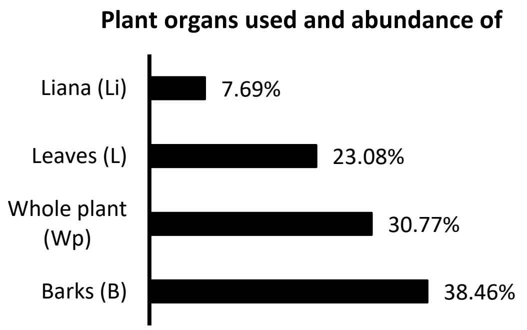

Figure 6. Plant organs used were screened for the relative abundance of bioactive chemical compounds

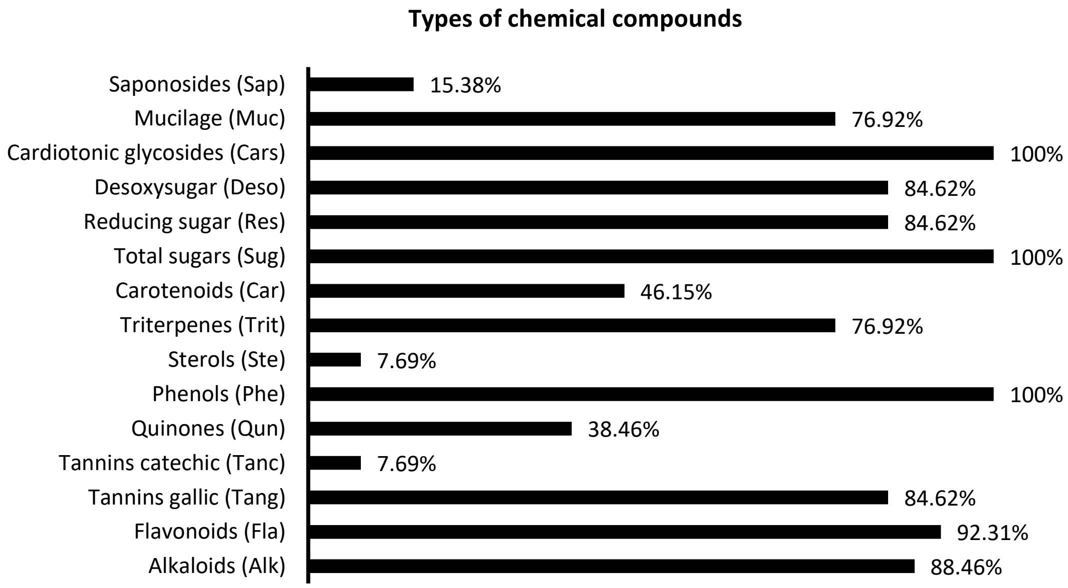

Figure 7. The affluence of different types of chemical compounds

Discussion

Snake envenomation is a neglected tropical disease that accounts for between 10,000 and 30,000 deaths per year (Chippaux 2011; Dhananjaya et al. 2016). The threat is particularly important in remote tropical and subtropical areas where health facilities are hardly available. When present, they are often poorly supplied with medical consumables and equipment. Inevitably, in these areas, traditional medicine becomes the medical approach of the first intention. The main signs developed after snakebite are characterized by inflammation, edema, necrosis, hemorrhage, and collapsing of the patient. Moreover, kidney and neuronal failure, respiratory dysfunction, and cardiotoxicity can all be experienced by the patient (Nalbantsoy et al. 2013; Gómez-Betancur et al. 2014; Pompermaier et al. 2018; Elgorashi and McGaw 2019). Hemorrhage is one of the most relevant signs of local and systemic envenoming by viper snakes (Gómez-Betancur et al. 2014).

In this study, we are reporting the results of an ethnobotanical survey we conducted in the district of Bissok (Northern Gabon). Of the 29 species of plants collected, 24 of them were reported in a number of studies to be used against snakebites (Ezuruike and Prieto 2014; Molander et al. 2014). More specifically, *Manihot esculentus* Crantz (Lebbie and Turay 2017) in Sierra Leone, *Lantana camara* L. and *Carica papaya* L. (Kamatenesi et al. 2011; Kodi et al. 2017) in Uganda, *Zanthoxylum gilletii* (De Wild Waterman) in Kenya (Okeyo et al. 2011), *Cissus quadrangularis* L. in South Sudan (Doka and Yagi 2009), have been reported for treating snakebites.

