



## Review

# The use of plants in the traditional management of diabetes in Nigeria: Pharmacological and toxicological considerations

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## ABSTRACT

**Ethnopharmacological relevance:** The prevalence of diabetes is on a steady increase worldwide and it is now identified as one of the main threats to human health in the 21st century. In Nigeria, the use of herbal medicine alone or alongside prescription drugs for its management is quite common. We hereby carry out a review of medicinal plants traditionally used for diabetes management in Nigeria. Based on the available evidence on the species' pharmacology and safety, we highlight ways in which their therapeutic potential can be properly harnessed for possible integration into the country's healthcare system.

**Materials and methods:** Ethnobotanical information was obtained from a literature search of electronic databases such as Google Scholar, Pubmed and Scopus up to 2013 for publications on medicinal plants used in diabetes management, in which the place of use and/or sample collection was identified as Nigeria. 'Diabetes' and 'Nigeria' were used as keywords for the primary searches; and then 'Plant name – accepted or synonyms', 'Constituents', 'Drug interaction' and/or 'Toxicity' for the secondary searches.

**Results:** The hypoglycemic effect of over a hundred out of the 115 plants reviewed in this paper is backed by preclinical experimental evidence, either *in vivo* or *in vitro*. One-third of the plants have been studied for their mechanism of action, while isolation of the bioactive constituent(s) has been accomplished for twenty three plants.

Some plants showed specific organ toxicity, mostly nephrotoxic or hepatotoxic, with direct effects on the levels of some liver function enzymes. Twenty eight plants have been identified as *in vitro* modulators of P-glycoprotein and/or one or more of the cytochrome P450 enzymes, while eleven plants altered the levels of phase 2 metabolic enzymes, chiefly glutathione, with the potential to alter the pharmacokinetics of co-administered drugs.

**Conclusion:** This review, therefore, provides a useful resource to enable a thorough assessment of the profile of plants used in diabetes management so as to ensure a more rational use. By anticipating potential toxicities or possible herb–drug interactions, significant risks which would otherwise represent a burden on the country's healthcare system can be avoided.

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**Abbreviations:** AAN, aristolochic acid nephropathy; ADME, absorption, distribution, metabolism and excretion; CYT P450, cytochrome P450; DPP-IV, dipeptidyl peptidase IV; GLP1, glucagon like peptide 1; GLUT4, glucose transporter 4; GSH, glutathione; GST, glutathione-S-transferase; IDDM, insulin dependent diabetes mellitus; NIDDM, non-insulin dependent diabetes mellitus; P-GP, P-glycoprotein; PPARγ, peroxisome proliferator activated receptor gamma; STZ, streptozotocin; WHO, World Health Organization

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## 1. Introduction

### 1.1. Diabetes

Diabetes is a chronic metabolic disorder characterized by high blood glucose levels. This is either as a result of insufficient endogenous insulin production by the pancreatic beta cells (otherwise known as type-1 diabetes); or impaired insulin secretion and/or action (type-2 diabetes). type-1 diabetes is an autoimmune disease characterized by T-cell mediated destruction of the pancreatic beta cells. In type-2 diabetes, there is a gradual development of insulin resistance and beta cell dysfunction, strongly associated with obesity and a sedentary lifestyle (Zimmet et al., 2001). Due to a higher incidence of the risk factors, the prevalence of diabetes is increasing worldwide, but more evidently in developing countries. Current estimates indicate a 69% increase in the number of adults that would be affected by the disease between 2010 and 2030, compared to 20% for developed countries (Shaw et al., 2010).

Administration of exogenous insulin is the treatment for all type-1 diabetic patients and for some type-2 patients who do not achieve adequate blood glucose control with oral hypoglycemic drugs. Current drugs used in diabetes management can be categorized into three groups. Drugs in the first group increase endogenous insulin availability. These include the sulphonylureas such as glibenclamide, the glinides, insulin analogs, glucagon-like peptide 1 (GLP-1) agonists and dipeptidyl peptidase-IV (DPP-IV) inhibitors. The first two members of this group act on the sulphonylurea receptor in the pancreas to promote insulin secretion. GLP-1 agonists and DPP-IV inhibitors on the other hand act on the ileal cells of the small intestine. The second group of drugs enhance the sensitivity of insulin. This includes the thiazolidinediones, which are agonists of the peroxisome proliferator-activated receptor gamma (PPAR $\gamma$ ) and the biguanide metformin. The third group comprises the  $\alpha$ -glucosidase inhibitors such as acarbose, which reduce the digestion of polysaccharides and their bioavailability (Chehade and Mooradian, 2000; Sheehan, 2003). All the existing therapies however have limited efficacy, limited tolerability and/or significant mechanism based side effects (Moller 2001; Rothenstein et al., 2012).

