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Preliminary study to identify anti-sickle cell plants in Niger's traditional pharmacopoeia and their phytochemicals

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The management of sickle cell disease is a major challenge at the international level. In many African countries, sickle cell anemia is one of the major causes of mortality and is a critical public health problem in Niger. In this part of the continent, the estimated prevalence is around 18 to 22%, which is amongst the highest in Africa. Nowadays, despite the existence of some ways to improve the prognosis of sickle cell anemia as allograft, it turns out that these resources are expensive and out of reach of underdeveloped countries. The purpose of this study was to identify the preliminary anti-sickle cell plants in Niger's traditional pharmacopoeia. To do this, an ethnobotanical survey was conducted among the patients consulting the National Reference Center for Sickle Cell Disease (CNRD) and the traditional healers in the city of Niamey. At the end of this survey, 29 plant species were identified. The phytochemical study of 12 plants showed the presence of large chemical groups known for important biological properties (polyphenols, alkaloids, gallic tannins, sterols and polyterpenes).

Key words: Phytochemical study, sickle cell disease, Niger, medicinal plants, ethnobotanical survey.

INTRODUCTION

Sickle cell disease is a genetic, hereditary disease that attacks red blood cells and deforms them (Pliya, 1994). It is due to a point mutation of the gene coding for the synthesis of the β chain of hemoglobin. This results in the replacement of glutamic acid by valine (André and Marc, 1988). Abnormal hemoglobin (Hbs) deforms red blood cells that take the form of a lunar crescent (sickle cell). These sickle cells block the fine vessels of certain organs: lungs, eye, brain, etc., hence the clinical manifestations of sickle cell disease (Pliya, 1994). Sickle cell anemia modifies the membrane flexibility of erythrocytes making them more sensitive and fragile against free radicals. In black Africa, sickle cell disease is one of the leading causes of infant mortality; almost 95%

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of children die before the age of 4 (Tshilolo et al., 2019; Mamounata et al., 2006). In Niger, the prevalence of sickle cell trait is between 18 and 22% (Issaka, 2012). This justifies the creation of the National Reference Center for Sickle Cell Disease (CNRD) in August 2009 (Issaka, 2012).

Recently conducted survey on the screening and management of medicinal plants in four localities of Niger through the traditional practitioners revealed that 110 species in 89 genera and 47 families are used in the tradItional pharmacopoeia, among them plants with potential effect against sickle cell disease (Mounkaila et al., 2017). The work of Souchet and Louis (2013) reported that in West Africa, 93 species are potential plants with effect against sickle cell disease. Among them *Cajanus cajan*, *Carica papaya*, *Piper guineense*, *Pterocarpus osun*, *Sorghum bicolor*, *Syzygium aromaticum*, *Zanthoxylum zanthoxyloides*, *Justicia secunda*, *Moringa oleifera* and *Vinga unguiculata* seem to be the most promising species for sickle cell disease treatment.

Plants are naturally sourcing of various bioactive compounds thought with various health benefits such as prevention of blood sickle cell disease. Plant metabolites can be divided into primary metabolites associated with nutrition and secondary metabolites, which perform several functions like interaction between a plant and its environment, and also involves in many drug formulation or preparation (Uko et al., 2019). Secondary metabolites included a group of compounds known as phenolic (Raji et al., 2019). In Africa, medicinal plants have a good reputation, as nearly 75% of the population uses these plants for their medical care (Grosse et al., 2011; Mamounata et al., 2006). Nigeriens use traditional medicine more than the modern, because of the low monthly income of parents of sickle cell patients and the high cost of modern medicine (Karl Rachid, 2013). This study aimed to identify, through an ethnobotanical survey in the region of Niamey (Niger), the medicinal plants used for the treatment of sickle cell disease and carry out the phytochemical screening of these plants.

