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## **An overview of anti-diabetic plants used in Gabon: Pharmacology and Toxicology**

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Abstract

*Ethnopharmacological relevance:*

The management of diabetes mellitus management in African communities, especially in Gabon, is not well established as more than 60% of population rely on traditional treatments as primary healthcare. The aim of this review was to collect and present the scientific evidence for the use of medicinal plants that are in current use by Gabonese traditional healers to manage diabetes or hyperglycaemia based here on the pharmacological and toxicological profiles of plants with anti-diabetic activity are presented in order to promote their therapeutic value, ensure a safer use by population and provide some bases for further study on high potential plants reviewed.

*Materials and methods:*

Ethnobotanical studies were sourced using databases such as Online Wiley library, Pubmed, Google Scholar, PROTA, books and unpublished data including PhD and Master thesis, African and Asian journals. Keywords including 'Diabetes', 'Gabon', 'Toxicity', 'Constituents',

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“hyperglycemia’ were used.

#### *Results:*

A total of 69 plants currently used in Gabon with potential anti-diabetic activity have been identified in the literature, all of which have been used in *in vivo* or *in vitro* studies. Most of the plants have been studied in human or animal models for their ability to reduce blood glucose, stimulate insulin secretion or inhibit carbohydrates enzymes. Active substances have been identified in 12 out of 69 plants outlined in this review, these include *Allium cepa* and *Tabernanthe iboga*. Only eight plants have their active substances tested for anti-diabetic activity and are suitable for further investigation. Toxicological data is scarce and is dose-related to the functional parameters of major organs such as kidney and liver.

#### *Conclusion:*

An in-depth understanding on the pharmacology and toxicology of Gabonese anti-diabetic plants is lacking yet there is a great scope for new treatments. With further research, the use of Gabonese anti-diabetic plants is important to ensure the safety of the diabetic patients in Gabon.

Key words: Diabetes mellitus, Gabon, Medicinal Plants, Anti-diabetic activity, Toxicity.

## **Introduction**

Diabetes is a chronic metabolic disorder where management is a global problem. Diabetes is forecasted to become one of the world’s main disablers and killers in less than 25 years (Malviya et al., 2010). The total number of persons affected globally is projected to rise from 371 million

in 2011 to 552 million in 2030, if prevention measures are not scaled up (IDF, 2011). Gabon, a small country with a population of 1.7 million, is the third country in sub-Saharan Africa that is the most affected by diabetes mellitus, with a national prevalence of more than 9% (Ntyonga-Pono, 2015).

Many factors are responsible for the rise of diabetes in Gabon. These factors include urbanisation, lifestyle changes with high fat food and few physical activities, obesity and the fact that more people are being diagnosed. In urban areas, diabetes is well managed, and patients have easy access to medicines. However, the expensive cost of treatments and their poor availability, as well as, the culture and religious beliefs of the population are leading to patients relying more on traditional healers and medicinal plants for the management of diabetes, especially in rural areas (Ntyonga-Pono, 2015).

In Africa, even in Gabon, plant based traditional medicine is widespread. These plants are used to treat all type of common pains and diseases, including those that modern medicines deal with such as cancer, renal insufficiency (Yokozawa *et al.*, 2002), HIV (Helfer *et al.*, 2014) and diabetes (Osabede *et al.*, 2014). Several diabetes medicines used today have been developed or derived from plants that were once used in traditional medicine such as metformin, a biguanide derived from *Galega officinalis* L. (Fabaceae) (Osabede *et al.*, 2014). Inversely, certain natural compounds from medicinal plants such as *Tabernanthe iboga* act like sulfonylureas, organic compounds that enhance insulin release from pancreatic beta cells (Souza *et al.*, 2011).

Despite the World Health Organisation (WHO) recommendations, the reduced cost of herbal medicines and the easy access of plants (many plants are cultured in gardens or surrounding villages), a large number of reported medicinal plants in Gabon are used by the population

without any scientific supportive data (Osabede et al., 2014). Data which could represent a valuable source of information to limit toxicity-related issues, monitor plants and population safety and provide a good number of compounds for drug development in diabetes, are needed. Current therapies for diabetes including insulin and various oral antidiabetic agents such as sulphonylureas and biguanides have limitations including hypoglycaemia and weight gain (Panda et al., 2011; Gupta et al., 2016). Medicinal plants have previously been reported to be beneficial in hyperglycaemia control worldwide and have largely been used as anti-diabetic remedies (Patel et al., 2012). Anti- hyperglycaemic effects of plants claimed to be anti-diabetic have been mainly attributed to their ability to re-establish pancreatic tissues functions by increasing insulin production such as sulfonylureas, inhibiting glucose intestinal absorption such as acarbose an oligosaccharide, or increasing metabolism of insulin-dependent means (Kuate and Efferth, 2010; Talreja and Kaur, 2014).

### **Biodiversity and Ethnobotanical uses of medicinal plants in Gabon**

Gabon is a country covered with more than 80% of forest, and many plants are traditionally used for the treatment of various diseases (Mengome *et al.*, 2009). Despite considerable progress in the management of several pathologies, including diabetes mellitus by conventional medicines, over 60% of Gabonese population is still dependent on plant remedies for economic and cultural reasons. In Gabon, rural areas are surrounded by wild vegetation, as Gabonese population density is low; people living in cities have easy access to domesticated or wild plants such as *Irvingia gabonensis* which is used as anti-inflammatory remedy (Vliet, 2014; Kuate et al., 2007). Medicinal plants use and knowledge have been mastered by traditional healers for a long time in

sub-Saharan Africa, including Gabon.

Ethnobotanical information indicates that more than 20 000 medicinal plants used for numerous pathologies (Iwu, 2014) are known in Africa while less than 1% of them have been scientifically investigated for their biological activities (Iwu, 2014). The use of medicinal plants is a cultural practice which represents the primary healthcare of 80% of the population of developing nations, including Gabon according to the World Health Organization (WHO) (Eyong, 2007; Swargiary *et al*, 2013).

In Gabon, more than 1600 medicinal plants have been reported (Vliet, 2012), however, little data is available in the literature. Among them, several herbs have shown their potential anti diabetic properties including *Irvingia gabonensis* (Odika or wild mango) (Hossain *et al.*, 2012), *Pseudospondias longifolia*, *Antrocaryon klaineinum* and *Tabernanthe iboga* (Mebale *et al.*, 2013; Souza *et al.*, 2011).

The aim of this review was to collect and present the scientific evidences for the use of medicinal plants that are in current use by Gabonese traditional healers to manage diabetes or hyperglycaemia based, and outline any known pharmacological, toxicological and safety profiles. This review therefore provides a valuable source of information and highlights scientific gaps in knowledge of Gabonese plants used in the management of diabetes.

## **Materials and methods**

Relevant information on medicinal plants occurring in Gabon and traditionally used for the management of diabetes and / or hyperglycaemia were mostly obtained from ethnobotanical

studies. These studies were made in different regions of Gabon (Estuaire, Ogooué-Lolo, Haut-Ogooué) with traditional healers, and in local markets of the capital and largest city, Libreville, where one third of the Gabon population lives. Traditional healers or market saleswomen/salesmen did not use the term ‘Diabetes mellitus’. However, they easily described symptoms such as ‘excessive urination with ants and flies gathering around it’, ‘abnormally feeling thirsty’, ‘loosing weight’, principally to diagnose the disease. Also, we selected published papers using databases such as Online wiley library, Pubmed, GoogleScholar, SciFinder, Sciences direct, Scopus, Pubchem using ‘Diabetes’, ‘Gabon’, ‘Toxicity’, ‘Constituents’ as main keywords. Other web sources such as the Plant List, Kew Botanical Garden, PROTA, African and Asian journals were also used alongside books, PhD and MSc dissertations and unpublished data. We shortlisted potential anti-diabetic plants found in the literature or not, which were acknowledged by traditional healers or saleswomen/ salesmen (vernacular name cited) in Gabon, with one or more experimental evidence (*in vivo* and/or *in vitro*) in animal models validating the anti-diabetic activity except for certain plants such as *Antrocaryon klaineinum*. Plants have been listed according to the family alphabetic order, local name, plants part(s) used and the traditional preparation, *in vivo* and/or *in vitro* anti-diabetic activity and other pharmacological activities applied traditionally in Table 1, and toxicity and chemical constituents in table 2.

## **Results / Discussion**

All 69 medicinal plants have been presented in both Table 1 and 2, with known information from the literature outlined and cited. The data has been obtained from ethnobotanical studies originating from different regions in Gabon and from published research papers. Among these

plants, 37 families were recorded with *Apocynaceae* being the most cited with 6 plant species, followed by *Annonaceae*, *Malvaceae* and *Poaceae* with 4 plant species each and *Anacardiaceae*, *Asteraceae*, *Euphobiaceae*, *Fabiaceae*, *Leguminosaeae* and *Mimosoideae* with 3 plant species each.

Generally, plant potential anti-diabetic activity was assessed by *in vivo* (animal models and humans) and *in vitro* (islets and hepatocytes) sugar (usually glucose) lowering effect. From a scientific perspective, only experimental validations at known doses and in specific design, may provide a good idea of a plant safety and efficacy. While, in traditional approach, the taste of the urine and the well-being of the patient after treatment prove plant preparations efficacy.

The majority of plants reviewed here (74%) has *in vivo* and/ or *in vitro* studies that evidenced anti-diabetic properties and support their use by traditional healer for the management of diabetes. However, 26% of reviewed plants including *Antrocaryon klainenum*, *Voacanga Africana* and *Aucoumea klaineana*, have no experimental evaluation of their anti-diabetic effects, either *in vitro* or *in vivo*. Although, these plants contained molecules such as flavonoids, alkaloids and saponins (Table 2), that have known anti-diabetic properties which can justify their use in the management of hyperglycaemia in traditional medicine.

Several reviews on medicinal plants and/or anti-diabetic plants from different parts of the world exist and highlight medicinal herbs value for the management of number of diseases including diabetes (Patel et al. 2012; Ezuruike and Prieto, 2014; Lakshmi et al., 2016; Tjeck et al., 2017).

Ethnobotanical surveys result's and data collected from literature on plants used for the management of diabetes in Gabon showed that plants are used either alone or in combination, such as with *Alstonia congensis* and *Xylophia aethiopica*, *Rauvolfia vomitoria* and *Citrus aurantium*. In traditional medicine, plants combination is the favourite preparation, although, not



easy to assess in laboratory animal model or in tissue. Only one plant, *Petroselinum crispum*, out of 69 was used in combination with a conventional anti-diabetic drug, glibornuride, a sulfonylurea.

Out of 69 plants, 47 plants had literature outlining *in vivo* experimental data in established Type 1 diabetic animal (alloxan or streptozotocin(STZ)-induced diabetes) models, Table 1. type 1 Depending on the dose used, streptozotocin and alloxan chemically destroy a significant number of beta cells in pancreas to induce type 1 diabetes.

Although most Gabonese plants were assessed experimentally in Type 1 animal models, 8 plants have been assessed in Type 2 animal models. For example, *Milicia excelsia* aqueous extract at 50 and 100 mg/kg administered orally prevented insulin resistance and blood glucose rise in dexamethasone-induced insulin resistance in rats (Dzeuffiet et al., 2014) and *Zea mays* corn extract at 50 mg/kg increased C-peptide levels, prevented pancreatic  $\beta$ -cells damage and increased their insulin content in type 2 model C57BL/KsJ db/db mice (Huang et al., 2015). This encouraging data demonstrated that some plants are targeting parameters that contribute to Type 2 Diabetes development and occur in pre-diabetics, such as insulin resistance. Thus, type 2 Diabetes can be managed at a very early stage by these plants. Type 2 diabetes is the most prevalent type of diabetes mellitus worldwide with increasing morbidity (Motala and Ramaiya, 2010). Thus, the Type 1 animal models used in most reviewed studies are not adequate to assess plants efficacy used to treat type 2 diabetic parameters such as insulin resistance or glucose tolerance. Numerous pharmacological experiments reviewed here involved aqueous (39 studies) plant extracts, negative and positive controls with glibenclamide, tolbutamide or metformin as anti-diabetic drug of reference. Organic extracts were not often used even though, they could be more efficient than water extract; e.g.: the leaves ethanol (400 mg/kg bw) and chloroform (800

mg to 1 g/kg bw) extract of *Vernonia amygdalina* Del. which exerted effective improvement in glucose tolerance and decreased Fasting Blood Glucose (FBG) in STZ-induced diabetic rats. The traditional most cited formulations were decoction (40 plants), maceration (22 plants) and infusion (11 plants), which can support the use of water extract over organic's, to investigate the effects claimed by traditional healers. Negative control was including in most of studies reviewed, however, the positive control was missing for some investigations; for example, in the study of the root aqueous extract at 500 and 1000 mg/kg bw of *Newbouldia laevis* (P. Beauv.) Seem by Okonkwo and Okoye in 2009. Thus, the experiment was incomplete.

Only 5 plants reviewed had data in diabetic patients; *Allium cepa*, *Rauwolfia vomitoria*, *Jatropha curcas*, *Irvingia gabonensis* and *Ipomea batatas*. This was surprising given that a large number of Gabonese plants had known safe doses and showed significant *in vivo* and/or *in vitro* anti-diabetic efficacy data in animal models justifying a clear rationale for the management of diabetes and a controlled clinical trial evaluation, such as *Allium sativum*, *Alstonia boonei* and *Euphorbia hirta*. It can be explained as numerous pharmacological studies reviewed have problematic methods including high doses and poor experimental design. Even though, high doses reported were usually for spices such as *Persea americana*, they need to be adapted from animal models to patients in clinical trials; e.g. *Zea mays*, *Ipomea batatas* and *Allium sativum* (Table 1).

Fourteen plants out of 69 have *in vitro* experimental data that could support part or all of their anti-diabetic mechanism of action. It is well recommended that *in vitro* experiments are carried out to determine the mechanism of anti-diabetic action of the plant. Moreover, due to ethical considerations associated with animal testing, it is greatly advised, where possible, to use non-animal model to validate experiments. The most potential reviewed plants are *Mangifera indica*

kernel flour which inhibited  $\alpha$ -amylase,  $\alpha$ -glucosidase and aldose reductase, enzymes that contribute to prevent / reduce carbohydrates digestion, thus less absorption of sugar by intestine and less blood glucose levels (Ironi et al., 2014). *Tabernanthe iboga*, which induced insulin secretion from  $\beta$ -cells in high glucose concentration (Souza et al., 2011), Akuammicine from *Picralima nitida* which increased glucose uptake in adipocytes (Kazeem et al., 2013), quercetin from *Psidium guajava* which increased glucose uptake in hepatocytes (Fang-Chui et al., 2009), and *Allium sativum* that enhanced glucose transporter GLUT-4 gene expression (Montasser and Fehresty, 2011).