Despite the existing pharmacotherapy, it is still difficult to attain adequate glycemic control amongst many diabetic patients due to the progressive decline in  $\beta$ -cell function (Wallace and Matthews, 2000). In Nigeria, polytherapy with two or more hypoglycemic agents to achieve better glucose control is common practice (Yusuff et al., 2008). There is also a high incidence of diabetic complications and hyperglycemic emergencies (Gill et al.,

2009; Ogbera et al., 2007, 2009). In the presence of these, the number of prescribed drugs increases to an average of four per day for each patient (Enwere et al., 2006). This need for the chronic intake of a large number of drugs with their attendant side effects in addition to their high costs which is often borne by the patients themselves is the identified reason for non-adherence to therapy amongst diabetic patients. As a result, patients often have recourse to alternative forms of therapy such as herbal medicines (Yusuff et al., 2008).

### 1.2. Traditional herbal medicines in diabetes management

A number of reviews on medicinal plants used in the management of diabetes in different parts of the world (Bailey and Day, 1989; Marles and Farnsworth, 1995), as well as those used specifically in certain regions, such as in West Africa (Bever, 1980), Central America (Andrade-Cetto and Heinrich, 2005) and Asia (Grover et al., 2002) exist. These reviews have highlighted the dependence of a large percentage of the world population on traditional medicine for diabetes management. This is also corroborated by the WHO fact sheet (No. 134), which estimates that about 80% of the population in African and Asian countries rely on traditional medicine for their primary healthcare (WHO, 2008). It also recognizes traditional medicine as 'an accessible, affordable and culturally acceptable form of healthcare trusted by large numbers of people, which stands out as a way of coping with the relentless rise of chronic non-communicable diseases in the midst of soaring health-care costs and nearly universal austerity' (WHO, 2013).

Ethnobotanical surveys of plants traditionally used in diabetes management in different parts of Nigeria have been carried out (Abo et al., 2008; Etuk and Mohammed, 2009; Gbolade, 2009; Soladoye et al., 2012). These medicinal plants are used either alone as a primary therapeutic choice, or in conjunction with conventional medicines. On an average, approximately 50% of diabetic patients visiting hospitals in urban cities like Lagos and Benin have used some forms of traditional medicine during the course of their disease management (unpublished results of field work conducted by first author). Unfortunately, clinicians are either unaware of their patients' herb use or the identity of the herbal product being taken. To complicate matters further, herbal practitioners are usually unwilling to divulge the identity of the constituents of their preparations to patients. Most patients are also not interested in finding this out as they consider herbal preparations to be 'safe'; thereby making it difficult to ascertain if the herb may have a significant contributory role to the efficacy or failure of the treatment.

In a systematic review of herbs and supplements clinically used for glycemic control, *Allium sativum*, *Aloe vera* and *Momordica charantia* were the only identified plants used in Nigeria. This inclusion was however based on clinical studies carried out outside Nigeria (Yeh et al., 2003). This indicates the lack of information about the clinical use (or monitoring thereof) of plants in diabetes management in Nigeria, despite widespread traditional use.

In line with the increasing importance of traditional medicine in various healthcare systems around the world, the WHO Traditional Medicine Strategy has recently been updated. 'The goals of the strategy for the next decade (2014–2023) are to support Member States in (a) harnessing the potential contribution of traditional medicine to health, wellness and people-centered health-care; and (b) promoting the safe and effective use of traditional medicine by regulating, researching and integrating traditional medicine products, practitioners and practice into health systems where appropriate' (WHO, 2013).