MATERIALS AND METHODS

Niamey region is located at the extreme West of Niger Republic where the National Reference Center for Sickle Cell Disease created in 2009 is located; and at the same time the place where the survey was conducted with the patients or their parents of CNRD but also with traditional healers (Issaka, 2012). The data collection was carried out using an ethnobotanical survey through a direct interview. To carry out this survey, two questionnaires were prepared for sickle cell patients and traditional healers. The questions have been translated into local languages, Hausa and Zarma (the two most spoken languages in Niamey region). The inventory survey questions were mainly focused on the anti-sickle cell plants, the manifestations of the disease, the parts of the plants used and the methods of drug preparation. The names of the plants listed are given in vernacular languages and for each plant species, a sample was collected for identification and phytochemical study. The identification of the plants species was carried out by the Biology Laboratory of the Faculty of Science and Technology, Abdou Moumouni University of Niamey, with help of Niger Republic national plant nomenclature and Professor Mahamane Saadou. In total, fifty-three (53) sickle cell patients (28 female and 25 male) from the CNRD and seven (7) all-male traditional healers were questioned for ethnobotanical survey. As for the patients, the survey focus more on the age of the patient, sex, origin, electrophoresis, type of hemoglobin, age of diagnosis of the disease, major symptoms of the disease, names of plants used, parts of plants, method of preparation, and locality of plants.

Chemical characterization

The plants organs depending on the part needed were collected from 15 to 30th December, 2013 during the day in the Tillabery (Niger) region at 115 km far from Niamey and 527 km away from Ouagadougou Burkina Faso. The plants were authenticated by a botanist professor Mahamane Saadou, Department of Biology at the Faculty of Science and Technology, Abdou Moumouni University of Niamey, Niger and were given voucher numbers from HI/011 to HI/039. After harvesting the different parts of the plant's materials, they were then cleaned and dried in an aerated area at room temperature for two weeks. The dried plant materials were grinded, sieved and the given powder were pulverized followed by extraction of the secondary metabolites using three different solvents petroleum ether, methanol and distilled water. Different chemical characterizations were performed as described in the work of Ronchetti and Russo (1971). The sterols and polyterpenes were characterized by the reaction of Liebermann, and the polyphenols content was determined through the reaction with ferric chloride ($FeCl_3$). The cyanidine reaction was used to characterize the flavonoids. The tannins, quinones and alkaloids content were determined using Stiasny, Bornstraëgen and Dragendorff's reagents, respectively. Picrosodium and foam test were used to characterize the cyanogenic glycosides and saponosides respectively.

RESULTS AND DISCUSSION

Plant organs and prescription

The survey revealed 29 plant species distributed among 20 families used in the treatment of sickle cell disease. The results of the ethnobotany survey are summarized in Table 1. Capparidaceae and Rubiaceae are the most represented (10.34%), followed by Bombacaceae, Meliaceae, Combretaceae, Convolvulaceae and Anacardiaceae (6.89%). At the end, the least-mentioned families are Lilliaceae, Vitaceae, Cyperaceae, Asclepiadaceae, Cochlospermaceae, Malvaceae, Acanthaceae, Bignoniaceae, Scrophulariaceae, Caesalpiniaceae, Mimosaceae, Sterculiaceae and Poaceae (3.45%). Depending on the size of the organs used, the leaves are the most recommended (41%), followed by the leafy stems (17%), the barks of the trunk (14%), the roots (10%), root barks (7%), fruits and seeds (4%) and finally, pods (3%). Figure 1a shows the percentages of utilized plant organs. The massive use of leaves is explained by their richness in primary and secondary metabolites, through photosynthesis. Indeed,