Interestingly, only three plants, i.e. *M. indica*, *E. prostrata*, and *P. umbrellatum* have been shown through experimental data to have anti-venom activities against snake venom enzymes and/or toxins (Nanjaraj et al. 2014; Singh et al. 2017). Indeed, aqueous extract of *E. prostrata* known in Brazil and China as an antidote against snakebite was successfully tested against South American rattlesnake venom (Félix-Silva et al. 2017). Furthermore, antimyotoxic, antihemorragic, antiproteolytic and anti-phospholipase properties of those plant extracts were revealed (Hasan et al. 2016; Strauch et al. 2019). Aqueous stem bark extracts of *M. indica* have been shown to inhibit the toxic and lethal effect of the *Indian Russell's viper* venom (Dhananjaya et al. 2011). Moreover, many secreted phospholipase A2 (sPLA2) inhibitors have been isolated from various medicinal plants (Kim et al. 2020; Fatahiya et al. 2021). Other studies have shown antivenom activity of aqueous stem bark extract of *M. indica* by inhibiting NN-XIb-PLA2 of *India cobra* venom with IC_{50} = 7.6 µg/ml (Dhananjaya et al. 2016). Extracts and pure compounds derived from various parts of *P. umbellatum* have shown several pharmacological activities, including anti-inflammatory, analgesic, anti-atherogenic, cytotoxic, anti-platelet, anti-rheumatism, antimalarial, antifungal, antibacterial, anti-leishmanial, pain, oedema, and anti-trypanosomal activities (Agbor et al. 2012; da Silva et al. 2014; 2016; Didjour et al. 2019). Several studies from *P. umbellatum* have shown the presence of alkaloids, flavonoids, sterols, and terpenes. Many of them are found in essential oil and other classes of secondary metabolites (Didjour et al. 2019). These results suggest that knowledge on virtues of traditional medicine is shared across countries, continents and support our findings.

As previously reported elsewhere, medicinal plants were used either alone or in combination. During our interviews, we were unable to clearly decipher why particular plants were required to be used in combination with others. However, we hypothesize that these plants act synergistically in order to prevent snakebite-induced tissue damages. We were further interested in knowing which type of plants and plant parts were commonly used by local populations in the District of Bissok to manage cases of snakebite. Overall, our results showed that herbaceous plants were mostly used, whilst leaves and stem barks were the most used part of the plant. These results are in accordance with our previous report (Mengome et al. 2010) and those from other authors (Bajin et al. 2016a) showing that herbaceous plants and leaves are the prominent plants and parts used. Nevertheless, it is important to note that the use of either plant type or plant part depends on the anatomical place where the injury occurs and, on the availability and accessibility of the material.

It is obvious that plants' secondary metabolites drive their biological activities (Khameneh et al. 2019). Regarding plant-based management of snakebite, Singh et al. (2017) investigated the effect of plant secondary metabolites on either snake products or venom-induced damages. Their report highlighted the role of alkaloids, terpenoids, flavonoids, steroids, and coumestans in the inhibition of the snake enzyme PLA2 on a snake bite-related injury. For instance, alkaloids extracted from the *Azadirachta indica* (neem) have been shown to inhibit PLA2 activity from various snakes' venoms (Yirgu and Chippaux 2019); other coumarin-type polyphenols isolated from leaves of *Ageratum conyzoides* act against visceral hemorrhages (Jasvidianto et al. 2020). In addition, *Emilia coccinea* has shown to be effective for treating infectious diseases (Prinsloo et al. 2018).

In this study, our preliminary qualitative analysis of chemical compounds in our batches of plants revealed the presence of phenols, total sugars, cardiotonic glycosides, flavonoids, tannins gallic, alkaloids, reducing sugar, deoxy sugars, terpenes, and mucilages. To a lesser extent, our plant extracts contained sterols, quinones, carotenoids, and saponosides. The relative abundance of chemical compounds in our plant extracts shows the presence of compounds with biological activity against snake envenomation. That observation is supported by results published by many other research teams. Indeed, over a decade ago, a team of researchers isolated alkaloids from the leaves of *Rauwolfia vomitoria* to treat edema (Fidele et al. 2014; Jasvidianto et al. 2020). More recently, reserpine alkaloids were isolated from *R. vomitoria* and showed to exhibit sedative properties on patients. Furthermore, it is documented that triterpenoids (lupeol acetate) neutralize the venom activity of *Naja kaouthia* by canceling the lethality, cardiotoxicity, neurotoxicity, and respiratory injury effects of the venom (Shabbir et al. 2014).