*In vitro* experiments are often designed to reproduce existing drugs mechanism of action used for the management of diabetes, such as sulfonylureas. Such mechanistic studies support an easier identification of potential medicinal plants with therapeutic value and have identified natural compounds. However, this experimental approach is only based on known targets and exclude extracts that might act on unknown targets through new mechanisms. Also, for remedies composed of plants mixture, it would not be appropriate to assess plants efficacy by *in vitro* experiments alone, as multiple active metabolites, and multiple targets may be involved.

In the Table 2, the majority of reviewed plants have revealed several bioactive compounds that elicit anti-diabetic effects such as alkaloids, terpenes, phenolic compounds. However, few of them have their isolated active natural product constituents tested for anti-diabetic effects. Indeed, only 12 medicinal herbs have had their anti-diabetic active constituents identified including the xanthone glycosides mangiferin from *Mangifera indica*, akuammicine alkaloids and its analogues from *Picralima nitida* and *Alstonia boonei* which stimulates glucose uptake, indole alkaloids ibogaine and its analogues from *Tabernanthe iboga* which increased beta cells insulin

release and flavonoids neohesperidin and naringin from *Citrus aurantium* which regulate glucose metabolism enzymes. Furthermore, flavonoids are known to exert antioxidant effects, which is beneficial against many diabetes complications such as arteriosclerosis, nephropathy, neuropathy, retinopathy associated with high oxidative stress state (Ezuruike and Prieto, 2014). Certain natural product constituents cited in Table 2 may help to evidenced specific beneficial effects in diabetes by assessing compounds that have previously been studied such as the alkaloids and flavonoids from *Antrocaryon klaineinum*. Moreover, knowing plants active principles could support a better dosage and quality control of plants remedies. Thus, these 12 plants with isolated compounds offer great potential anti-diabetic plants for further investigations. Also, it is important to note that a large number of plants reviewed here are currently being taken by diabetic patients alone or in combination with conventional anti-diabetic drugs in Gabon. Toxicological issues might therefore be associated with plants consumption at wrong dosage or due to compounds interactions. It is well understood that medicinal plants are an abundant source of bioactive compounds that can elicit various biological, pharmacological and toxicological effects within the body. The risk of medicinal plants toxicity is one of the main reason why physicians hesitate to consider medicinal plants as alternative therapeutics in Gabon. Various plants reviewed here have specific organ toxicity such as nephrotoxicity, hepatotoxicity or cardiotoxicity effects (Table 2). However, most of these effects are only seen at high doses which encourage the use of medicinal plants at appropriate safe doses. Among the plants reviewed, the oral lethal dose that kills 50% of the population ( $LD_{50}$ ) is greater than 2000 mg/kg while the intraperitoneal (IP)  $LD_{50}$  is as low as 1 mg/ml (Table 2). Acute and subacute toxicities with dose-related information need to be detailed before the use of medicinal plants. Thirteen plants reviewed have no toxicological information. It is important to highlight that all plants

listed in this review are continuously consumed by the Gabonese population. Thus, it is vital to assess plants toxicity and acknowledged dose efficacy and activities before their use, to avoid unwanted compounds interactions and harm.

## Conclusion

This review is the first to present all known literature on the Gabonese medicinal plants and highlights the use of specific plants in the treatment of diabetes. While it is of interest to identify new plants for research, this review also outlines the lack of scientific evidence on Gabonese medicinal plants claimed to be anti-diabetic and currently used by the Gabonese population. Numerous plants are reported in Gabon to be anti-diabetic and are used by traditional healers to treat the population. While 69 plants have been described in the literature, there is very little preliminary data, although there is a great deal of potential for novel diabetic therapy. The lack of reproducible investigations with poor general design and unrealistic doses showed the huge work to be done before getting to phytomedicines from the plants cited. Nevertheless, the results gathered in this review represent a valuable start point to further investigate the medicinal plants already used for the management of diabetes in Gabon. Many points have to be resolved such as the reproducibility of traditional preparation, the appropriate animal model, the experimental design and so on. Although, most of the plants listed in this review reduced blood glucose levels in animal or human model, this parameter alone is not sufficient to prioritise the most potential anti-diabetic plants. The mechanism of action of these plants should be investigated to allow standardised phytomedicines to be available. Toxicological data was also scarce, and the pharmacological and natural compound information of Gabonese anti-diabetic plants is not sufficient. Ibogaine and its congener alkaloids from *Tabernanthe iboga* need particular attention as their anti-diabetic potential can easily be studied. Further investigations are needed to validate

the mechanism of action, clinical efficacy and toxicology of all these plants and to ensure the safety of the Gabonese population.

Above all, this work was done to make available local information to enable future investigations with Gabonese potential anti-diabetic plants and promote Gabonese traditional knowledge.

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Table 1: Anti-diabetic plants used in Gabon

<b>Family: Scientific name</b>	<b>Vernacular name</b>	<b>Plant part(s) used/ Traditiona l preparatio n</b>	<b>Antidiabetic activities</b>	<b>Other pharmacological activities</b>
Amaryllidaceae : <i>Allium cepa</i> L.	Nyonda	Bulb / Crude	<i>In vivo</i> : The consumption of 100 g of onion crude extract reduced FBG in type 1 diabetic patients compared to insulin and lower FBG in type 2 diabetic patients comparing to glibenclamide, after 4 hours. Also, the same dose reduced significantly reduced hyperglycemia in type 1 diabetic patients compared to water and insulin and in type 2 diabetic patients compared to water and glibenclamide, after	Hypotensive, Anti-inflammatory, Antimicrobial Anticarcinogenic, Antimutagenic, Antihyperglycemic, Antioxidant, Neuroprotective, Anticonvulsion (Naseri <i>et al.</i> , 2008; Kaiser <i>et al.</i> , 2009; Nishimura <i>et al.</i> , 2006; El-Demerdash <i>et al.</i> , 2005; Santas <i>et al.</i> , 2010).

			4h (Taj Eldin et al., 2010). The use of 200 mg/kg bw of S-methylcysteine sulfoxide (SMCS) for 2 months in alloxan-induced diabetic rats ameliorated diabetic conditions compared to glibenclamide and insulin. Also, these doses exhibited antioxidant effects on lipid peroxidation. (Akash et al., 2014).	
Amaryllidaceae : <i>Allium sativum</i> L.	Garlic	Cloves / Maceration	<i>In vivo</i> : Oral doses of 0.1, 0.25 and 0.5 g/kg bw reduced serum glucose, TC, TG levels on diabetic rats comparing to glibenclamide for 14 days (Eidi et al., 2006). <i>In vitro</i> : Increasing doses of alliin (0, 10, 20 and 50 uM) incubated with SOD (Superoxide dismutase) at 0.2 mg/ml in presence of glucose (0.5M) or 10 mM MG (Methylglyoxal) or both for 10 days and 37° C showed the therapeutic potential of alliin to prevent glycation-mediated diabetic complication comparable to quercetin effects (Anwar et al., 2017).	Antimicrobial, Antiviral, Antiparasitic, Antiinflammatory, Antihyperlipidemic (Nwokocha et al., 2011; Capasso, 2013; Ashraf et al., 2005; Adler, 2002; Yousuf, 2011; Bayan et al., 2014)
Anacardiaceae: <i>Antrocaryon</i>	Osome élé, onzabili	Stem bark / Decoction,	Not available in	Antinociceptive and anti-inflammatory



<i>klaineinum</i> Pierre		Maceration	literature	(Fongang et al., 2017)
Anacardiaceae: <i>Mangifera</i> <i>indica</i> L	Mwiba mutangani	Leaves, Stem- bark, roots, seed / Decoction	<i>In vivo and in vitro:</i> The ethanol extract of mango peel at 100, 150 and 200 mg/kg bw administered once for 60 days to STZ- induced diabetic rats reduced FBG, fructosamine and glycolated haemoglobin levels comparable to metformin. The same doses inhibited alpha- amylase and alpha- glucosidase activities with IC <sub>50</sub> of 4.0 and 3.5 ug/ml respectively (Gondi and Prasada Rao, 2015). In high-fat diet/ STZ-diabetic rats, 20% of MIKF ( <i>Mangifera indica</i> Kernel Flour) - supplemented diets, improved fasting blood glucose, hepatic glycogen, glycolated haemoglobin, lipid profile, plasma electrolytes, monaldehyde, and liver function biomarkers in diabetics compared to control and metformin groups, after 21 days of treatment (Ironi et al., 2016).	Antioxidant, Immunostimulant, Anti-allergic, Anti- inflammatory, Antitumor, Antimicrobial, Antiviral (Wauthoz <i>et al.</i> , 2007)

Anacardiaceae: <i>Pseudospondias longifolia</i> Engl.	Ofoss	Stem bark / Decoction, maceration	Not available in literature	Antioxidant and antimicrobial properties (Obiang et al., 2016)
Annonaceae: <i>Xylopi aethiopica</i> (Dunal) A. Rich.	Mugana	Fruits Leaf / Decoction	<i>In vivo</i> : Acetone fraction of <i>Xylopi aethiopica</i> (XA) at 150 and 300 mg/kg bw in type 2 diabetic and non-diabetic rats significantly lowered blood glucose level in a dose-dependent manner, serum fructosamine, insulin resistance, serum insulin and glucose tolerance were also improved compared to metformin after 4 weeks' study (Mohammed et al., 2016). Aqueous leaf extract of XA at 200mg/kg bw for 25 days showed beta- cells recovery/regenerative effect, blood glucose decrease in STZ- induced diabetic rats which improved insulin secretion compared to non- treated STZ-diabetic rats (Ofusori et al., 2016).	Antimicrobial, Analgesic, Antioxidant, Antimalarial, Diuretic Hypotensive (Ilusanya <i>et al.</i> , 2012; Woode <i>et al.</i> , 2012; Mohammed <i>et al.</i> , 2015; Karioti <i>et al.</i> , 2004; Titanji <i>et al.</i> , 2008; Somova <i>et al.</i> , 2001) Antidepressant potential, epilepsy, inflammatory disorders, haemorrhoids, bronchitis, rheumatism, anti-inflammatory effects, analgesic, sedative, anticonvulsant, antiproliferative effects (Biney et al., 2016) antioxidant (Tjeck et al., 2017)
Annonaceae: <i>Annickia chlorantha</i> (Oliv.) Setten & Maas	Mwamba jaune, Muambebeng ue	Stem barks/ Decoction	Not available in literature	Antimalarial, jaundice, yellow fever, hepatitis B, conjunctivitis, infected wounds, ulcers (Olivier et al., 2015)

Annonaceae: <i>Annona muricata</i> L.	Soursop	Stem barks/ Decoction	<i>In vivo</i> : Leaves aqueous extract at 100 and 200 mg/kg orally administered to normal and STZ-induced diabetic rats, reduced significantly blood glucose levels in diabetic animals by 75% at 100 mg/kg and by 58.22% at 200 mg/kg, after 28 days of treatment, compared to initial value and control group (Ngueguim et al., 2014)	Antimicrobial, anti-inflammatory, antioxidant, larvicide, cytotoxic to tumour cells (Coria-Télez et al., 2016)
Annonaceae: <i>Anonidium mannii</i> (Oliv.) Engl. & Diels	Ebom	Stem barks/ Decoction	Not available in literature	Antibacterial activity (Djeussi et al., 2013) and cytotoxic properties (Tjeck et al., 2017)
Apiaceae: <i>Petroselinum crispum</i> (Mill.) Fuss	Persil	Leaves/ Chewing	<i>In vivo</i> : Parsley extract (2g/kg) and Glibornuride (5mg/kg bw) were given daily to STZ-diabetic rats for 28 days. Blood glucose levels, liver non-enzymatic glycosylation decreased in both groups compared to controls. However, liver lipid peroxidation increased in glibornuride group (Ozsoy-Sacan et al., 2006)	Diuretic activity (Ozsoy-Sacan et al., 2006) Antioxidant and antibacterial properties (Tjeck et al., 2017)
Apocynaceae: <i>Alstonia boonei</i> De Wild.	Emien	Stem barks/ Decoction	<i>In vivo</i> : Water extract at 200 and 500 mg/kg bw given orally for 30 days to	Diuretic (Tjeck et al., 2017), antioxidant, antimalarial, anti-

			<p>dexamethasone-induced-hyperglycaemia rats reduced blood glucose level, TG, TC, ALT, AST compared to non-treated rats and comparable to glibenclamide and metformin groups (Nkono Ya Nkono et al., 2014).</p> <p><i>In vitro</i>: Ethyl acetate extract orally administered to Wistar rats significantly reduced blood glucose level within 2h and was the most potent inhibitor of <math>\alpha</math>-amylase (IC<sub>50</sub>: 3.17 mg/ml) and <math>\alpha</math>-glucosidase (IC<sub>50</sub>: 0.70 mg/ml) (Kazeem and Ashafa, 2015)</p>	<p>infective, treat arthritis and infertility (Ezuruike and Prieto, 2014)</p>
<p>Apocynaceae: <i>Alstonia congensis</i> Engl</p>	<p>Mukuka</p>	<p>Root / Decoction, maceration</p>	<p><i>In vivo</i>: Mixture of hydroalcoholic extract of <i>Alstonia congensis</i> (AC) bark and <i>Xylopiya aethiopica</i> fruit (1:1) given once daily, reduced blood glucose levels in Swiss albino healthy mice between doses 50 and 250mg/kg bw after 30 days treatment, compare to the control (Ogbonnia et al., 2008).</p>	<p>Antioxidant Antimalarial (Ogbonnia et al., 2008; Awah et al., 2012; Awe et al., 2009)</p>