Given that diabetes is now considered as one of the main threats to human health in the 21st century (Zimmet et al., 2001), there might be an even greater reliance by diabetic patients in Nigeria on herbal medicines used in its management. Unfortunately, pharmacological and toxicological evidences validating the safety and efficacy of these medicinal plants are not readily available. The objective of this paper is to collate as much as possible, available information about medicinal plants traditionally used in diabetes management in Nigeria. In doing so, we aim to promote the rational use of these plants based on pharmacological evidence for their therapeutic use and their toxic/interaction profile.

## 2. Ethno-pharmacological data collection

### 2.1. Method

Information about medicinal plants traditionally used in the management of diabetes in Nigeria was obtained from published papers and texts on ethnobotanical studies, as well as those investigating the effect of plant(s) used in diabetes management, in which the place of use and/or sample collection was identified as Nigeria. A literature search of electronic databases such as Google Scholar, Pubmed and Scopus up to 2013 was carried out using 'Diabetes' and 'Nigeria' as keywords for the primary searches; and then 'Plant name – accepted or synonyms', 'Constituents', 'Drug interaction' and/or 'Toxicity' for the secondary searches.

In order to highlight medicinal plants traditionally used in diabetes management with the potential for integration into the healthcare system, not all identified plants were included in this paper. Only those with (1) more than one reference to its use in diabetes management in Nigeria based on ethnobotanical studies were retained; and/or (2) experimental evidence in one or more diabetes experimental models validating its activity. This review is therefore not exhaustive for all the plants used traditionally for diabetes management in Nigeria.

### 2.2. Results

Data for one hundred and fifteen plants traditionally used in diabetes management in Nigeria were obtained, either from previously conducted ethnobotanical studies (Abo et al., 2008; Aiyelaja and Bello, 2006; Ajibesin et al., 2008; Etuk and Mohammed, 2009; Gbolade, 2009; Igoli et al., 2005; Lawal et al., 2010; Ogbonnina and Anyakora, 2009; Okoli et al., 2007; Olowokudejo et al., 2008); or

from primary research papers (as indicated in Table 1). These are tabulated according to their accepted Latin Name (based on <http://www.plantlist.org>). Synonyms are included for plants which were not identified with their accepted names in the primary research paper. For each of the identified plants, the family name, common name(s), identified region of use in diabetes management, experimental evidence of activity (where available), other medicinal uses, plant part(s) used, traditional method(s) of preparation, identified active constituent(s), other relevant phytochemical constituents, as well as data on interaction and toxicity studies are included [Table 1].

Out of the 115 plants reviewed in this paper, only twelve of them have no experimental evaluation of their blood sugar reducing effects, either *in vivo* or *in vitro*. In selecting studies to be included, priority was given to investigations carried out with samples collected in Nigeria. Certain publications were not included if the study design of the experimental evidence was not appropriate enough for validating the effect of the plant, such as the absence of a suitable control or the use of improper doses. Two-thirds of the identified plants with experimental evidence for their biological activity involved samples collected from Nigeria. For the remaining one-third, although the studies were not carried out with plant samples sourced from within Nigeria, these were still included, as the experimental evidence could provide some information validating their use in diabetes management, since they are widely used in Nigeria. The ethnobotanical research carried out on *Moringa oleifera* provides a rationale for including information from studies carried out in different countries, as some of these locally available plants could have been initially sourced from elsewhere (Popoola and Obembe, 2013).

*In-vitro* experimental studies as well as phytochemical studies carried out on the plant species regardless of the source of the plant samples were also included. These together could provide more insight into the biological activity(s) of the plant, which would in turn help to promote a more rational use of the plant in diabetes management, either in the presence or absence of other co-morbidities. For completeness, reports on the antioxidant properties of many of the identified plants have been included as this has become a popular parameter in assessing the beneficial effects of a plant in diabetes management.

## 3. Pharmacological evidence and its clinical implications

### 3.1. *In vivo* hypoglycemic activity

Reducing blood sugar level is the classical clinical target in all forms of diabetes. Thus, the *in vivo* sugar lowering effect of putative hypoglycemic plants is therefore a premise to infer their potential clinical efficacy. *In vivo* validation also provides an indication of the relative toxicity of the plant. Although most herbal medicines have a long history of traditional use, only their experimental validation at known doses may give a clearer idea about its safety and efficacy, in line with the objectives of the WHO Traditional Medicine Strategy (WHO, 2013).