Flavonoids are recognized for their numerous biological properties including, but not limited to anti-inflammatory, anticancer, cardioprotective, antioxidant, and veino-tonic activities (Mpondo et al. 2012; Borah et al. 2019). Moreover, flavonoids isolated from root aqueous extracts obtained from the plant *Ophirrhiza mungos* showed to inhibit PLA2 contained in the venom of *Daboia russelii* (Krishnan et al. 2014; Vanessa et al. 2020). Also, rutin, a flavonoid glycoside is effective in increasing the survival time of rats injected with cobra venom. Rutin, quercetin, hesperidin, and bioflavonoids produce significant antinociceptive and/or anti-inflammatory activities (Gòmez-Betancur et al. 2014). Phenolic compounds also present in our plant extracts are frequently mentioned in the literature as being responsible for inhibiting damaging activities induced by snake venoms (Gomes et al. 2010; Ambikabothy et al. 2011; da Silva et al. 2016; de Moura et al. 2018). *In vitro* assays of the polyphenol compounds obtained from aqueous extracts of seeds of *Pithecellobium dulce* and *Pentace burmanica* and nutgalls of *Quercus infectoria* indicated that these chemicals were able to neutralize cobra venom (Pereañez et al. 2011; Shabir et al. 2014). Similarly, several sesquiterpene types and flavonoids isolated from *Artemisia* species have shown to exhibit anti-inflammatory properties (Emami et al. 2010; Ruikar et al. 2011). In addition, many studies on polyphenolic compounds, including flavonoids and phenolic acids, have reported various activities for these secondary metabolites, including anti-ulcer, anti-inflammatory, and antioxidant (Kumar and Pandey 2013; da Silva et al. 2016; Borah et al. 2019). Tannins have an astringent activity that promotes vasoconstriction, an important parameter in hemostasis. These hemostatic and vasoconstrictor effects on small vessels, justify the use of tannins against varicose veins, wounds, and hemorrhoids (Ghedadba et al. 2014; Dibong et al. 2015). Tannins are typically used orally to assure vasoconstrictive function and limit the loss of body fluid (Pereañez et al. 2011; Ghedadba et al. 2014; Dibong et al. 2015). Tannins have also an inhibitory effect on snake venom enzymes (Gomes et al. 2010; Ambikabothy et al.

2011; Pereañez et al. 2011; Silva et al. 2016; de Moura et al. 2018). Not only tannins interfere with enzymatic activities of the snake venoms, but they also chelate metal ions such as zinc, copper, and iron found for instance in the venom of *Bothrops* (Patiño et al. 2012). The chelating effect of the extracts of *Aniba fragrans* was confirmed by SDS-PAGE when mixing the *Bothrops atrox* venom with the plant extracts (de Moura et al. 2018). Tannins isolated from aqueous extract of *Mimosa pudica* roots displayed inhibitory effects on the lethality, myotoxicity, and enzyme activities of *Naja kaouthia* venom (Sia et al. 2011; Pereañez et al. 2011). Detoxification, neutralization of neurotoxic and hemorrhagic effects of tannins were revealed from extracts of young persimmon fruits of *Diospyros kaki* (Ying and Chun 2016). Although sterols are not abundant in species we analyzed, it appears however that β-sitosterol and stigmasterol isolated in root extracts of *Pluchea indica* using methanol as solvent carry protective effects against the lethality of *Naja kaouthia*. Moreover, they showed to have neutralizing effects on respiratory dysfunction, neurotoxicity, cardiotoxicity, and on phospholipase A2 activity. Interestingly, sterols increased anti-serum activity by up to 35.5% (Shabir et al. 2014). Taken altogether, these results confirm the interest in medicinal plants as potential remedies against snakebites. In addition, this study opens new avenues for the use of natural compounds in clinical settings.

In conclusion, several plants have been mentioned to be traditionally used for the treatment of snakebite envenomation. However, only a few of them have been experimentally and scientifically validated. This report on medicinal plants used for treating snakebites in Gabon opens new avenues for the use of natural compounds in clinical settings. Further investigation at a national scale would bring new insight into ancestral knowledge and practices regarding the management of snakebites. Moreover, experimental studies would be of interest to scientifically valid or not, the use of plants that require such validation in treating snakebites in rural areas.

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