<p>Apocynaceae: <i>Picralima nitida</i> (Stapf) T. Durand &amp; H. Durand</p>	<p>Dugundu or Ebam</p>	<p>Leaves, fruits, stem bark, seed / Infusion, maceration, decoction</p>	<p><i>In vivo</i>: Antidiabetic activity of methanol extract of leaves of <i>Picralima nitida</i> (PN) (300 mg/kg) in STZ-induced diabetic rats showed significant blood glucose reduction compared to control and glibenclamide groups after 90 min of glucose load (Teugwa et al., 2013).</p> <p><i>In vitro</i>: Akuammicine (3-93 <math>\mu</math>M) from the chloroform extract of PN seeds stimulated the increase in glucose uptake in fully differentiated 3T3-L1 adipocytes (Shittu et al., 2010). The acetone leaf extract (2.5-10 mg/ml) showed inhibition of alpha-amylase and alpha-glucosidase activities (IC<sub>50</sub> of 6.50 and 3.00 respectively) (Kazeem et al., 2013).</p>	<p>Antimalarial, Antipyretic, Analgesic, Anti-inflammatory, Antimicrobial, Antiulcer, Antioxidant, Antiparasitic (Inyanga et al., 2006; Erharuyi et al., 2014; Yessoufou et al., 2013)</p>
<p>Apocynaceae: <i>Rauvolfia vomitoria</i> Afzel.</p>	<p>Mupitugu</p>	<p>Leaves, root bark / Decoction, maceration</p>	<p><i>In vivo</i>: 6 weeks' administration of mixture of <i>Rauvolfia vomitoria</i> (RV) and <i>Citrus aurantium</i> (0.5 ml/kg bw) to genetic diabetes mice resulted in</p>	<p>Antitumor, Anticonvulsivant, Antimicrobial, Analgesic, Hepatoprotective, Antimalarial Antipsychotic, Antioxidant</p>

			normalisation of blood glucose levels and pancreas protection as compared to control groups (Campbell et al., 2006). Decreased of post prandial and fasting plasma glucose levels in type-2 diabetic patients given daily a mixture of RV and <i>Citrus aurantium</i> (tea) for 4 months (Campbell-Tofte et al., 2011). Hypoglycaemic effect at 500, 700 and 1000 mg/kg bw in healthy mice after 4g/kg glucose load (N'doua et al., 2015).	(Olatokunboh <i>et al.</i> , 2009; Yu <i>et al.</i> , 2013; Amole <i>et al.</i> , 2006; Ezejindu <i>et al.</i> , 2013; Momoh <i>et al.</i> , 2014; Nwodo <i>et al.</i> , 2003; Bisong <i>et al.</i> , 2011; Okolie <i>et al.</i> , 2011)
Apocynaceae: <b><i>Tabernanthe iboga</i> (Bail.)</b>	Iboga, diboga	Stem root, stem bark / Decoction, maceration	<i>In vitro</i> : Aqueous extract of <i>Tabernanthe iboga</i> root barks induced insulin secretion in isolated islets at 1ug/ml in presence of stimulatory glucose concentration [11.1 mM] (Souza et al, 2011)	Anti-addictive, spasmolytic, anti-HIV1, ant fatigue, anti-hunger, anti-psychological troubles (Souza et al., 2011)
Apocynaceae: <b><i>Voacanga Africana</i> Stapf ex Scott-Elliot</b>	Ondou or Ontueles	Roots/ Maceration	Not available in literature	Antioxidant and antimicrobial activities (Tjeck et al., 2017)
Aracaceae: <b><i>Cocos nucifera</i> L.</b>	Coco	Fiber/ Decoction	<i>In vivo</i> : <i>Cocos nucifera</i> influorescence (CNI) methanol extract at 100, 200 and 400 mg/kg bw were	Anti-diarrhea, dysentery (Naskar et al., 2011), cytoprotective and antimalarial activities (Tjeck et al., 2017)

			administered to groups of STZ-induced diabetic male rats for 45 days. CNI extract at 200 mg/kg bw showed better antihyperglycemic effect compared to diabetic control. CnI methanol extract improved glucose metabolism in this study (Renjith et al., 2013)	
Asteraceae: <b><i>Ageratum conyzoides</i> L.</b>	Kumba djuma	Whole plant, leaves / Fresh juice, infusion	<i>In vivo</i> : Aqueous extract doses of 100, 200 and 300 mg/kg given orally to STZ-rats for 3 weeks lowered serum glucose and improved lipid profile compared with controls (Nyunai et al., 2015). Methanol extract of leaves, stem and root at 100 mg/kg administered orally to normal and STZ-rats reduced FBG, TC, TG, LDL and HDL compared with control and untreated group, after 14 days' treatment (Atawodi et al., 2017).	Analgesic, Antimicrobial, Anti-inflammatory, Spasmolytic, Emmenagog, Anti-Cancer, Radioprotective, Antioxidant, Cardiovascular activity, Gastrointestinal activity, Antimalarial, Antidiabetic, Anticoccidial, Schistosomicidal (Singh <i>et al.</i> , 2013 ; Adebayo <i>et al.</i> , 2010 ; Kamboj <i>et al.</i> , 2008).
Asteraceae: <b><i>Tithonia diversifolia</i> (Hemsl.) A. Gray.</b>	Daisy	Leaves/ Chewing	<i>In vivo</i> : Aqueous leaf extract at 500 mg/kg bw showed hypoglycaemic effect in normal mice and lowered significantly blood glucose levels,	Antioxidant, antimalarial, antimicrobial properties, treat hepatitis, infectious dermatitis, fever, diarrhea, ascariasis (Poonsit et

			TC, TG and LDL-cholesterol in alloxan-diabetic mice after 30 days' treatment compared to control and glibenclamide treated mice (Thongsom et al., 2013)	al., 2016)
Asteraceae: <b><i>Vernonia amygdalina</i></b> Del.	Ndolé	Leaves / Decoction	<i>In vivo</i> : Leaves ethanol extract at 400 mg/kg given for 28 days exerted the most effective improvement in glucose tolerance, decrease in FBG, in TG and TC levels and exerted pancreatic beta-cells protective effect with slight increase in insulin level of STZ-induced diabetic rats compared to metformin treated rats. This study showed that 400 mg/kg extract increased GLUT4 translocation to plasma membrane suggesting skeletal muscle's glucose uptake stimulation (Ong et al., 2011). Leaves chloroform extract (800 mg-1 g/kg) showed blood and serum glucose-decrease effects in non-diabetic and STZ-induced diabetic rats, in a similar way	Antimicrobial, Antimalarial, Antiparasitic, Antiviral, Antimutagenic, Analgesic, Antipyretic, Anti-Inflammatory, Antioxidant, Hepatoprotective, Anti-cancer (Yeap <i>et al.</i> , 2010; Akah <i>et al.</i> , 2004)



			of metformin and compared to control, after 14-day administration (Atangwho et al., 2013). A mixture (1:1:1) of leaves 1:3 (weight:water) of <i>Vernonia amygdalina</i> , <i>Ocimum gratissimum</i> and <i>Gongronema latifolium</i> decreased significantly blood glucose concentrations compared to baseline, when given 45 min before OGTT in normoglycemic patients (Ejike et al., 2013).	
Bignoniaceae: <i>Newbouldia laevis</i> (P. Beauv.) Seem	Ossome-dzo	Stem barks / Decoction	<i>In vivo</i> : Aqueous extract of root at 500 and 1000 mg/kg bw significantly reduced serum glucose levels in normal and alloxan-induced diabetic rats after 4h to 6h (Okonkwo and Okoye, 2009). Dichloromethane-methanol extract (DME), hexane fraction (HF), ethylacetate fraction (EF) and methanol fraction (MF) at 250, 500 and 1000 mg/kg decreased significantly, in a dose-dependent manner blood glucose in alloxan-	Cancers, infectious diseases, male infertility, anti-hemorrhagic (Kuetete et al., 2014), antioxidant, antimicrobial potential, anti-inflammatory, anti-malarial (Anaduaka et al., 2014)

			induced diabetic rats compared to control and metformin-treated rats, from 3h after drug administration. Sub-fraction of MF at 50, 100 and 200 mg/kg showed significant blood glucose reduction compared to glibenclamide (Osigwe et al., 2015)	
Bignoniaceae : <i>Spathodea campanulata</i> P. Beauv.	Tulipier du Gabon	Stem bark, leaves / Decoction	<i>In vivo</i> : Aqueous-methanol extract at 800 mg/kg significantly reduced blood glucose in healthy rats after 2h administration. At 200, 400 and 800 mg/kg, the extract after glucose-induced hyperglycaemia, exerted moderate reduction of blood glucose. However, in alloxan-induced diabetic rats the extract significantly reduced blood glucose levels with the highest effect at 400 mg/kg comparable to those of control and chlorpropamide (Tanayen et al., 2014)	Antioxidant, Antimicrobial, Analgesic, Anti-inflammatory, Antimalarial, Anticonvulsant, Wound Healing, Hepatoprotective (Coolborn et al., 2015; Rajesh et al., 2010; Ilodigwe et al., 2009; Ilodigwe et al., 2010; Dhanabalan et al., 2008; Niyonzima et al., 1999; Houghton et al., 2005; Dadzeasah 2012).
Burseraceae: <i>Aucoumea klaineana</i> Pierre	Okoumé	Stem barks / Maceration	Not available in literature	Anti-inflammatory (Pérez et al., 2011), antioxidant (Koudou et al., 2009)
Burseraceae: <i>Santiria</i>	Ebo, Nkungu	Roots / Decoction	Not available in	Antimicrobial activity (Tjeck et al., 2017),

<i>trimera</i> (Oliv.) Aubrév.			literature	HIV/AIDS (Feuya Tchoua et al., 2015)
Caesalpinioidea e: <i>Eurypetalum</i> <i>tessmannii</i> Harms	Anzillim	Stem barks / Decoction	Not available in literature	
Caesalpinioidea e: <i>Guibourtia</i> <i>tessmannii</i> (Harms) J. Leonard	Kévazigo	Stem barks / Decoction	<i>In vitro</i> : 70 ug/ml of aqueous extract induced insulin secretion in beta cells at high glucose concentration (11.1 mg/ml) (Research in progress, PhD Bayissi Bading-Taika)	Hypotensive and antioxidant activities (Madingou et al., 2011)
Calophyllaceae: <i>Mammea</i> <i>Africana</i> Sabine	Oboto	Stem barks / Decoction	<i>In vivo</i> : CH <sub>2</sub> -Cl <sub>2</sub> -MeOH stem bark extract from 19 to 300 mg/kg administered to STZ-induced type 1 diabetes rats reduced blood glucose levels after 5h. The maximal anti-diabetic effects, better than those produced by glibenclamide, were obtained at 75 mg/kg during a 21-day period (Tchamadeu et al., 2010)	Anti-malarial fever, anti-microbial, antiplasmodial (Okokon et al., 2007), hepatoprotective, anti-inflammatory, anti-hypertensive, cardioprotective, hypolipidemic, vasorelaxant, analgesic, antioxidant, anti-diarrheal, immunomodulatory, nephroprotective (Okokon et al., 2016)
Cannabaceae: <i>Celtis</i> <i>tessmannii</i> Rendle	Diania	Stem barks / Decoction	Not available in literature	
Capparaceae: <i>Buchholzia</i> <i>coriacea</i> Engl.	Magic cola	Seeds / Maceration	<i>In vivo</i> : Ethanol extract and butanol fraction of	Antiinflammatory, Antimicrobial, Antiparasitic, Antiulcer,

			<p><i>Buchholzia coriacea</i> at 250 mg/kg bw each (EEBC and BFBC) decreased FBG in hyperglycemic STZ-mice and normoglycemic rats 4 and 12h, respectively, after administration. EEBC, BFBC and glibenclamide administration significantly reduced FBG level in STZ-rats by 55%, 64%, and 56% respectively (Adisa et al., 2011). Aqueous and methanol extracts at 100, 200 and 400 mg/kg bw administered twice daily, showed a dose-dependent decrease of blood glucose concentration in alloxan-induced diabetic albino rats after 14-days treatment, compared to control and glibenclamide treated rats (Obiudu et al., 2015)</p>	<p>Antispasmodic (Ezike et al., 2015; Adisa et al., 2011; Ajaiyeoba et al., 2003; Fred-Jaiyesimi et al., 2011; Erhirhie et al., 2015; Anowi et al., 2012)</p>
<p>Caricaceae: <i>Carica papaya</i> L.</p>	<p>Mulolu</p>	<p>Leaves, fruit pulp, seed / Infusion, decoction, juice</p>	<p><i>In vivo</i>: Leaf aqueous extract of <i>Carica papaya</i> at 0.75, 1.5 and 3g/100 ml has shown antihyperglycemic and hypolipidemic potentials in alloxan-induced diabetic rats after 30 days</p>	<p>Antioxidant, Antimicrobial, Anticancer, Anti-Inflammatory, Wound Healing, Antiparasitic, Diuretic, Hepatoprotective, Dengue Fever (Sudhakar et al., 2010; Krishna et al., 2008;</p>

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compared to controls and hypoglycemic effect at 100, 200 and 400 mg/kg bw in STZ-induced diabetic rats compared to glibenclamide group after 21 days (Maniyar and Bhixavatimath, 2012 and Juárez-Rojop et al., 2012). Leaf extract (3-125 mg/kg bw) preserves pancreatic islets, improves insulin secretion in STZ-induced diabetic animals compared to insulin after 20 days (Miranda-Osorio et al., 2016)

*In vitro*: Healthy pancreatic cells cultured in a presence of leaf aqueous extract (3-12 mg) and/or STZ (6 mg) for 3 days revealed higher insulin levels in the medium containing *Carica papaya* leaf extract comparing to the medium where cells received only STZ (Miranda-Osorio et al., 2016)

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Convolvulaceae : <i>Ipomoea batatas</i> (L.) Lam.	Mongu	Whole plant, leaves, tubers / Juice extract, infusion, powder	<i>In vivo</i> : 4g/day given orally to 61 type 2 diabetic patients decreased significantly fasting blood glucose after 12 weeks. Also after the 2h-glucose levels were significantly lowered in the (4g) group compared to the placebo group (Ludvik et al., 2004). Moreover, (4g/day) treatment improved glucose tolerance due to the amelioration of insulin sensitivity (Ludvik et al., 2003). Aqueous extract of whole plant decreased dose dependently (100-400 mg/kg) blood glucose levels in normal and STZ-induced diabetic rats compared to control and glibenclamide groups (Olowu et al., 2011)	Antimicrobial, Antioxidant, Antidiabetic, Wound Healing Antiulcer, Hepatoprotective, Anti-inflammatory, Antiproliferative, Immunostimulant (Pochapski <i>et al.</i> , 2011; Ogunrinola <i>et al.</i> , 2015; Panda <i>et al.</i> , 2011 ; Panda <i>et al</i> 2012).
Combretaceae: <i>Combretum micranthum</i> G. Don	Kinkêliba	Leaves / Infusion	<i>In vivo</i> : Aqueous leaf extract at 100, 200 and 400 mg/kg were administered to normal, sub-diabetic and alloxan-induced diabetic rats. Dose of 100 mg/kg showed significant hypoglycemic and anti-hyperglycemic effects comparable to glibenclamide at 0.6 mg/kg (Chika and Bello, 2010)	Antibacterial (Tjeck et al., 2017)