Ninety six out of the one hundred and fifteen plants here reviewed have been evaluated in various *in vivo* animal models of diabetes, mostly using alloxan and/or streptozotocin (STZ)-induced diabetic animals, which are the most frequently used animal diabetes models worldwide (Fröde and Medeiros, 2008). These chemical agents are cytotoxic to the  $\beta$ -cells of the pancreatic islets, generating a state of insulin deficiency (akin to type-1 diabetes) with subsequent hyperglycemia (Szkudelski, 2001). The

**Table 1**  
Medicinal plants used in the management of diabetes in Nigeria.

S/ no.	Plant name	Family	Common name	Local Nigerian name(s) <sup>a</sup>	Region of use for diabetes <sup>#</sup>	Experimental evidence for its use in diabetes management	Other medicinal uses	Plant part (s) used	Traditional preparation method	Identified active constituent(s)	Other relevant phytoconstituents identified in the plant	Interaction/toxicity studies
1	<i>Abelmoschus esculentus</i> (L.) Moench	Malvaceae	Okro/Okra; Lady's fingers	Ila (Y); Okweje (I); Kubewa (H)	SW, SS	100 and 200 mg/kg of the seed and peel powder decreased blood glucose in STZ induced diabetic rats (Sabitha et al., 2011) <sup>§</sup> ; Antioxidant effects of the aqueous extract of the leaves (Tsumbu et al., 2011)	Infections, Immuno-modulatory, Fevers, Spasms, Gonorrhoea, Dysentery	Fruit, Seed	Decoction, Maceration food vegetable		$\beta$ -1,3-D-glucans (Sheu and Lai, 2012); Hydroxy cinnamic derivatives, Oligomeric catechins, Isorhamnetin glycosides, Quercetin, Myricetin and Kaempferol and their glycosides (Arapitsas, 2008); Abelesculin (Kondo and Yoshikawa, 2007); Rhamnogalacturonans (Deters et al., 2005), Oleic, Stearic, Palmitic, Capric, Caprylic, Lauric, Myristic, Arachidic and Linoleic acids, Gossypol (Al-Wandawi, 1983)	Water soluble fraction of the fruits decreased oral metformin absorption <i>in-vivo</i> (Khatun et al., 2011)
2	<i>Abrus precatorius</i> (L.)	Leguminosae	Cat's eye, Jequirity beans	Ojuologbo (Y), Otoberebere (I), Idozakara (H), Nneminua (Ib)	SW	Inhibited $\alpha$ -amylase and $\alpha$ -glucosidase enzymes and antioxidant effects (Vadivel et al., 2011); 100 and 200 mg/kg aqueous extract of the seeds produced a dose dependent decrease in STZ-induced diabetic rats (Nwanjo, 2008)	Anti-infective, Convulsion, Rheumatism, Abortifacient, Cold/Cough, Conjunctivitis, Contraceptive, Aphrodisiac, Ulcers, Anemia	Leaves, Seeds, Root	Decoction, Maceration	Trigonelline extracted from the seeds decreased blood glucose levels in alloxan induced diabetic rats (Monago and Nwodo, 2010)	Epicatechin, Syringic acid, Caffeic acid (Vadivel et al., 2011); Abruquinones (Kuo et al., 1995); Abrusosides (Choi et al., 1989); Trigonelline, Hypaphorine, Precatorine, Abrine (Ghosal and Dutta, 1971)	Abrin-Toxic component (Kirsten et al., 2003)