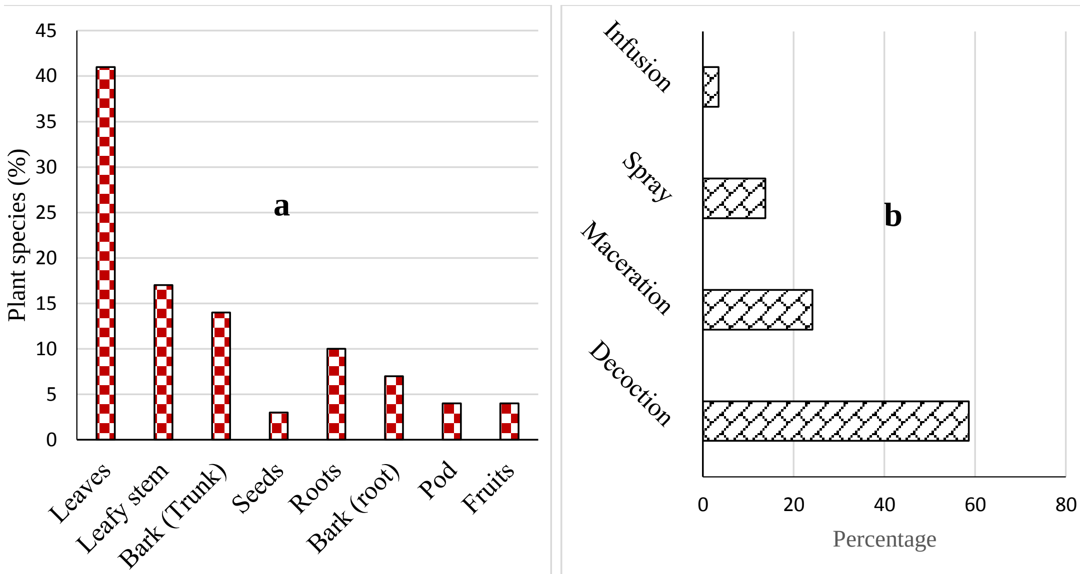

Figure 1. Percentages of plants species and methods of drug preparation from ethnobotanical survey of anti-sickle cell plants

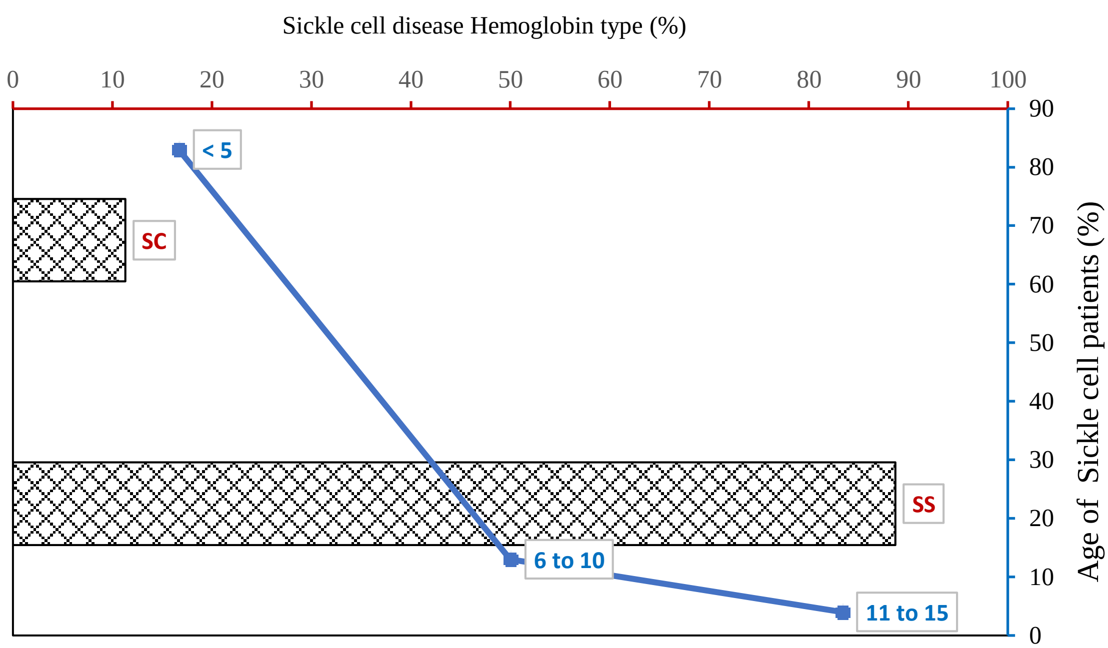

Figure 2. Sickle cell disease hemoglobin type and age of patients.

plants ensure the synthesis and storage of these metabolites with their chlorophyllian pigment. Secondary metabolites have very important biological interests (N'Guessan et al., 2009) which justifies in general, the use of leaves by the traditional healers in the treatment of sickle cell disease.