Euphorbiaceae: <i>Alchornea cordifolia</i> (Schumach & Thonn.) Mull.Arg.	Dumbundzen	Leaves / Decoction	<i>In vivo</i> : Increasing hypoglycaemic effects at 200, 400 and 800 mg/kg comparing to Glibenclamide in STZ-induced diabetic wistar rats after 28 days (Mohammed et al., 2013).	Anti-Inflammatory, Antimicrobial, Wound Healing, Analgesic, Immunostimulant, Antipyretic, Hepatoprotective, Antioxidant, Antimalarial (Manga <i>et al.</i> , 2004; Okeke <i>et al.</i> , 1999 ; Agyare <i>et al.</i> , 2014; Kouakou e <i>et al.</i> , 2013; Ishola <i>et al.</i> , 2012; Effo <i>et al.</i> , 2013; Olaleye <i>et al.</i> , 2006; Togola 2002)
Euphorbiaceae: <i>Euphorbia hirta</i> L.	Ambèningo	Leaves, whole plant / Decoction, maceration	<i>In vivo</i> : Ethanolic leaves extract (400 mg/kg bw) reduced blood glucose levels in STZ-induced diabetic rats after 21-days treatment in comparison to glibenclamide (Maurya et al., 2012).  <i>In vitro</i> : Alpha-glucosidase inhibitory activity and sucrose tolerance effect of quercetrin, dimethoxy quercetrin, hirtacoumaroflavonoside and hirtaflavonoside-B ethyl acetate fraction from <i>Euphorbia hirta</i> methanolic extract in comparison to acarbose (Manjur et al., 2015)	Anti-allergic, Anti-inflammatory Diuretic, Antioxidant, Antitumor Antiparasitic, Antimicrobial, Antihypertensive, Antimalarial, Immunostimulant, Anxiolytic, Sedative (Huang <i>et al.</i> , 2012; Patil <i>et al.</i> , 2009)
Euphorbiaceae:	Puluka	Seeds,	<i>In vivo</i> : Roots	Antioxidant,

<i>Jatropha curcas</i> L.		leaves, root, stem bark, whole plant / Decoction, maceration	aqueous extract (250 and 450 mg/kg bw) decreased fasting blood glucose levels in alloxan-induced diabetic rats compared to untreated and Glucophage rats, after 15 days (Aladodo et al., 2013). Blood glucose level reduction or anti-hyperglycemic potential activity compared to control, in alloxan-induced diabetic female rats by aqueous extract of <i>Jatropha curcas</i> leaves at 100, 200 and 300 mg/kg bw after 21 days of treatment (Nwamarah et al., 2015).	Antibacterial, Anti-Inflammatory, Anti-ulcer, Antiparasitic, Anti HIV, Gastroprotective, Antitumor, Wound healing, Coagulant and anticoagulant (Sharma et al., 2012; Laxane et al., 2013; Dahake et al., 2013)
Fabaceae: <i>Acacia auriculiformis</i> Benth.	Akasmani	Leaves / Infusion	Not available in literature	Antifilarial and antioxidant effects (Tjeck et al., 2017)
Fabaceae: <i>Mimosa pudica</i> L.	Bodji	Leaves / Decoction	<i>In vivo</i> : Ethanolic leaves extract at 600 mg/kg given to alloxan-induced Wistar rats decreased significantly blood glucose level compared to metformin at 500 mg/kg 5h after treatment (Sutar et al., 2009)	Antimicrobial and hypolipidemic properties (Tjeck et al., 2017)
Fabaceae: <i>Phaseolus vulgaris</i> L.	Bean	Fruit / Decoction	<i>In vivo</i> : Aqueous extract at 400 mg/kg administered to	Antioxidant, antiproliferative (Ombra et a., 2016)



			normal and alloxan-induced diabetic rats daily for 14 days showed hypoglycemic and anti-diabetic properties compared to control group (Luka et al., 2013)	
Gentianaceae: <i>Anthocleista vogelii</i> Planch.	Givindu	Root, leaves, stem bark / Decoction, maceration	<i>In vivo</i> : Leaves, stem bark and roots methanol extracts (1g/kg) given orally to albino rats for 7 days exhibited blood glucose reduction (Olubomehin et al., 2013). Ethanolic extract of roots (100, 200 and 400 mg/kg) and fractions (ethyl acetate, dichloromethane and hexane) at 200 mg/kg each administered to STZ-induced diabetic rats exerted anti-diabetic and anti-hyperlipidemic activity comparing with glibenclamide (Sunday et al., 2017)  <i>In vitro</i> : Alpha-amylase inhibitory activity of leaves, stem bark and roots methanol extract (1ml of 250 mg/ml) (Olubomehin et al., 2013)	Antimicrobial Antimalarial, Analgesic, Hepatoprotective (Iroanya et al., 2015; Gboeloh et al., 2014; Osadebe et al., 2014; Mbiancha et al., 2014; Alaribe et al., 2012)
Gnetaceae: <i>Gnetum africanum</i>	Nkumu	Leaves / Cooking	Not available in literature	Chemoprotection potential and antimicrobial (Tjeck et

Welw.				al., 2017)
Hyperaceae: <i>Harungana madagascariensis</i> Lam. ex Poir.	Atsui	Leaves / Chewing	<i>In vivo</i> : Leaves extract at 200 mg/kg bw administered to alloxan-induced diabetic guinea pig for 28 days reduced significantly blood glucose compared to glibenclamide (0.25 mg/kg bw) group (Kadima et al., 2016)	Anti-inflammatory and antioxidante properties (Tjeck et al., 2017)
Irvingiaceae: <i>Irvingia gabonensis</i> (Aubry-Lecomte ex O'Rorke) Baill.	Mwiba, Africa mango, ndôc	Seeds, fruit, leaves, stem bark, roots / Decoction, maceration	<i>In vivo</i> : IGOB131 from <i>Irvingia gabonensis</i> (150 mg) given in a double blinded manner to overweight/obese volunteers 30-60 minutes before lunch and dinner significantly improved a variety of parameters characteristic including blood glucose (Ngondi et al., 2009). Single oral administration of methanol extract of seeds at doses 150 and 250 mg/kg significantly reduced plasma glucose levels in STZ-induced diabetic rats 2h after administration, with 250 mg/kg more efficient than 150 mg/kg (Ngondi et al., 2006). Long-term anti-diabetic effects of aqueous extract of	Antimicrobial, Hepatoprotective, Anti-inflammatory, Antiulcer, Analgesic (Kuete et al., 2007; Omonkhua et al., 2012; Gbadegesin et al., 2014; Okolo et al., 1995)

			stem bark at 200 mg/kg bw in STZ-induced diabetic rats was revealed for 24 weeks by a sustained reduction of fasting blood glucose in treated diabetic rats (Omonkhua et al., 2012).	
Lauraceae: <i>Persea americana</i> Mill.	Muvoka	Seeds, leaves / Decoction, maceration	<i>In vivo</i> : Aqueous extract of seed given to alloxan-induced wistar rats at 20, 30 and 40 g/L showed hypoglycaemic activity compared to glibenclamide, also anti-diabetic and protective effects on pancreas, kidneys and liver after 21 days (Ezejiofor et al., 2013). Hydro alcoholic extract of leaves at 0.15 and 0.3g/kg/day given orally to STZ-induced diabetic rats for 4 weeks exhibited reduction in fasting blood glucose levels in comparison with glibenclamide, and improvement in metabolic state via a regulation of glucose uptake in liver and muscles by PKB/Akt activation (Lima et al., 2012)	Vasorelaxant activity, Analgesic, Anti-inflammatory, Antiulcer Anticonvulsant, Hypotensive, Antiviral, Antioxidant, Antimicrobial, Wound healing, Antihepatotoxic (Yasir <i>et al.</i> , 2010; Gomez-Flores <i>et al.</i> , 2008; Lima <i>et al.</i> , 2012)
			<i>In vitro</i> : The in-vitro (rat pancreas) assessment of	

			5mg/ml of aqueous extract of <i>Persea americana</i> inhibitory effect on alpha-amylase and alpha-glucosidase activities showed that the minimum of leaves extract concentration exhibit the highest IC <sub>50</sub> (0.28 mg/ml) for α-amylase and peel extract exhibited the highest IC <sub>50</sub> (0.080 mg/ml) for α-glucosidase (Adelusi et al., 2014)	
Leguminosae: <b><i>Senna alata</i></b> (L.) Roxb. Syn: <i>Cassia alata</i> Linn	Gitsamuna	Leaves, roots, seed / Decoction	<i>In vitro</i> : Alpha-glucosidase inhibitory effect of methanol extract (IC <sub>50</sub> = 63.75 ug/ml) compared to acarbose (IC <sub>50</sub> = 107.31 ug/ml) with higher effect of the ethyl acetate (IC <sub>50</sub> = 2.95 ug/ml) and n-butanol (IC <sub>50</sub> = 25.80 ug/ml) fractions (Varghese et al., 2013)	Antimicrobial, Antioxidant, Anti-inflammatory, Wound Healing, Bronchorelaxant, (Sule et al., 2011; Ouédraogo et al., 2013; Sagnia et al., 2014; Midawa et al., 2010; Yakubu et al., 2015; Adedoyin et al., 2015)
Leguminosae: <b><i>Senna occidentalis</i></b> (L.) Link Syn: <i>Cassia occidentalis</i> Linn	Muwiwisi	Leaves, root / Decoction	<i>In vivo</i> : Aqueous extract of whole plant reduced significantly FBG levels in normal and alloxan-driven diabetic rats at 200 mg/kg bw during 21 days and promote pancreas regeneration compared to control (Verma et al., 2010).	Antimicrobial, Antioxidant, Hepatoprotective, Antimalarial, Anti-inflammatory, Analgesic, Antipyretic, (Vijayalakshmi et al.; 2013)

			Root ethanol extract has hypoglycaemic activity at 250 and 500 mg/kg bw in STZ-induced diabetes mice compared to control mice and metformin after 21 days (Sharma et al., 2014)	
Leguminosae: <i>Tetrapleura tetraptera</i> (Schum. & Thonn.) Taub.	Gyaga	Seeds, leaves, roots, stem bark / Decoction, infusion	<i>In vivo</i> : Fruit aqueous extract (50-800 mg/kg p.o.) reduced in a dose-dependent manner blood glucose concentrations on normal and STZ-diabetic rats compared to chlorpropamide (250 mg.kg) (Ojewole and Adewunmi, 2004). Methanolic leaves extract at 50 mg/kg bw decreased plasma glucose levels after 7 days, compared to glibenclamide and normal. Also, hepato protective effect in alloxan-induced diabetic rats was revealed (Atawodi et al., 2014)	Antihypertensive, Antioxidant, Antidyslipidemia, Wound Healing, Antimicrobial, Anti-inflammatory, Analgesic, Anticonvulsant, Antimalarial (Ojewole 2005; Okokon <i>et al.</i> , 2007; Bella <i>et al.</i> , 2012; Effiong <i>et al.</i> , 2014; Uchechi 2010; Aderibigbe <i>et al.</i> , 2010)
Malvaceae: <i>Abelmoschus esculentus</i> (L.) Moench	Nèfu	Fruit, seed / Decoction, food powder, maceration	<i>In vivo</i> : <i>Abelmoschus esculentus</i> seed powder (AESP) and <i>Abelmoschus esculentus</i> peel powder (AEPP) at 100 and 200 mg/kg reduce blood sugar	Antioxidant, Antiulcerogenic, Diuretic, Antimicrobial, Gastroprotective, Antispasmodic, Nephroprotective (Ngoc <i>et al.</i> , 2008;

			<p>levels comparable to glibenclamide and also, reduced hyperlipidemia in STZ-induced rats for 28 days (Sabitha et al. 2011).</p> <p>Antihyperglycemic effect of powder (100 mg/kg) and water extract (100 mg/kg) on alloxan-induced diabetic rats compared to normal and glibenclamide (5 mg/kg) treated rats, after 14 days (Ben-Chioma et al., 2015).</p>	Gemedede <i>et al.</i> , 2014)
Malvaceae: <b><i>Ceiba pentandra</i></b> (L) <b>Gaertn.</b>	Fromage	Barks, leaves, roots	<p><i>In vivo</i>: Root methylene chloride/methanol extract at 40 and 75 mg/kg bw single dose significantly reduced blood glucose 5h after administration in a time-dependent manner in both normal and STZ-induced diabetic Wistar rats compared to glibenclamide treated rats. Also, the administration twice daily to diabetic rats at the same doses (40 and 75 mg/kg) for 3 days showed significant decreased of blood and urine glucose compared to insulin (Djomeni et al., 2006). Ethyl acetate fraction at 200 mg/kg bw</p>	Antiulcer, Hepatoprotective, Anti-inflammatory, Hypolipidaemic, Antiparasitic, Antioxidant (Elumalai <i>et al.</i> , 2012; Anosike <i>et al.</i> , 2014)

			decreased significantly blood glucose in alloxan-induced diabetic albino rats compared to normal and glibenclamide treated rats after 12 days (Muhammad et al., 2015). Leaves and bark ethanol extract at 200 and 400 mg/kg exhibited remarkable reduction of blood glucose in alloxan-induced diabetic rats (Muhammad et al., 2016) and STZ-induced diabetic rats compared to normal and glibenclamide rats (Satyaprakash et al., 2013).	
Malvaceae: <i>Duboscia macrocarpa</i> Bocq.	Akak	Stem barks / Decoction	Not available in literature	Treat toothache, tuberculosis (PROTA)
Malvaceae: <i>Hibiscus sabdariffa</i> L.	Bukulu	Calix / Infusion, decoction, maceration	<i>In vivo</i> : Aqueous calyxes extract at 100 mg/kg bw, administered to STZ-induced Sprague Dawley rats for 28 days, decreased BGL and increased insulin levels in diabetic treated rats compared to normal control and non-treated diabetic rats. Also, this extract prevented liver injury associated with diabetic condition (Husin et al., 2017).	Antibacterial, Antifungal, Antiparasitic, Antipyretic, Antinociceptic, Antioxidant, Anti-Inflammatory, Hepatoprotective, Nephroprotective, Diuretic, Cancer-Preventive, Anti-Hypertensive Anti-Anaemic (Da-Costa-Rocha et al., 2014)