3	<i>Acacia nilotica</i> (L.) Delile	Leguminosae	Gum arabic, Egyptian thorn	Bagaruwa (H)	NC	50 mg/kg of the ethyl acetate fraction of the methanol extract of the leaves produced greater blood glucose reducing effect (> 50%) in alloxan-induced diabetic rats than the n-butanol fraction (Tanko et al., 2013)	Anti-parasitic, Male sterility, Inflammation, Anti-microbial, Hypertension, Anti-spasms, Insomnia	Leaves, Pods, Root, Bark, Seeds	Maceration, Infusion, Decoction		Catechin and gallic acid derivatives (Malan, 1991); Androstene steroid (Chaubal et al., 2003); D-Pinitol (Chaubal et al., 2005); Kaempferol (Singh et al., 2008); Polygalloyltannin (Jigam et al., 2010); Lupenone, Acanilol A and B (Ahmadu et al., 2010)	Co-incubation of 0.01% of the extract in Caco-2 cell monolayers decreased the integrity of the monolayer and the secretory transport of CsA indicating possible inhibition of P-gp (Deferme et al., 2003)
4	<i>Adansonia digitata</i> L.	Malvaceae	African baobab tree	Ose (Y), Kuka (H), Bokki (Fulani)	NE, SW	100 mg/kg of the methanol extract of the stem bark decreased blood glucose levels by 51% in STZ-induced diabetic rats (Tanko et al., 2008)	Anti-sickling, Galactagogue, Inflammation, Antipyretic, Analgesic, Antiparasitic, Constipation, Skin lubricant, Asthma, Nutritive value	Stem bark, Leaves, Fruit pulp, Seeds			Oleic, Linoleic and Myristic acids (Eteshola and Oraedu, 1996); Epicatechin, Epicatechin procyanidins, Dihydroxy and Trihydroxy flavan-4-one glycosides, Quercetin glycosides, $\alpha$ -amyrin, $\beta$ -amyrin palmitate, Ursolic acid, Adansonin, $\beta$ -sitosterol, Stigmasterol (Refaat et al., 2013)	
5	<i>Aframomum melegueta</i> K. Schum.	Zingiberaceae	Alligator pepper, Grains of paradise	Atare (Y), Ose-orji (I), Citta (H)	SW	Inhibitory effects on $\alpha$ -amylase and $\alpha$ -glucosidase enzymes, Antioxidant activity (Adefegha and Oboh, 2012) 200 & 400mg/kg aqueous seed extract decreased blood glucose in alloxan-induced	Stimulant, Inflammation, Diarrhoea, Antifungal, Insect repellent, Skin conditions, Malaria, Analgesic	Seed, Fruits, Leaves	Maceration, Tincture		6-Gingerol, 6-shogaol, 6-paradol (Ilic et al., 2010); Linalool, 1,8-cineole, Citral, 2-heptyl acetate, 2-heptanol (Ukeh and Umoetok, 2011)	Inhibition of Cyp 3A4, 3A5 and 3A7 enzyme activity (Agbonon et al., 2010); Elevated levels of liver function enzymes with chronic dosing (Ilic et al., 2010)