The majority of prescriptions against sickle cell disease are decoctions (58.62%) (Figure 1b). The most requested method of preparation has to do with efficiency in the extraction of a sufficient quantity of secondary metabolites (Detemmerman et al., 2018; Seca and Pinto, 2018). This result is close to that established by N'Guessan et al. (2009) who showed that the decoction is mainly used (42.30%) (Figure 2). It was found that the detection of sickle cell disease was early in most of the sickle cell patients (83%), which explains the importance of creating

Table 1. Different plant species cited by traditional healers and sickle cell patients.

N°	Botanical names	Family	Vernacular (Hausa)	Vernacular (Zarma)	Plant part	Preparation Method	Frequency
01	*Adansonia digitata*	Bombacaceae	Kuuka	Kôgna	F	Macération	01
02	*Allium sativum*	Lilliaceae	Tafarnua	Tafarnua	G	Décoction	01
03	*Ampelocissus africana*	Vitaceae	Kabakura	komnitanda	F	Décoction	01
04	*Anogeissus leiocarpus*	Combretacea	Marké	Gonga (kodjal)	F	Décoction	01
05	*Azadiracta indica*	Meliaceae	Bédi	Turiforta	F	Macération	02
06	*Bombax costatum*	Bombacaceae	Bagaye	Forgo	ER	Décoction	01
07	*Boscia angustifolia*	Capparidaceae	Agajini	Hasukoirey	F	Décoction	01
08	*Boscia senegalensis*	Capparidaceae	Anza	Anza	F	Décoction	01
09	*Cajanus cajan*	Cyperaceae		Dobudobugna	F	Pulvérisation	03
10	*Calotropis procera*	Asclepiadaceae	Tunfafiya	Sagaye	ER	Décoction	01
11	*Capparis corymbosa*	Capparidacea	Bagaye	kubi nya	F	Décoction	03
12	*Cochlospermum tinctorium*	Cochlospermaceae	Lawaga	Bagarbey	R	Pulvérisation	01
13	*Combretum micranthum*	Combretaceae	Géza	Kubu	F	Décoction	02
14	*Crossopteryx febrifuga*	Rubiaceae	hincin'morgo	hincin'morgo	F	Décoction	01
15	*Faidherbia albida*	Mimosaceae	Bagarbey	Kokoye	ET	Macération	01
16	*Gardenia sokotensis*	Rubiaceae	Gaud'in geza	tondifara	F	Décoction	01
17	*Hibiscus sabdarifa*	Malvaceae	Yakwa	waraou	Gr	Décoction	03
18	*Hygrophila senegalensis*	Acanthaceae	Djan tanki	banguizé	TF	Décoction	01
19	*Ipomoea asarifolia*	Convolvulaceae	Dumankada	Talhana	TF	Infusion	06
20	*Ipomoea batatas*	Convolvulaceae	Dankaly	Kudaku	TF	Pulvérisation	01
21	*Khaya senegalensis*	Meliaceae	madachi	farré	R	Macération	01
22	*Kigelia africana*	Bignoniaceae	Yawirya	Combey	Fr	Décoction	01
23	*Lannea microcarpa*	Anacardiaceae	Malga	Falunfa	ET	Macération	01
24	*Mitragyna innermis*	Rubiaceae	giayia	kabey	ET	Macération	01
25	*Sclerocarya birrea*	Anacardiaceae	dânia	Diney	ET	Décoction	01
26	*Striga hermontica*	Scrophulariaceae	kujiji	mâlu	TF	Pulvérisation	01
27	*Tamarindus indica*	Caesalpiniaceae	Tsamiya	bôsey	F	Décoction	01
28	*Walteria indica*	Sterculiaceae	Ankufuwa	Nunebasi	R	Décoction	01
29	*Zea mays*	Poaceae	Massara	kolgoti	TF	Macération	03