			Ethyl acetate fraction at 100 and 200 mg/kg bw administered for 4 weeks to STZ-induced diabetic rats lower FBG when measured once a week in comparison to non-treated rats. Intra-peritoneal GTT made after 4 weeks showed that 200 mg/kg of the ethyl acetate fraction improved FBG and postprandial blood glucose levels compared to STZ-treated rats (Seung et al., 2018)	
Mimosoideae: <i>Cylicodiscus gabunensis</i> Harms	Okan	Stem barks / Decoction	Not available in literature	Antiplasmodial, antimicrobial and antimalarial properties (Tjeck et al., 2017)
Mimosoideae: <i>Entada gigas</i> (L.) Fawcett and Rendle	Coeur de mer	Stem barks / Decoction	Not available in literature	Diarrhoea and antimicrobial (Tjeck et al., 2017)
Mimosoideae: <i>Piptadeniastrum africanum</i> (Hook.f.) Brenan	Dabéna	Stem barks / Decoction	Not available in literature	Antifungal property, gastroprotective and healing ulcer activity (Tjeck et al., 2017)
Moraceae: <i>Milicia excelsa</i> (Welw.) C.C. Berg	Obiga	Stem barks / Decoction	Not available in literature	Wound healing and antibacterial properties (Tjeck et al., 2017)
Musaceae: <i>Musa paradisiaca</i> L.	Digondi	Fruits, roots, leaves, ripe fruits, stem	<i>In vivo</i> : Stem juice at the dose of 500 mg/kg bw produced rise in blood glucose	Immunostimulant, Antiulcerogenic, Wound healing, Antirolithiatic,



		juice / Maceration	level after 6h of oral administration in normal rats. However, the same dose produced a lower rise in blood glucose levels within 1h during glucose tolerance test in sub diabetic rats and even a decrease after 4h in fasting blood glucose levels in severe diabetic animals compared to normal control (Singh et al., 2007). Ethanolic extract of banana peels at 500 mg/kg exhibited minor reduction of blood glucose in normal rats compared to normal, 120 min after extract administration. Also, the same dose showed anti-hyperglycemic effects compared to normal during OGTT and from 90 min (Navghare and Dhawale, 2017)	Hepatoprotective, Antioxidant (Swathi <i>et al.</i> , 2011)
Myrtaceae: <b><i>Psidium guajava</i> L.</b>	Guava	Stem bark, leaves / Decoction, maceration	<i>In vivo</i> : Water leaf (250 and 500 mg/kg/d) administration to high fructose treated rats for 8 weeks, improved insulin resistance, dyslipidaemia and hypertension in a dose-dependent	Anti-Inflammatory, Antioxidant, Wound Healing, Antimalarial, Antitussive, Hepatoprotective, Antimutagenic, Antitumor, Cardiovascular activity, Hypotensive, Antinociceptive

			manner compared to normal control (Mathur et al., 2015).	(Ravi <i>et al.</i> , 2014; Gutierrez <i>et al.</i> , 2008)
			<i>In vitro</i> : Aqueous leaves extract at 50, 100, 200 or 400 µg/ml enhanced glucose uptake in rat clone 9 hepatocytes compared to control and insulin group (Fang-Chui et al., 2009).	
Pandaceae: <b>Microdesmis puberula Hook.f. ex Planch.</b>	Inko	Stem barks / Infusion	Not available in literature	Analgesic and anti-stress (Tjeck et al., 2017)
Piperaceae: <b>Peperomia pellucida (L.) Kunth</b>	Pepper-elder	Leaves / Infusion	<i>In vivo</i> : Rats chow was supplemented with (100g) 10% w/w and (200g) 20% w/w of fine powder of leaves for 28 days to alloxan-induced diabetic rats and normal rats. Blood glucose levels in treated groups was significantly reduced compared to control and at levels comparable to glibenclamide group (Hamzah et al., 2012)	Antimicrobial, anticancer, antioxidant, analgesic and anti-inflammatory (Tjeck et al., 2017)
Poaceae: <b>Cymbopogon citratu (DC.) Stapf</b>	Ditsotsu	Leaves / Decoction, infusion	<i>In vivo</i> : Leaves aqueous extract of lemon grass lower in a dose-dependent manner FPG (125-500 mg/kg bw) with the most significant	Antimicrobial, Antioxidant, Antiparasitic, Antimalarial, Anti-Inflammatory, Antimutagenicity, Neurobehaviorial (Shah

			hypoglycaemic effect activity at 500 mg/kg/day compared to non-treated rats after 42 days (Adeneye and Agbaje, 2007). Leaves aqueous extract (1,5 ml/100g bw) reduced elevated blood glucose at week 4 of study in alloxan-induced diabetic rats compared to diabetic non-treated group (Ewenighi et al., 2013). Ethanol and aqueous extract at 200 mg/kg bw each, for a period of 30 days, on normal Wistar rats reduced blood glucose levels compared to normal control (Ademuyiwa et al., 2015)	<i>et al.</i> , 2011; <i>Manvitha et al.</i> , 2014)
Poaceae: <b><i>Pennisetum purpureum</i></b> Schumach.	Mikuku	Stem / Maceration	Not available in literature	Antioxidant, nutritional and berbicial (Tjeck et al., 2017)
Poaceae: <b><i>Saccharum officinarum</i></b> L.	Sugar cane	Wine, leaves / Fermentati on	<i>In vivo</i> : Anti-hyperglycaemic effect of 400 mg/kg bw in alloxan-induced diabetic male rats compared to non-treated and glibenclamide-treated groups, during 21 days (Ojewunmi et al., 2013).	Antimicrobial, Antioxidant Diuretic, Antiinflammatory (Eneh <i>et al.</i> , 2015; Ojewunmi <i>et al.</i> , 2013; Palaksha <i>et al.</i> , 2015; <i>Ghiware et al.</i> , 2012)
			<i>In vitro</i> : The 30%	

			hydroalcoholic fraction at 0.01, 0.05 and 0.1 mg/ml showed significant alpha-glucosidase, sucrase and maltase inhibition and improved glucose uptake in HepG2 cells compared to rosiglitazone (10 µM) and acarbose (10µM) (Zheng et al., 2017).	
Poaceae: <b><i>Zea mays</i> L.</b>	Putu	Corn silk, leaves stigma / Decoction	<i>In vivo</i> : Polysaccharides of corn silk at 300, 400 and 500 mg/kg bw administered daily on STZ-induced diabetic rats during 4 weeks, reduced blood glucose and serum lipid levels compared to normal and dimethylbiguaninide rats. It also improved glucose tolerance in normal and diabetic rats (Zhao et al., 2012). Anthocyanin-rich purple corn extract at 50 mg/kg lowered FBG, increased c-peptide levels, prevented pancreatic beta cells damage and increased insulin content in type 2 animal model C57BL/KsJ db/db mice during 8 weeks' study and compared to diabetic control and pinitol groups	Antioxidant, Antiinflammatoire, Diuretic Nephroprotective, Antimicrobial Antifatigue, (Balasubramanian <i>et al.</i> , 2012; Miura <i>et al.</i> , 1996; Parle milind <i>et al.</i> , 2013; Nessa <i>et al.</i> , 2012)

(Huang et al., 2015).

*In-vitro*: Aqueous and ethanol extracts of ZM kernels (0.67 mg/ml both) inhibited rat intestine  $\alpha$ -glucosidase (13 %) with less efficacy than *S. cerevisiae*  $\alpha$ -glucosidase (55%) and compared to acarbose. However, extracts were capable of scavenging NO at the level of 0.25 mg/ml and only aqueous extracts were capable of scavenging  $O_2^-$  (Lee et al., 2010)

Rubiaceae: <i>Morinda lucida</i> Benth.	Dungatsi, Akeng	Bark, leaves / Decoction	<i>In vivo</i> : Aqueous and 50% ethanolic extract both at 120 and 210 mg/kg bw lowered significantly blood glucose levels in alloxan-induced diabetic rats compared to non-treated diabetic and control groups. Aqueous extract, at both doses, was more effective than 50% ethanol extract (Bamisaye et al., 2013).	Analgesic, Hypotensive, Antiplasmodial, Antimicrobial, Antiparasitic, Gastrointestinal activity (Olajide <i>et al.</i> , 1999; Lawal <i>et al.</i> , 2012).
Rubiaceae: <i>Nauclea diderrichii</i> (De Wild.) Merr.	Bilinga	Leaves, bark / Maceration	<i>In vitro</i> : Barks aqueous extract fractions (1 mg/ml) exhibited very potent inhibitory activity of alpha-glucosidase	Anti-diarrhoea, fever and stomach pains (Lamidi et al., 1995), malaria (Iyamah and Idu, 2015).

			compared to acarbose (10 mM) in human MCF-7 cell line (Agnaniet et al., 2016).	
Rutaceae: <i>Citrus aurantium</i> L.	Mwali	Peel of fruit, leaves, root, stem bark, stem twigs / Juice, decoction	<i>In vivo</i> : Mixture of extract of <i>Citrus aurantium</i> fruit and RV foliage given orally at 875 mg for 6 weeks, lowered serum glucose levels in diabetes type 2 model db/db mice compared to non-treated diabetic mice (Campbell et al., 2006). The same mixture given orally, daily for 4 months to type 2 diabetic patients lowered fasting and post prandial plasma glucose comparable to oral anti-diabetic agents (Campbell-Tofte et al., 2011). Alcohol extract of fruit peel at 500 mg/kg significantly reduced blood glucose levels in normal and alloxan-induced diabetic rats compared to tolbutamide (100 mg/kg bw) after 21 days (Sharma et al., 2008).	Antimicrobial, Antimalarial, Anti-Cancer (Trabelsi et al., 2014; Khodabakhsh et al., 2015 ; Bapna et al., 2014; Sharma et al., 2008; Karimi et al., 2012 )
Simaroubaceae: <i>Quassia amara</i> L.	Gisimigali or Mukèdji	Wood powder, stem wood, leaves /	<i>In vivo</i> : Aqueous extract of wood powder at 200 mg/kg bw given to normal	Antiparasitic, Antiviral, Anti-inflammatory, Antitumor, Antiulcer, Gastrointestinal activity

		<p>Maceration and alloxan-induced diabetic rats decreased blood glucose levels in a similar manner to metformin during an OGTT from 90 min (Ferreira et al., 2013). Methanol extract of stem wood at 100 and 200 mg/kg bw reduced significantly elevated fasting blood glucose levels in Nicotinamide-STZ-induced diabetic rats after 14 days of treatment, compared to normal and diabetic rats treated with glibenclamide (10 mg/kg) Also, these doses improved glucose tolerance in normal rats after oral glucose tolerance test (Husain et al., 2011).</p>	<p>(Ajaiyoba <i>et al.</i>, 1999; Apers <i>et al.</i>, 2002; Toma <i>et al.</i>, 2003; Kupchan <i>et al.</i>, 1976; Toma <i>et al.</i>, 2002)</p>	
<p>Urticaceae: <b><i>Musanga cecropioides</i></b> <b>R.BR. ex Tedlie</b></p>	<p>Asèng</p>	<p>Leaves, stem bark / Decoction, macertion</p>	<p><i>In vivo</i>: Daily oral administration of the aqueous and ethanol extract of <i>Musanga cecropioides</i> (MC) stem bark at 250, 500 and 1000 mg/kg for 14 days significantly decreased fasting blood glucose in normal and alloxan-induced diabetic rats with higher effect with ethanol extract, compared to metformin (Adeneye et al., 2007). The</p>	<p>Hepatoprotective, Hypotensive, Antioxidant, Anti-inflammatory, anti-nociceptive (Adeneye 2009 ; Feuya Tchouya <i>et al.</i>, 2015 ; Sowemimo et al., 2015 ; Aziba 2004 ; Ajayi <i>et al.</i>, 2013 ; Emoji <i>et al.</i>, 2014)</p>

			water ethanol extract of MC stem bark at 300 mg/kg bw reduced significantly glucose-load induced hyperglycemia in normal wistar rats and at 200, 300, and 400 mg/kg bw in STZ-induced diabetic rats. The extract effects were less efficient than those of glibenclamide (Nyunai et al., 2016).	
Verbenaceae: <b><i>Lantana camara</i> L.</b>	Filawa	Leaves, roots / Decoction, Infusion	<i>In vivo</i> : Aqueous ethanol extract, n-butanol and aqueous fractions at 800mg/kg exhibited significant anti-hyperglycemia in normal and alloxan-induced diabetic rats compared to glibenclamide, after 28 days of treatment (Jawonisi and Adoga, 2015)	Antioxidant, Antimicrobial, Anti-ulcerogenic, Wound Healing, Antipyretic, Anti-Hypertensive (Ganesh, 2010; Saxena et al., 2012; Kumar et al., 2015)
Zingiberaceae: <b><i>Zingiber officinale</i> Roscoe</b>	Nungutsi mabala	Rhizome, roots / Maceration	<i>In vivo/in vitro</i> : Aqueous rhizomes extract at 100, 300 and 500 mg/kg bw administered orally and daily for 30 days to STZ-induced diabetic rats exerted a dose-dependent anti hyperglycaemic effect with a significant decreased of plasma glucose and increased in glucokinase, phosphorfructokinase	Anticancer, Antiemetic, Anti-Inflammatory, Antinociceptive, Antioxidant, Cardiovascular, Gastrointestinal activity, Antitussive, Immunostimulant, Antiarthritic, Antimicrobial, Radioprotective, Antigenotoxic (Mishra et al., 2012; Asha et al., 2011)



and pyruvate kinase activities in treated animals compared to normal rats (Abdulrazaq et al., 2011). Ethanol extract of rhizome at 200 mg/kg bw improved significantly insulin sensitivity in a high-fat high-carbohydrate diet-fed rat model with metabolic syndrome after 10 weeks, in comparison with metformin. Also, (S)- [6]-gingerol exerted a dose-dependent (50 to 150  $\mu$ M) increased of AMPK alpha-subunit phosphorylation in L6 skeletal muscle cells compared to control (Li et al., 2014).