Table 1 (continued)

S/ no.	Plant name	Family	Common name	Local Nigerian name(s) <sup>a</sup>	Region of use for diabetes <sup>#</sup>	Experimental evidence for its use in diabetes management	Other medicinal uses	Plant part (s) used	Traditional preparation method	Identified active constituent(s)	Other relevant phytoconstituents identified in the plant	Interaction/toxicity studies
6	<i>Ageratum conyzoides</i> (L.) L.	Compositae	Goat weed	Imi esu (Y), Urata njele (I), Ebegho- edore (Bi)	SW, NC	diabetic rats (Adesokan et al., 2010) 100, 200 and 300 mg/kg of the aqueous extract of the leaves decreased blood glucose levels in both normal rats, STZ-induced diabetic rats and glucose-loaded rats (Nyunai et al., 2009) <sup>§</sup> ; 100, 200 and 400 mg/kg of the ethanol extract of the shoot decreased blood glucose levels in normal and alloxan induced diabetic rats (Egunyomi et al., 2011)	Wound ulcers, Antimicrobial, Skin infections, Analgesic, Anti-spasm, Insecticidal, Diarrhoea, Gonorrhoea, Emetic	Whole plant, Leaves	Fresh Juice extract, Infusion		Eugenol, $\alpha$ -pinene, 1,8- cineole, $\beta$ -caryophyllene, Ocimene, Limonene, Precocene I and II, Encecalin derivatives, Coumarin, Quercetin and its glycosides, Kaempferol and its glycosides, $\beta$ - sitosterol, Friedelin, Stigmasterol, Echinatine, Lycopsamine, Polymethoxylated and Polyhydroxy flavones (Okunade, 2002)	
7	<i>Alchornea cordifolia</i> (Schumach and Thonn.) Mull.Arg.	Euphorbiaceae	Christmas bush	Ipa (Y), Mbom (Ib), Upia (Ige), Uwanwe (Es), Osokpo (I)	SE, SW, SS	Antioxidant activity and hepatoprotective effects (Olaeye and Rocha, 2007, 2008); Significant decrease in blood glucose levels in STZ- induced diabetic rats administered 200, 400 and 800 mg/kg of the n-butanol fraction of the aqueous extract of the leaves (Mohammed et al., 2012a, 2012b)	Wound, Ulcers, Infections, Anti- parasitic, Liver disorders, Rheumatism, Fevers, Diuretic, Purgative, Analgesic, Gonorrhea, Cough	Stem bark, Leaves, Seeds, Root	Decoction		Alchornoic acid (Kleiman et al., 1977); Quercetin and its glycosides, Gallic acid, Triisopentenyl guanidine, Protocatechuic acid (Lamikanra et al., 1990); Ellagic acid (Banzouzi et al., 2002); Daucosterol, $\beta$ - sitosterol, Acetyl aleuritic acid, Di(2- ethylhexyl) phthalate (Mavar-Manga et al., 2008); Caryophyllene, Eugenol, Nanocosaine, Cadinol, Linalool, $\alpha$ - bergamone (Okoye et al., 2011)	
8	<i>Allium cepa</i> L.	Amaryllidaceae	Onion	Alubosa (Y)	SE	100 and 300 mg/kg aqueous extract of the bulb administered for 30 days decreased blood glucose levels in alloxan-induced diabetic rabbits and restored decreased levels of antioxidant enzymes (Ogunmodede et al., 2012)	Convulsion, Rheumatism, Vermifuge, Hypertension	Bulb		Anti-diabetic effects of S-methylcysteine sulfoxide isolated from onion in alloxan-induced diabetic rats (Sheela et al., 1995)	Quercetin and its glycosides, Kaempferol, Cepaenes, S-methylcysteine sulfoxide (SMCS), $\beta$ - chlorogenin (Corzo- Martínez et al., 2007); Trapeosides, Ascalonicoside, Sitosterol, Amyrin, Oleanolic acid, Taxifolin, Diosgenin, Gitogenin, Apigenin, Luteolin, Myricetin (Lanzotti, 2006)	
9	<i>Allium sativum</i> L.	Amaryllidaceae	Garlic	Aayu (Y), Ayo-ishi (I), Tafarunua (H)	SS, SE	200–300 mg/kg aqueous extract of the cloves decreased blood glucose levels in alloxan-induced diabetic rats after one week (Eyo et al., 2011); 250 and 500 mg/kg ethanol extract of the cloves administered for 14 days produced a dose- dependent decrease in serum glucose, lipid levels and liver	Hypertension, High cholesterol, Stomach ache, General debility, Hemorrhoids, Tumours, Asthma, Anti-microbial	Cloves		Anti-diabetic effects of S-allylcysteine sulfoxide isolated from garlic in alloxan-induced diabetic rats (Sheela et al., 1995)	S-allylcysteine sulfoxide (SACS), Allyl sulfides, Allicin and its breakdown products, Allixin, Eruboside B, Vitamin B <sub>6</sub> and B <sub>12</sub> (Corzo-Martínez et al., 2007); Sativosides, Proto-desgalactotigonin, Apigenin, Quercetin, Myricetin, N-feruloyl	Components of aged garlic extract did not produce significant inhibition of Cytochrome P450 enzymes <i>in vitro</i> (Greenblatt et al., 2006); and in humans (Markowitz et al., 2003)



Table 1 (continued)