TF = Leafy stem: ER = bark of the roots; F = leaves; Gr = seed; G = pod; Fr = fruit; ET = bark of the trunk; Org. = Body; No. = number; Freq: frequency of the species mentioned.

the CNRD in Niamey. Similar findings by Gernet (2010) stated that the neonatal diagnosis was the major (59%) method of sickle cell disease screening. At the CNRD Reference Center, it was revealed that the SS-type sickle cell disease was the highest (88.70%) recorded (Figure 2). Concomitantly, the work of Gernet (2010) and Dreux (2012) on the sickle cell patients are similar to these results in which the SS-type were respectively 90 and 71%, although these show the predominant nature of hemoglobin S in Africa (Tshilolo et al., 2019).

Phytochemical screening of the plants

The phytochemical screening carried out during this work revealed the presence of a set of chemical groups in these identified plants as shown in Tables 1 and 2. In addition, the laboratory analysis revealed the presence of secondary metabolites either isolated or in combination such as tannins, sterols and polyterpenes, alkaloids, saponosides, flavonoids, quinones, polyphenols and cyanogenic glycosides (Tables 1 and 2). However, the literature review on the phytochemical study of some of these plants in the survey showed the presence of other chemical groups, namely, cardiotonic glycosides, anthocyanins and coumarins (Salma et al., 2018). The numerous therapeutic properties of secondary metabolites may justify the use of these plants in the treatment of sickle cell disease (Raji et al., 2019). Indeed, alkaloids and derivatives are used as painkillers and have vasodilator properties (Raji et al., 2019). They also show an anti-edematous action, causing a marked increase in blood pressure with a strong diuresis (Nurain et al., 2016; N'Guessan et al., 2009). Moreover, the anthocyanins promote antifalcemic action of sickle cells (Gbolo et al.,

Table 2. Phytochemical screening of the twelve (12) plants.

Plants			Secondary metabolites								
			Sterols and polyterpenes	Polyphenols	Flavonoids	Tannins		Quinones	Alkaloids (Dragendorff)	Saponosides (Cm)	Glycosides cyanogenic
Names	Org.	Extracts				Gallic	Catechin				
Bombax costatum	ER	EMA	++ - +++	+ ++ ++	++ - +++	- + ++	- + -	- - -	+++ - ++	4.5	++ ++
Boscia angustifolia	F	EMA	+ - +++	+ +++ +++	++ - ++	- +++ +	- +++ -	- - -	+++ ++ +++	0.0	- -
Calotropis procera	ER	EMA	++ - +++	++ - +	+ + -	- - +	- + +	- - -	++ +++ +++	5	- -
Capparis corymbosa	F	EMA	+++ - ++	++ ++ +++	+ + -	- + ++	- +++ ++	- - -	+++ +++ +++	5.5	- -
Hygrophila senegalensis	TF	EMA	+++ +++ +++	+ +++ +++	++ - +++	- +++ +++	- ++ ++	- - -	+++ +++ +++	2.5	- ++
Ipomea asarifolia	TF	EMA	++ + +++	++ +++ +++	+ - -	- +++ +++	- ++++ -	- - -	+++ + ++	2	- -
Ipomea batatas	TF	EMA	+++ +++ +++	- +++ +++	- + -	- +++ +	- +++ -	- - -	+++ +++ +++	00	- -
Kigelia africana	Fr	EMA	+++ - ++	+++ +++ +++	+ - -	- +++ +++	- - +++	- - -	+++ + ++	3	- -
Mitragyna innermis	ET	EMA	+++ - +++	++ +++ +++	++ +++ +++	- - ++	- - -	- ++ ++	+++ - ++	2.5	+ +++
Striga hermontica	TF	EMA	- +++ ++	+++ +++ +++	- - -	- + +++	- +++ -	- - -	+++ +++ +++	3.5	+++ -
Walteria indica	R	EMA	+++ - +++	++ +++ +++	- +++ -	- +++ +++	- +++ +++	- - -	+++ +++ +++	0.0	- -

Table 2. Contd.