*Abbreviations:* IP: intraperitoneal; bw: body weight; STZ: streptozotocin; GLUT: Glucose transporter; mRNA: messenger RiboNucleic Acid; FBG: Fasting Blood Glucose; FPG: Fasting Plasma Glucose; TG: Triglycerides; TC: Total Cholesterol; OGTT: Oral Glucose Tolerance Test; GTT: Glucose Tolerance Test; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; IC<sub>50</sub>: half maximal Inhibitory concentration; HbA: Hemoglobin A; AMPK: Adenosine Monophosphate Protein Kinase; NA: sodium; p.o.: per os; LD<sub>50</sub>: Lethal median dose

Table 2: Toxicology and active constituents of some Gabonese anti-diabetic plants

<b>Family: Scientific name</b>	<b>Toxicology</b>	<b>Identified active constituents or relevant phytoconstituents from the plant</b>
Amaryllidaceae: <i>Allium cepa</i> L.	<i>Acute toxicity:</i> 5 Groups of rats were treated orally or by IP with 300, 600, 1200, 2400 and 4800	Allyl propyl disulphide (Lakshmi et al., 2016), S-methylcysteine sulfoxide,

	mg/kg bw of methanol bulb extract. LD <sub>50</sub> >4800 mg/kg (Oyewusi <i>et al.</i> , 2015)	quercetin (Akash <i>et al.</i> , 2014)
Amaryllidaceae: <b><i>Allium sativum</i> L.</b>	<i>Acute toxicity:</i> Rats were given aqueous garlic bulbs extract orally at doses of 100, 1 000, 2 500 and 5 000 mg/kg. LD <sub>50</sub> was more than 5 000 mg/kg  <i>Subacute toxicity:</i> 3 groups of rats received respectively 300, 600 and 1 200 mg/kg daily for 5 weeks. No significant changes or alterations have been noticed (Lawal <i>et al.</i> , 2016)	S-Allyl cysteine sulfoxide (Lakshmi <i>et al.</i> , 2016), alliin (Anwar <i>et al.</i> , 2017)
Anacardiaceae: <b><i>Antrocaryon klaineinum</i> Pierre</b>	Not available in literature	Flavonoids, alkaloids, reductor compounds, tannins and saponins (Abogo Mebale <i>et al.</i> , 2013); proanthocyanidins, phenolic acids (Fongang <i>et al.</i> , 2017)
Anacardiaceae: <b><i>Mangifera indica</i> L</b>	<i>Acute toxicity:</i> No toxicity of leaves extract in mice and rats at maximal dose of 18.4 g/kg bw  <i>Subacute toxicity:</i> 3 groups of rats were treated for 12 weeks with 100, 300 and 900 mg/kg bw of leaves extract and no toxicity has been reported (Zhang <i>et al.</i> , 2014)	Mangiferin- a xanthone glycoside  (Rakesh <i>et al.</i> , 2015)
Anacardiaceae: <b><i>Pseudospondias longifolia</i> Engl.</b>	Not available in literature	Flavonoids, alkaloids, reductor compounds, tannins and saponins (Abogo Mebale <i>et al.</i> , 2013)
Annonaceae: <b><i>Xylophia aethiopica</i> (Dunal) A. Rich.</b>	<i>Acute toxicity:</i> LD <sub>50</sub> was 1258.92 mg/kg in mice  <i>Subacute toxicity:</i> Oxytotic activity on guinea pig uterus	Rich content of alkaloids, flavonoids, tannins, saponins, phenol (Ofusori <i>et al.</i> , 2016)

	(Omodamiro et al., 2012). Aqueous extract of fruit from 100 to 300 mg/kg shown toxic effects on liver and kidney Wistar rats (Ozoko et al., 2015)	
Annonaceae: <b><i>Annickia chlorantha</i></b> <b>(Oliv.) Setten and Maas</b>	<i>Acute and sub-acute toxicity</i> of the aqueous stem-bark extract were evaluated on Swiss mice (oral doses of 1000, 3000 and 5000 mg/kg) for seven days and rats (daily doses of 250, 500, and 1000 mg/kg) for 42 consecutive days. No death in acute toxicity test. At doses from 1000 mg/kg in the sub-acute toxicity study, animals presented histopathological signs in the liver, lungs and kidneys, and alterations in ALT, AST and platelet counts (Tan <i>et al.</i> , 2007)	Flavonoids, terpenes, glycosides, sterols, acetogenins and alkaloids (Olivier et al., 2015)
Annonaceae: <b><i>Annona muricata</i> L.</b>	<i>Acute toxicity:</i> Rats received 200 and 5000 mg/kg and oral LD <sub>50</sub> was estimated to be >5000 mg/kg (Ngueguim et al., 2014)  <i>Subacute toxicity:</i> Doses of 100, 1000, and 2500 mg/kg were administered daily for 14 days. The extract did not produce any toxic effect but higher doses could cause kidney damage and induce negative effect on uterine function (Arthur <i>et al.</i> , 2011). In a more recent study, 200, 400 and 800 mg/kg bw were administered daily by gavage for 4 weeks. No death or toxicity sign was recorded (Ngueguim et al., 2015)	Alkaloids, acetogenins, phenolic compounds, vitamins, carotenoids, amides cyclopeptides and megastigmanes (Coria-Téllez et al., 2016)
Annonaceae: <b><i>Anonidium mannii</i></b> (Oliv.) <b>Engl. &amp; Diels</b>	Not available in literature	Alkaloids, phenols, polyphenols, saponins, sterols, tannins and triterpenes (Djeussi et al., 2013)

<p>Apiaceae: <b><i>Petroselinum crispum</i></b> <b>(Mill.) Fuss</b></p>	<p><i>Acute toxicity:</i> No mortality found up to dose 2000 mg/kg on mice of ethanolic and methanolic leaf extracts (Vannamalar and Jaykar, 2016)</p>	<p>Sulphonylureas (glibornuride) (Ozsoy-Sacan et al., 2006) phenolics compounds, flavonoids (apigenin, apiin and 6''-Acetylapiin), essential oil (myristicin and apiol) and coumarins (Farzaei et al., 2013)</p>
<p>Apocynaceae: <b><i>Alstonia boonei</i> De Wild.</b></p>	<p><i>Subacute toxicity:</i> 200, 500 and 1000 mg/kg of aqueous stem bark extract were orally administered daily for 4 weeks to rats. The aqueous extract is toxic on liver and kidney at high doses (Nkono Ya Nkono <i>et al.</i>, 2015)</p>	<p>Saponins and indole alkaloids. Alkaloids, tannins, steroids, glycosides, flavonoids, and terpenoids. Triterpenes (Tjeck et al., 2017)</p>
<p>Apocynaceae: <b><i>Alstonia congensis</i> Engl.</b></p>	<p>Not available in literature</p>	<p>Alkaloids, polyphenols and terpenoids (Ogbonia et al., 2008)</p>
<p>Apocynaceae: <b><i>Picralima nitida</i> (Stapf) T. Durand &amp; H. Durand</b></p>	<p><i>Acute toxicity:</i> Oral administration of 600, 750, 1000, 1500 and 3000 mg/kg to mice did not exert any mortality</p> <p><i>Subacute toxicity:</i> Toxic effect on the liver, kidneys and the lungs (Kouitcheu Mabeku <i>et al.</i>, 2008). Pancreas degeneration in methanol seeds extract treated groups (Akinloye et al., 2014)</p>	<p>Akuammicine, 10-deoxyakuammicine, akuammicine, akuammidine, burnamine and picraline (Teugwa et al., 2013)</p>
<p>Apocynaceae: <b><i>Rauvolfia vomitoria</i> Afzel.</b></p>	<p><i>Acute toxicity:</i> No toxicity up to a concentration of 5000 mg/kg bw in mice by oral route (N'doua et al., 2015)</p> <p><i>Subacute toxicity:</i> Teratogenic (Eluwa <i>et al.</i>, 2013) and possible toxicity on liver and kidney (Eteng <i>et al.</i>, 2009)</p>	<p>Reserpine, Yohimbine, Ajmaline, Ajmalicine, Alstonine, Serpentine Apigenin rhamnoside, Naringin (Campbell-Tofte et al., 2011)</p>
<p>Apocynaceae: <b><i>Tabernanthe iboga</i> (Bail.)</b></p>	<p><i>Acute toxicity:</i> LD<sub>50</sub> of ibogaine is 263 mg/kg of mouse b.w. and</p>	<p>Ibogaine, tabernanthine, ibogamine, iboluteine and</p>

	LD <sub>50</sub> of noribogaine is 630 mg/kg of mouse bw (Kubilienė et al., 2008). LD <sub>50</sub> of ibogaine is respectively 82 mg/kg b.w., (IP), 327 mg/kg bw (intragastric) and 145 mg/kg (IP) for guinea pig and rats (Goutarelet et al., 1993)	ibogaline (Mačiulaitis et al., 2008)
Apocynaceae: <b><i>Voacanga Africana</i> Stapf ex Scott-Elliot</b>	The <i>subacute toxicity</i> was evaluated after a daily oral dose of aqueous leaf extract (100, 400 and 800 mg/kg) for 28 days to animal's study. No gross abnormalities or histopathological changes were observed among any the groups treated (Igbe <i>et al.</i> , 2015)	Anthranoids, anthraquinone, cardiac glycosides, phenols, phlobatanins, starch and tannins. Ibogamine, voacamine, vobasine, voacangine, voacristine, 19-epi-voacristine and 19-epi-heyneanine (Tjeck et al.2017)
Aracaceae: <b><i>Cocos nucifera</i> L.</b>	<i>Acute toxicity</i> : A single dose of 175, 550, 2000 and 5000 mg/kg of Fermented Virgin Coconut Oil was administered orally in rats and no mortality or gross toxicity were seen (Ah <i>et al.</i> , 2016)	Phenolic compounds, flavonoids, resins, alkaloids, carbohydrate, proteins, and fibers. Tannins, saponins, glycosides, steroids and anthraquinones (Tjeck et al., 2017)
Asteraceae: <b><i>Ageratum conyzoides</i> L.</b>	<i>Acute toxicity</i> : Groups of rats received orally doses of 1, 2, 4, 8, 12 and 16 g/kg of aqueous extract from the whole plant. The LD <sub>50</sub> was 10.1 g/kg  <i>Subacute toxicity</i> : For 4 weeks', 2 groups of rats received 0.5 and 1 g/kg of extract respectively. No changes in the general condition was noticed (Igboasoiyi et al., 2007)	Alkaloids and cardenolides (Agunbiabe et al., 2012). Coumarin, Quercetin and its glycosides, Kaempferol and its glycosides, β- sitosterol, Friedelin, Stigmasterol, Echinatine, Lycopsamine, Polymethoxylated and Polyhydroxy flavones (Okunade, 2002)
Asteraceae: <b><i>Tithonia diversifolia</i> (Hemsl.) A. Gray.</b>	<i>Acute toxicity</i> : 3 groups of rats received orally 800, 400 and 1600 mg/kg of ethanolic aerial part extract. Haematological and toxic effects on the kidney and liver. The LD <sub>50</sub> was greater than 1600 mg/kg (Elufioye <i>et al.</i> ,	Flavonoids, tannins, saponins, steroids and terpens. Tannins and saponins. Sugars, sesquiterpenes lactones and phenolics (Tjeck et al., 2017)

	2009)	
Asteraceae: <b><i>Vernonia amygdalina</i> Del.</b>	<i>Acute toxicity:</i> I.P. LD <sub>50</sub> of 500 mg/kg. (Ojaiko and Nwanjo, 2006)  <i>Subacute toxicity:</i> 200, 400 and 600 mg/kg of aqueous leaves extract were administrated orally to rats for 29 days. No significant changes were recorded (Nabukenya <i>et al.</i> , 2014)	Dicaffeoyl-quinic acid, 1,5-dicaffeyol-quinic acid, chlorogenic acid and luteolin-7-O-glucoside (Atangwho <i>et al.</i> , 2013; Ong <i>et al.</i> , 2011)
Bignoniaceae: <b><i>Newbouldia laevis</i> (P. Beauv.) Seem.</b>	<i>Acute toxicity:</i> LD <sub>50</sub> on mice was 5400 mg/kg  <i>Subacute toxicity:</i> 3 groups of rats received 150, 300 or 500 mg/kg bw of the ethanolic leaf extract orally once daily for 28 days. No significant change was observed except for the platelet count that was high at high doses (Kolawole <i>et al.</i> , 2013)	Chrysoeriol, newbouldiaquinone; 2-acetylfuro-1,4-naphthoquinone, 2-hydroxy-3-methoxy-9,10-dioxo-9,10-dihydroanthracene-1-carbaldehyde, lapachol, beta-sitosterol-3-O-beta-D-glucopyranoside, oleanolic acid, canthic acid, newbouldiamide and 2-(4-hydroxyphenyl) - ethyltrioctanoate (Tjeck <i>et al.</i> , 2017) flavonoids, triterpenes, anthraquinones, phenols, saponins, alkaloids (Kuate <i>et al.</i> , 2014)
Bignoniaceae : <b><i>Spathodea campanulata</i> P. Beauv.</b>	<i>Acute toxicity:</i> No toxicity was found in Swiss albino mice at a dose of 250 mg/kg of ethanol leaves extract (Coolborn <i>et al.</i> , 2012)	Triterpernes (N'guessan <i>et al.</i> , 2009), steroids, flavonids, saponins, alkaloids and cardiac glycosides (Kulkarni <i>et al.</i> , 2014)
Burseraceae: <b><i>Aucoumea klaineana</i> Pierre</b>	Not available in literature	Momoterpenoids (Koudou <i>et al.</i> , 2009)
Burseraceae: <b><i>Santiria trimera</i> (Oliv.) Aubrév.</b>	Not available in literature	Triterpenes. Alpha-pinene, beta-pinene. Alpha-humulene and beta-caryophyllene (Tjeck

		et al., 2017)
Caesalpinioideae: <b><i>Eurypetalum tessmannii</i></b> <b>Harms</b>	Not available in literature	Not available in literature
Caesalpinioideae: <b><i>Guibourtia tessmannii</i></b> <b>(Harms) J. Leonard</b>	<i>Acute toxicity:</i> Mice received oral doses of aqueous stem bark extract (2 000, 3 000 and 5 000 mg/kg) LD <sub>50</sub> <i>per os</i> was greater than 5 000 mg/kg. At 150, 250, 300, 500 and 600 mg/kg bw given by IP LD <sub>50</sub> was 328.78 mg/kg  <i>Subacute toxicity:</i> After a single daily administration of extract at 150, 1 500 and 3 000 mg/kg <i>per os</i> for a period of 28 days, no significant changes have been recorded (Madingou <i>et al.</i> , 2016)	Triterpenes, sterols, alkaloids, tannins, polyphenols, sugars and saponosides (Madingou <i>et al.</i> , 2016)
Calophyllaceae: <b><i>Mammea Africana</i> Sabine</b>	<i>Acute toxicity:</i> Mice were treated by IP with doses ranging from 50 to 1000 mg/kg of the ethanolic stem bark extract. The intraperitoneal LD <sub>50</sub> was 387.3 mg/kg  <i>Subacute toxicity:</i> The extract was administered by gavage to three groups of 5 animals at 30, 60 and 90 mg/kg on alternate days for 21 days. No changes have been noticed (Antia <i>et al.</i> , 2006)	5, -7-dihydroxy-8-(12- methyl-butryl) – 4 –N - pencylcoumarins, 4-phenyl and 4-alkylcoumarins, mesuxanthone B (Okokon <i>et al.</i> , 2007; Okokon <i>et al.</i> , 2016)
Cannabaceae: <b><i>Celtis tessmannii</i> Rendle</b>	Not available in literature	Not available in literature
Capparaceae: <b><i>Buchholzia coriacea</i> Engl.</b>	<i>Acute toxicity:</i> 250, 500, 1000, 2000 mg/kg of the methanol seed extract was administered by IP. The LD <sub>50</sub> was greater than 2000 mg/kg. (Eze <i>et al.</i> , 2016)  <i>Subacute toxicity:</i> Animals were	Tannins, flavonoids, cardiac glycosides, saponins, alkaloids, and flavone glycosides (Adisa <i>et al.</i> , 2011; Obiudu <i>et al.</i> , 2015)

	<p>treated per os with 500, 250 and 125 mg/kg of methanolic seed extract once daily for 28 days. Anaemia, congestion of the liver and lungs and signs of liver atrophy were observed in male rats (Nweze <i>et al.</i>, 2012)</p>	
<p>Caricaceae: <b><i>Carica papaya</i> L.</b></p>	<p><i>Acute toxicity:</i> Fixed doses of 5, 50, 300 and 2000 mg/kg of leaves extract were administered to rats. No signs of toxicity and no deaths were recorded (Halim <i>et al.</i>, 2011)</p> <p><i>Subacute toxicity:</i> 0.01, 0.14, and 2 g/kg bw of the leaves extract were administered orally to rats for 13 weeks. The extract did not cause any significant toxic effect (Zakiah <i>et al.</i>, 2014)</p>	<p>Cryptoglavine, cis-violaxanthin and antheraxanthin (Lakshmi <i>et al.</i>, 2016)</p>
<p>Convolvulaceae: <b><i>Ipomoea batatas</i> (L.) Lam.</b></p>	<p><i>Acute toxicity:</i> Oral doses (10.0, 12.5, 15.0, 17.5, and 20.0 g/kg) of water extract from the whole plant were administered to mice. The extracts did not induce lethality or mortality up to 10 g/kg. However, a dose-dependent mortality effect between 12.5 g/kg and 17.5 g/kg was recorded giving an LD<sub>50</sub> of 12 g/kg</p> <p><i>Subacute toxicity:</i> Rats were orally administered 100, 200 and 400 mg/kg/day of the extract, for 14 days. No toxic effects have been recorded (Olowu, <i>et al.</i>, 2011)</p>	<p>Abietadiene (Lakshmi <i>et al.</i>, 2016)</p>
<p>Combretaceae: <b><i>Combretum micranthum</i> G. Don</b></p>	<p><i>Acute toxicity:</i> Rats were treated with 10, 170 100, 1000, 1250, 1750, 2500, 3500 and 5000mg/Kg of the aqueous leaf extract. No mortality up to 5000</p>	<p>Gallic acid, rutin trihydrate, (+) - catechin and benzoic acid. Alkaloids, saponins, tannins, anthraquinones, cardiac glycosides, flavonoids, and</p>



	mg/kg was observed.	steroids (Tjeck et al., 2017)
	<i>Subacute toxicity:</i> Rats were treated with dose of the extract at 500 and 1000mg/Kg once daily up to seven days. The results showed liver damage (Muttaka <i>et al.</i> , 2016)	
Euphorbiaceae: <b><i>Alchornea cordifolia</i></b> (Schumach and Thonn.) Mull.Arg.	<i>Acute toxicity:</i> Aqueous leaf extract LD <sub>50</sub> values were 8.6 g/kg and 3.8 g/kg in male and female mice respectively (Djimeli <i>et al.</i> , 2017)	Cyanogenetic glycosides, saponins, flavonoids, tannins, cardiac glycosides, steroids and triterpenoids (Mohammed et al., 2012)
	<i>Subacute toxicity:</i> Groups of rats were respectively administered 125, 250, 500 and 750 mg/kg bw of ethanolic leaf extract intra peritoneally daily for two weeks. The plant extract is relatively non-toxic but may induce hepatic injury at high doses (Ezeokeke <i>et al.</i> , 2017)	
Euphorbiaceae: <b><i>Euphorbia hirta</i> L.</b>	<i>Acute toxicity:</i> A single dose of 5000 mg/kg did not produce treatment related signs of toxicity or mortality in any of the animals tested during the 14-day observation period. The LD <sub>50</sub> was estimated to be greater than 5000 mg/kg	Quercetrin, dimethoxy quercetrin, hirtacoumaro-flavonoside and hirtaflavonoside-B (Manju et al., 2015), triterpenes, phytosterols, tannins, polyphenols and flavonoids (Kumar et al., 2010), saponin, alkaloids (N'Guessan et al., 2015)
	<i>Subacute toxicity:</i> In the repeated dose 90-day oral toxicity study, the administration of 50 mg/kg, 250 mg/kg, and 1000 mg/kg/day of <i>Euphorbia hirta</i> extract per b. w. revealed no significant morphological alteration of the organs (Ping <i>et al.</i> , 2013)	
Euphorbiaceae: <b><i>Jatropha curcas</i> L.</b>	<i>Acute toxicity:</i> LD <sub>50</sub> of 1 mg/kg on mice by IP. Haemorrhage of	Diterpenoids, alkaloids, flavonoids, phenols

	the liver, lungs and stomach leading to death was induced at high doses in mice (Abdu- Aguy <i>et al.</i> , 1986). LD <sub>50</sub> of 2500 mg/kg on mice by oral route and potential hepatotoxicity effect (Nwamarah <i>et al.</i> , 2015)	(Abdelgadir and Staden, 2013)
Fabaceae: <b><i>Acacia auriculiformis</i></b> <b>Benth.</b>	Not available in literature	Triterpenoid saponins. Proacaciaside and acacia mini. Tetrahydroxyflavanone, teracacidin, and trihydroxyflavanone, phenols, and tannins, proanthocyanidins (Tjeck <i>et al.</i> , 2017)
Fabaceae: <b><i>Mimosa pudica</i></b> <b>L.</b>	<i>Acute toxicity:</i> Animals were treated at different doses (5, 50, 300 and 2000 mg/kg). Behavioural changes were observed. At 2000 mg/kg (p.o.) the extract showed certain changes in activity and was devoid of any toxicity, thus >2000 mg/kg was taken as LD <sub>50</sub> (Vikram <i>et al.</i> , 2012)	C-glycosylflavones. Terpenoids, flavonoids, glycosides, alkaloids, quinines, phenols, tannins, saponins, and coumarins (Tjeck <i>et al.</i> , 2017)
Fabaceae: <b><i>Phaseolus vulgaris</i></b> <b>L.</b>	<i>Subacute toxicity:</i> Each animal received 10 mL/kg bw <i>via</i> oral intubation doses of 625, 1250, and 2500 mg/kg for a period of 31 days (males) or 32 days (females). No mortalities or significant changes have been observed (Chokshi, 2007)	Alkaloids, anthraquinone, catechic tannins, flavonoids, gallic tannins, glycosides, polyphenols, saponins, steroids and terpenoids (Ocho-Anin Atchibri <i>et al.</i> , 2010)
Gentianaceae: <b><i>Anthocleista vogelii</i></b> <b>Planch.</b>	<i>Acute toxicity:</i> 3 groups of rats were given 10, 100 and 1000 mg extract/kg body weight (p.o.) of root hydroethanolic extract. The LD <sub>50</sub> of extract was ≥ 5000 mg/kg (p.o.)  <i>Subacute toxicity:</i> Rats were given 100, 200 and 400 mg/kg of extract (p.o) daily for 28 days.	Secoiridoids, nor-secoiridoids, xanthonenes, phytosterols, triterpenes, alkaloids (Anyanvu <i>et al.</i> , 2015)

	No significant toxic effects have been recorded (Sunday <i>et al.</i> , 2016)	
Gnetaceae: <b><i>Gnetum africanum</i> Welw.</b>	<p><i>Acute toxicity:</i> 7 groups of mice were treated with 10, 100, 1000, 1500, 2000, 2500 and 3000 mg/kg methanol leaf extract. The results revealed an oral LD<sub>50</sub> of 3000 mg/kg</p> <p><i>Subacute toxicity:</i> 3 groups of rats were orally administered doses of the crude extract (100, 200 and 300 mg/kg) daily for 30 days. No adverse effects have been recorded (Ufelle <i>et al.</i>, 2016)</p>	Phenolic compounds, flavonoids, phytosterols, alkaloids, tannins, saponins, chlorophyll, and glycosides. $\beta$ -caryophyllene, (E)-phytol and trimethyl-2-pentadecanone (Tjeck <i>et al.</i> , 2017)
Hyperaceae: <b><i>Harungana madagascariensis</i> Lam. ex Poir.</b>	<p><i>Acute toxicity:</i> LD<sub>50</sub> of aqueous leaf extract were 11.6 g/kg and 13.2 g/kg bw for female and male mice respectively (Kengni <i>et al.</i>, 2013)</p> <p><i>Subacute toxicity:</i> 25, 50, 100, 200 mg/kg bw of the aqueous leaf extract were administrated orally to rats for 14 days. the extract induced hypercholesterolaemia and liver damage at high doses (Kengni <i>et al.</i>, 2016)</p>	Polyphenols, tannins, and triterpenes. Alkaloids, saponins, and flavonoids (Tjeck <i>et al.</i> , 2017)
Irvingiaceae: <b><i>Irvingia gabonensis</i> (Aubry-Lecomte ex O'Rorke) Baill.</b>	<p><i>Acute toxicity:</i> 6 groups of rats received orally leaf extract at 10, 100, 1000, 1600, 2900 and 5000 mg/kg bw. The LD<sub>50</sub> of the ethanolic leaf extract was above 5000mg/kg (Ewere <i>et al.</i>, 2016)</p> <p><i>Subacute toxicity:</i> Rats received orally 100, 1000 and 2000 mg/kg of aqueous leaf and stem bark extracts for 56 days. The plant may induce testicular</p>	Flavonoids, alkaloids, cardiac glycosides, terpenoids, tannins and saponins (Aw and Fi, 2010)

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	degeneration from 1000 mg/kg bw (Ezeasor <i>et al.</i> , 2017)	
Lauraceae: <b><i>Persea americana</i> Mill.</b>	<i>Acute toxicity:</i> 5 groups of rats were administered by oral gavage doses of 125, 250, 500, 1000, and 2000 mg/kg of ethanolic extract of seed. LD <sub>50</sub> was 1200 mg/kg (Padilla-Camberos <i>et al.</i> , 2013). Rats received orally a single dose of 2000 mg/kg of aqueous, methanolic and ethanolic extracts of the leaves. No death was recorded (Kamagate <i>et al.</i> , 2016)	Alkaloids, glycosides, saponins, tannins, and flavonoids (Ezejiofor <i>et al.</i> , 2013), kaempferol, phenol (Adelusi <i>et al.</i> , 2014)
Leguminosae: <b><i>Senna alata</i> (L.) Roxb.</b>	<i>Acute and subacute toxicity</i> were carried out with doses of 1,000, 2,000, and 3,000 mg/kg bw of alcoholic leaf extract, through oral administration for 15 days. This extract may be safe by oral route (Roy <i>et al.</i> , 2016)	Anthraquinone glycosides, chrysophanol, emodin, rhein, aloe-emodin and chrysophanic acid, sesquiterpene and phenolic compounds, wanthone, cassiollin, kaempferol (Ghani, 2003; Asolkar <i>et al.</i> , 1992; Fernand <i>et al.</i> , 2008)
Leguminosae: <b><i>Senna occidentalis</i> (L.) Link</b>	<i>Acute toxicity:</i> Seeds (beans) induced acute hepato toxicity and myoencephalopathy in children and brain, liver and striated muscles toxicity to animals; LD <sub>50</sub> >1 g/kg on mice and rats by IP (Vashishtha <i>et al.</i> , 2009). No toxicity of the ethanol extract up to 2000 mg/kg bw (Sharma <i>et al.</i> , 2014)	Flavonoids, alkaloids, phenolic, tannins, steroids, glycosides and anthraquinones (Kathirvel <i>et al.</i> , 2012)
	<i>Subacute toxicity:</i> 3 groups of rats were orally treated with 0.10, 0.50 or 2.5 g/kg/day for 30 days of hydroalcoholic extract from stem and leaves. The results showed no toxicity in	