Zea mays	TF	EMA	+++	-	-	-	-	-	+++	1.5	-
			+++	++	-	++	++	-	+++		-
			+++	+	-	-	-	-	+++		

Org.: Body; EMA: Aqueous methanolic ether; - = absent; + = present in small quantity; ++ = present in average quantity; +++ = present in large quantity.

2017); and the cyanogenic glycosides exhibit very high toxicity (Oluseyi, and Cohall, 2018). The combination of tannins and saponosides resulted to antibacterial properties (N'Guessan et al., 2009). As for the tannins, they have anti-inflammatory properties through their scavenging capacity on free radicals (Biseko et al., 2019; Amadou et al., 2012). Sudasinghe and Peiris (2018) reported in their phytochemical screening the presence of alkaloids, unsaturated sterols, triterpenes, saponins, flavonoids, tannins and proanthocyanidins present in the leaves of *Passiflora suberosa* L; and showed that the herbal preparations are capable of exercising glycaemic regulation with no significant toxic effects.

Generally known, the health benefits associated with polyphenols may be related to their various roles as scavenging agent and their ability to combat cell damage (Table 3). In addition, they possess hepatoprotective activity by preventing lipid peroxidation (Xing et al., 2019; Traoré, 2006), though polyphenols may also impact genes and gene expression, which make it an important candidate for combating sickle cell disease (Osei-Hwedieh et al., 2016; Amadou et al., 2012). Recent researches reported many health benefits through cell signaling pathways and antioxidant effects from flavonoids which are a group of plant metabolites. They are compounds that strengthen the inner lining of blood vessels, helping to help prevent circulatory disorders (Raji et al., 2019; N'Guessan et al., 2009). Traditionally used, naturally occurring substances around the world contain the coumarins which exhibit very important pharmacological activity such as an anti-oedematous, antithrombic, antioxidant and vasodilatory action (Traoré, 2006). In addition, it was established that the presence of phenolic compounds such as flavonoids, and tannin in the plant extracts can be considered to be responsible for inhibition of free radicals formed as a result of lipid peroxidation (Medini et al., 2014). The anthocyanin antioxidant efficacy can also be responsible for reduction of haemolysis of erythrocytes. Furthermore, compound with potent antioxidant efficacy and thus capable of preventing generation of free radicals (Mpiana et al., 2013) could be used as an antisickling drug. Bandara et al. (2018) revealed the presence of anthocyanin in the aqueous extract of *Passiflora suberosa* with potent antihaemolytic activity. Thus, antihaemolytic activity was found to be an important feature of antisickling agents.

The therapeutic effects of these different plants used may be related to their composition in secondary metabolites (polyterpenes, sterols, polyphenols, flavonoids, tannins, saponosides, alkaloids, quinones and anthocyanins). Previously, the antifalcemic activity of several plants such as *Fagara xanthoxyloïds* Lam and *Zizyphus mucronate* was demonstrated on *in vitro* blood sickle cell SS study, focusing on anthocyanins effect (Mpiana et al., 2009). The work of Baraka et al. (2018) showed the capacity of *Sterculia setigera* in preventing haemoglobin oxidation to form methaemoglobin, thus suitable for the management of sickle cell anaemia according to some traditional healers in northern Nigeria.

Conclusion

The study thus revealed that the ethnobotanical surveys carried out among sickle cell patients and traditional healers has enabled identifying of many ways of handling sickle cell cases, based on twenty-nine (29) plant species distributed among twenty (20) families. Several organs of these plant species have been used in the drug preparation to cope with sickle cell crises. These are manifested through several symptoms such as joint pain, headache, stomach, edema and jaundice. The plant parts analysis highlighted compounds like sterols and polyterpenes, polyphenols, flavonoids, tannins, saponosides, alkaloids, quinones, cyanogenic glycosides and anthocyanins. Natural substances also provide a basis for potential new drugs used against several diseases, including sickle cell anemia. Moreover, herbal medicine can currently be considered as a way of relieving anemia in general and sickle cell disease in particular.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

Table 3. Phytochemical screening of seventeen (17) other plants.