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	male and female Wistar rats (Silva <i>et al.</i> , 2011)	
Leguminosae: <b><i>Tetrapleura tetraptera</i></b> (Schum. & Thonn.) Taub.	<i>Acute toxicity:</i> Acetone fruit extract was administered intraperitoneally in a dose range of 7000-12500 mg/kg. LD <sub>50</sub> was 10 g/kg (Effiong <i>et al.</i> , 2015)	Aridanin (Ojewole and Adewunmi, 2004)
Malvaceae: <b><i>Abelmoschus esculentus</i></b> (L.) Moench	<i>Acute toxicity:</i> 5 groups of rats received 500, 1000, 2000, 3000 and 4000 mg/kg of gum suspension in normal saline orally. No mortality and toxic manifestations were observed (Kumar, 2014). Doses of ethanol fruit extract of 1000, 2000, 2300, 2400, 2500, 2600, 2700, 3000, 4000 and 5000mg/kg bw were administered to rats. The LD <sub>50</sub> was 2500mg/kg  <i>Subacute toxicity:</i> Single dose of 500 mg/kg was administered daily for 28 days. The results showed severe toxicity effect on the testes of albino wistar rats (Umoh <i>et al.</i> , 2013)	Flavonoid, glycoside, quercetin, coumarin, scopoletin (Lakshmi <i>et al.</i> , 2016)
Malvaceae: <b><i>Ceiba pentandra</i></b> (L) Gaertn.	<i>Acute toxicity:</i> Ethanol leaf extract was administered at 10, 100, 1 000, 1 600, 2 900, and 5 000 mg/kg to albino rats. Oral LD <sub>50</sub> >5000 mg/kg (Muhammad <i>et al.</i> , 2016)  <i>Subacute toxicity:</i> Daily oral doses of 100, 400 and 750 mg/kg were administered for 28 days to rats. The results showed no abnormalities in treated groups as compared to the controls (Gandhare <i>et al.</i> , 2013)	Flavonoids, tannins (Mohamed <i>et al.</i> , 2015)
Malvaceae: <b><i>Duboscia macrocarpa</i></b>	Not available in literature	Dubosane. Dubosciasides (Tjeck <i>et al.</i> , 2017)

**Bocq.**

Malvaceae:

***Hibiscus sabdariffa* L.**

*Acute toxicity:* 6 groups of rats were treated with doses of aqueous extract (200, 400, 800, 1600, 3200 and 6400 mg/kg). LD<sub>50</sub> found was 3200mg/kg in Wistar rats (Adeyemi *et al.*, 2014)

Flavonoids, tannins, alkaloids, saponins, triterpenes, steroids (Rosemary *et al.*, 2014) and coumarins (Adeyemi *et al.*, 2014)

*Subacute toxicity:* Rats were administered orally aqueous extract of calix at 1, 2, 3, 4 and 5g /kg bw respectively for 28 days. Results suggest that high dose of calyx extract may be toxic to liver and kidney (Abubakar *et al.*, 2010)

Mimosoideae:

***Cylicodiscus gabunensis*****Harms**

*Acute toxicity:* Plant extract was administrated to rats different concentrations (4, 8, 12 and 16 g/kg bw). LD<sub>50</sub> found were 11 and 14.5 g/kg p.o., respectively in female and male rats (Mabeku *et al.*, 2007)

Alkaloids and terpenes. Leucoanthocyanins, saponins, tannins, polyphenols, coumarins, cardiac glycosides, reducing sugars, steroids, flavonoids, sterols and or triterpenes. Gallic acid, oligosaccharides (Tjeck *et al.*, 2017)

*Subacute toxicity:* Ethyl acetate extract of the stem bark was administered to Wistar rats at 4 doses (0.75, 1.5, 3 and 6 g/kg p.o.) daily for 6 weeks. Significant physical, clinical and pathological changes were associated with the p.o. administration of the plant extract (Mabeku *et al.*, 2007)

Mimosoideae:

***Entada gigas* (L.) Fawcett and Rendle**

Not available in literature

Alkaloids, phenols, and tannins (Tjeck *et al.*, 2017)

Mimosoideae:

***Piptadeniastrum africanum* (Hook.f.)**

*Acute toxicity:* Rats received an oral single dose of methanolic leaf extract (4, 8, 12, 16 and 20

Total phenols, gallic acid, flavonoids, quercetin, tannins, tannic acid and

<b>Brenan</b>	g/kg bw). No death was recorded at all tested doses (Assob <i>et al.</i> , 2011)	proanthocyanidins procyanidin (Tjeck <i>et al.</i> , 2017)
Moraceae: <b><i>Milicia excelsa</i> (Welw.) C.C. Berg</b>	<i>Acute toxicity:</i> Ethanol stem bark extract at 100, 1000, 3000, 4000 and 5000 mg/kg bw were administered to the mice. LD <sub>50</sub> was greater than 5g/Kg.  <i>Subacute toxicity:</i> Doses of 250, 500 and 750 mg/kg were given to rats orally once daily for 28 consecutive days. The extract was not toxic at the doses investigated (Areola <i>et al.</i> , 2015)	Tannins, alkaloids, flavonoids and saponins. Melicilamide A. 3,4-dimethoxybenzyl beta-D-xylopyranosyl -beta-D-glucopyranoside, lupeol acetate, ursolic acid, triacontyl (E)-ferulate, and 2-(3,5-dihydroxyphenyl) benzofuran-5,6-diol. Polyphenol, phenol, triterpenes and glycosides (Tjeck <i>et al.</i> , 2017)
Musaceae: <b><i>Musa paradisiaca</i> L.</b>	<i>Acute toxicity:</i> 7 group of mice were administered different doses (10, 100, 200, 400, 600, 800 and 1000 mg/kg bw) of ethanol leaf extract. The LD <sub>50</sub> was 489.9 mg/kg (Asuquo & Udobi, 2016)  <i>Subacute toxicity:</i> Three extracts (petroleum ether, methanol and ethyl acetate) were administered daily at 200 mg/kg bw orally for 28 consecutive days. No noticeable toxicity was recorded in male albino rats (Bera <i>et al.</i> , 2013)	Cyclomusalenol, cyclomusalenone (Lakshmi <i>et al.</i> , 2016)
Myrtaceae: <b><i>Psidium guajava</i> L.</b>	<i>Acute toxicity:</i> No harmful effects in rats were recorded after 72h of oral administration of 10-50 mg/100g of leaves water extract (Etuk and Francis, 2003). LD <sub>50</sub> was 1352 mg/kg. Another study in rats and mice have given LD <sub>50</sub> of guava leaf extracts > 2g/kg (Fang-Chui <i>et al.</i> , 2009).	Quercetin (Fang-Chui <i>et al.</i> , 2009), strictinin, isostrictinin, pendunculagin (Lakshmi <i>et al.</i> , 2016)

	<i>Subacute toxicity:</i> Hepatotoxicity in long-term treatment (Onyekwe et al., 2011)	
Pandaceae: <b><i>Microdesmis puberula</i> Hook.f. ex Planch.</b>	<i>Acute toxicity:</i> Mice were respectively treated with ethanol root extract at 100, 500, 1000, 1600, 2900 and 5000 mg/kg orally. Oral LD <sub>50</sub> was higher than 5000 mg/kg	keayanidines A, B, C and keayanine A. Saponins, cardiac glycosides, deoxysugars, alkaloids and terpenes (Tjeck et al., 2017)
	<i>Subacute toxicity:</i> 200, 400 and 600 mg/kg of the ethanol root extract were administrated between the hours of 10 am and 12 noon daily for 14 days to rats. No significant toxic effect on liver and kidney functions as well as on haematological parameters were recorded. However, alterations in serum lipid profile were observed (Akpanyung et al., 2013)	
Piperaceae: <b><i>Peperomia pellucida</i> (L.) Kunth</b>	<i>Acute toxicity:</i> Doses of 6.0, 7.5, 9.5, 12.0, 15.0, 19.0, 24.0, 32.0 g/kg were given orally to mice. LD <sub>50</sub> in male and female adult mice after a 14-day period was 11.78 g/kg (Sio et al., 2001)	Phytol, 2-Naphthalenol, decahydro, hexadecanoic acid, methyl ester and 9,12-octadecadienoic acid (Z, Z) -, methyl ester. Alkaloids, tannins, resins, steroids, phenols and carbohydrate. Flavonoids, glycosides, saponins (Tjeck et al., 2017)
Poaceae: <b><i>Cymbopogon citratus</i> (DC.) Stapf</b>	<i>Acute toxicity:</i> Mice received orally 8000, 16000 and 32000 mg/kg of essential oil. LD <sub>50</sub> was estimated at 8,105 mg/kg	Borneol, estragole, methyleugenol, geranyl acetate, geraniol, beta-myrcene, limonene, piperitone, citronellalitrat-2, alpha-terpineole,
	<i>Subacute toxicity:</i> Four double dilutions below the LD <sub>50</sub> value were given to animals. Each group was received orally a test dilution, daily for 28 days. Histological changes were recorded in the lungs, liver,	pinene, farnesol, proximadiol and cymbodiacetal (Ademuyiwa et al., 2015)



	kidney and intestines (Nakavuma <i>et al.</i> , 2016)	
Poaceae: <b><i>Pennisetum purpureum</i></b> <b>Schumach.</b>	<i>Acute toxicity:</i> 4 groups of rats received orally 100 mg/kg, 1000 mg/kg, 5000 mg/kg and 10000 mg/kg of aqueous stem extract, respectively. LD <sub>50</sub> found was 7071 mg/kg (Brantley <i>et al.</i> , 2015).	Ascorbic acid, rutin, epicatechin, anthocyanins, p-coumaric acid, quercetin, and catechin. Alkaloids, cyanogenic glycosides, flavonoids, oxalates, phytals, saponins, and tannins (Tjeck <i>et al.</i> , 2017)
Poaceae: <b><i>Saccharum officinarum</i> L.</b>	<i>Acute toxicity:</i> 1000 and 2000 mg/kg of aqueous leaf extract were given to mice. No toxicity up to 2000 mg/kg bw was recorded (Ojewunmi, <i>et al.</i> , 2013).	Tricin 4-O-guaiacyl-glycerol ether-7-O-glucopyranoside, genistin, p-coumaric acid, quercetin and genistein (Zheng <i>et al.</i> , 2017)
Poaceae: <b><i>Zea mays</i> L.</b>	<i>Subacute toxicity:</i> Daily consumption of 9.354 and 10.308 g/day/kg bw for male and female rats respectively, did not reveal any observed adverse effect and the no-observed-adverse-effect level was 8.0% (Wang <i>et al.</i> , 2011).	Phenolic compounds such as kaempferol, morin, naringenin, ferulic acid, caffeic acid, quercetin, rutin and chloogenic acid (Thiraphattha-navong <i>et al.</i> , 2014).
Rubiaceae: <b><i>Morinda lucida</i> Benth.</b>	<i>Acute toxicity:</i> Toxicity via IP at doses of 500-1500 mg/kg bw (Bamisaye <i>et al.</i> , 2013). LD <sub>50</sub> > 6400mg/kg (Oduola <i>et al.</i> , 2010)	Steroids, cardiac glycosides, phenolics, tannins, flavonoids (Ndam <i>et al.</i> , 2014)
	<i>Subacute toxicity:</i> Hepatotoxicity at 120 and 240 mg/kg in alloxan-induced diabetes rats (Bamisaye <i>et al.</i> , 2013). Aqueous extract of stem bark was well tolerated at low doses (0.1, 1, and 5 mg/kg bw) and toxic at dose level of 5 g/kg bw at sub-acute administration (Agbor <i>et al.</i> , 2012). Also, anti-spermatogenic properties was	

	found (Raji et al., 2005)	
Rubiaceae: <i>Nauclea diderrichii</i> (De Wild.) Merr.	Not available in literature	Alkaloids, saponins, flavonoids (Agnaniet et al., 2016), cardiac glycosides, tannins and anthraquinone glycosides (Ibibia et al., 2015)
Rutaceae: <i>Citrus aurantium</i> L.	<i>Acute toxicity:</i> Oral acute toxicity was not revealed up to 5000 mg/kg (Sharma et al., 2008)  <i>Subacute toxicity:</i> Cardiovascular toxicity due to synephrine (Hansen et al., 2013; Calapai et al., 1999)	Neohesperidin, Naringin (Suryawanshi, 2011)
Simaroubaceae: <i>Quassia amara</i> L.	Not available in literature	Quassinoids: simalikalactone D, picrasin B, picrasin H, beoquassin, quassin, picrasin I and picrasin J (Houël et al., 2009)
Urticaceae: <i>Musanga cecropioides</i> R.BR. ex Tedlie	<i>Acute toxicity:</i> Ethanol leaf extract was administered at 1, 2 and 3 g/kg (p.o.) to mice. LD <sub>50</sub> >3 g/kg (Sowemimo et al., 2015)  <i>Subacute toxicity:</i> Daily oral dose of 750 mg/kg bw was administered to rats for 28 days. No subacute toxicity up to 750 mg/kg bw was recorded (Adeneye et al., 2006)	Alkaloids, phenolic compounds, catechic tanins, flavonoids, and triterpenes (Nyunäi et al., 2016)
Verbenaceae: <i>Lantana camara</i> L.	<i>Acute toxicity:</i> Single dose of 2 g/kg bw of methanol leaf extract was administrated by oral gavage to mice. No obvious toxicity was recorded after 2 weeks (Pour et al., 2011). In another study, 3 groups of rats were administered 10, 100 and 1000mg/Kg bw of the extract	Flavones, isoflavones, flavonoids, anthocyanins, coumatins, lignans, catechins, isocatechins, coumarins, alkaloids, tannins, saponins ans triterpenoids (Saxena et al., 2012)

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respectively, then in a second stage, 1600, 2900 and 5000mg/Kg. No toxicity up to 5000mg/kg bw was recorded.

*Subacute toxicity:* 100, 200 and 500 mg/kg doses were given to rats for 4 weeks. Toxicity at chronic stage was observed (asadu *et al.*, 2015)

Zingiberaceae:

***Zingiber officinale* Roscoe**

*Acute toxicity:* Oral LD<sub>50</sub> in rats was 4525.5 mg/kg (Abdulrazaq *et al.*, 2011). In another study, 2 groups of rats received orally 2 and 5 g/kg of ethanolic rhizome extract. The extract was safe in doses less than 5 g/kg (Bardi *et al.*, 2013)

*Subacute toxicity:* Both male and female rats were daily treated with ethanol extract at 500, 1000 and 2000 mg/kg bw by gavage for 35 days. No mortalities and abnormalities in general conditions were observed except a slight reduction of testes weight (Rong *et al.*, 2009)

Poly phenols, vitamin C,  $\beta$ -carotene (Lakshmi *et al.*, 2016)

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