Plants		Secondary metabolites								
Names	Org.	Sterols-polyterpenes	Polyphenols	Flavonoids	Tannins	Quinones	Alkaloids	Saponosides	Glycosides cyanogenic	Anthocyanes
Adansonia digitata	F	-	NT	+	-	+	-	+	+	+
	Gr	-	NT	+	+	+	-	-	-	+
	R	-	NT	-	-	-	-	-	+	-
	pulpe	-	NT	+	-	-	-	-	-	-
Allium sativum	G	-	+	-	+	-	+	+	NT	-
Ampelocissus africana	PA	+	NT	-	+	+	+	+	NT	NT
Anogeissus leiocarpus	F	-	NT	-	+	-	-	+	NT	NT
	ET	+	NT	-	+	-	-	+	NT	NT
	ER	+	NT	-	+	-	-	+	NT	NT
	Fle,F,Fr, Tg		NT	NT	+	NT	NT	NT	NT	NT
	PE	+	NT	-	+	-	-	-	NT	NT
Azadiracta indica	F	-	NT	+	-	-	-	-	NT	NT
	ET	-	NT	+	-	-	-	+	NT	NT
Boscia senegalensis	F	+	NT	-	+	-	-	+	NT	NT
	Gr	-	NT	-	+	-	+	+	-	-
Cajanus cajan	ER	-	NT	+	+	-	-	+	NT	NT
	ET	-	NT	+	+	-	-	+	NT	NT
	F	-	NT	-	-	-	-	-	NT	NT
Cochlospermum tinctorium	F	+	NT	-	+	+	-	-	NT	NT
	R	+	+	+	+	NT	NT	+	NT	NT
Combretum micranthum	TF	NT	NT	NT	NT	NT	+	NT	NT	NT
	F	+	+	+	+	+	+	NT	NT	NT
Crossopteryx febrifuga	F	+	+	+	+	-	+	+	NT	NT
	ER	+	+	+	+	-	+	+	NT	NT
	F	+	NT	-	+	-	-	-	NT	NT
	ET	-	NT	-	+	-	-	-	NT	NT
	ER	+	NT	-	-	-	-	-	NT	NT
Faidherbia albida	F	+	+	-	+	-	-	+	-	NT
Gardenia sokotensis	F	+	NT	-	+	-	+	+	NT	NT
Hibiscus sabdarifa	Gr	+	NT	-	-	+	+	+	-	-
		+	NT	-	-	-	+	+	+	-
	T	+	+	+	+	NT	+	+	-	+
	F	+	+	+	+	NT	+	+	+	+
	R	+	+	+	+	NT	+	+	+	-

Table 3. Phytochemical screening of seventeen (17) other plants.

	Gr	+	+	+	+	NT	+	+	-	-
	Gr	+	+	+	+	NT	+	+	+	+
Khaya senegalensis	F	+	NT	+	+	-	-	+	-	+
Lannea microcarpa	ET	+	-	-	NT	-	-	+	-	+
	Fle, F, T, Fr	NT	NT	NT	+	NT	NT	NT	NT	NT
Sclerocarya birrea	F	+	NT	+	+	-	-	+	NT	NT
	PE	+	-	+	+	-	+	+	-	-
	Fle, F, T, Fr	NT	NT	NT	+	NT	NT	NT	NT	NT
Tamarindus indica	Fle, F, T, Fr	NT	NT	NT	+	NT	NT	NT	NT	NT

Org.: Body; - = absent; + = present; NT = not tested; Fle = Flower; PE = whole plant; F = sheet; Fr = fruit; R = root; ER = root bark; ET = bark of the trunk; T = stem; Gr = seed; G = pod; PA = aerial part.
Source: Mounkaila et al. (2017).

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