S/ no.	Plant name	Family	Common name	Local Nigerian name(s)	Region of use for diabetes <sup>#</sup>	Experimental evidence for its use in diabetes management	Other medicinal uses	Plant part (s) used	Traditional preparation method	Identified active constituent(s)	Other relevant phytoconstituents identified in the plant	Interaction/toxicity studies
10	<i>Aloe vera</i> (L.) Burm.f.	Asparagaceae	Barbados aloe	Ahon erin (Y)	SE	function enzyme levels and increased serum insulin levels in STZ-induced diabetic rats (Eidi et al., 2006) <sup>§</sup> 150 mg/kg of the dried pulp extract/exudate administered to STZ-induced diabetic rats decreased fasting blood glucose levels and improved the levels of the antioxidant enzyme (Nwanjo, 2006); 1 mg/ml aloe vera whole gel extract prevented the onset of hyperglycaemia in alloxan-induced diabetic rabbits (Akinmoladun and Akinloye, 2007); 350 mg/kg of a polyphenol-rich gel extract administered to insulin resistant mice for 4 weeks improved insulin tolerance and fasting blood glucose levels (Pérez et al., 2007) <sup>§</sup>	Skin diseases, Laxative, Immune booster, Wound ulcers, Tumours, Guinea worm, Amenorrhoea	Leaves	Juice extract		tyrosine, N-feruloyl tyramine (Lanzotti, 2006)	
11	<i>Alstonia boonei</i> De Wild.	Apocynaceae	Stoolwood, Devil tree, Australian fever bush	Ahun (Y), Egbu (I)	SW <sup>c</sup>	<i>In vitro</i> antioxidant effects (Akinmoladun et al., 2010)	Malaria, Infertility, Arthritis, Anti-infective	Stem bark	Decoction, Tincture, Maceration		Mannose-6-phosphate, Barbaloin, Emodin, Aloin, Aloe emodin, Aloesin, $\beta$ -sitosterol, Diethylhexyl phthalate (Choi and Chung, 2003); Aloetic acid, Veracylglyceran A, B and C, Acemannan, Anthranol, Isobarbaloin, Arabinogalactan, Cinnamic acid ester, Aloeride, Malic acid, Isorabaichromone, Neoloesin A, Isoaloesin D, 8-C-glucosyl derivatives of aloediol, aloesol, noreugenin, Ascorbic acid, $\beta$ -carotene, $\alpha$ -tocopherol (Hamman, 2008); Myricetin, Kaempferol, Quercetin (Sultana and Anwar, 2008) B-amyrenone, $\beta$ -amyren acetate, Lupeol, Sitosterol (Faparusi and Bassir, 1972); Echitamine, Echitamine (Kucera et al., 1972); $N\alpha$ -formyl echitamine (Oguakwa, 1984); $\alpha$ -amyren and its esters, Lupeol and its esters (Rajic et al., 2000); $N\alpha$ -formyl-12-methoxy echitamine, Voacangine, Akuammidine, Ursolic acid, Loganin, Boonein (Adotey et al., 2012) Echitamine, Echitamine, Nor-echitamine, 17-O-acetyl nor-echitamine, Akuammicine and its 12-Methoxy derivative, Tubotaiwine, 12-methoxy tubotaiwine and its 12-methoxy derivative, Akuammidine, Angustilobine A and B, Seco angustilobine A and B, Anugustilobine-B-N-oxide (Caron et al., 1989) 6-Alkyl salicylic acids (Anacardic acids), 5-alkyl resorcinols (Cardols), 3-alkyl phenols	Causes an opening of the tight junction between adjacent epithelial cells thereby increasing paracellular transport, with the potential to increase oral drug absorption (Hamman, 2008)
12	<i>Alstonia congensis</i> Engl.	Apocynaceae	Pattern wood Alstonia	Egbu ora (I), Awogbo ahun (Y)	SW	Administration of 1 g/kg of a 1:1 mixture of a hydroethanolic extract of <i>Alstonia congensis</i> bark and <i>Xylopi aethiopica</i> fruits decreased blood glucose levels in normal mice (Ogbonnia et al., 2008a); <i>In vitro</i> antioxidant effects (Awah et al., 2012)	Malaria, Diuretic, Analgesic, Astringent, Hypertension	Stem bark, Root, Leaves	Decoction, Maceration			Possible nephrotoxic effects; Decreased creatinine levels in normal mice (Ogbonnia et al., 2008a).
13	<i>Anacardium occidentale</i> L.	Anacardiaceae	Cashew	Kasu (Y), Sashu (I), Kanju (H)	SW, NC	Stimulated glucose uptake in C2C12 myoblasts and rat liver mitochondria (Tedong et al., 2010) <sup>§</sup> ; 200 mg/kg methanol	Cough, Malaria, Skin infections, Anti-parasitic, Fevers, Anti-helminthic	Stem bark, Leaves, Seed, Nuts	Decoction, Maceration			

Table 1 (continued)

S/ no.	Plant name	Family	Common name	Local Nigerian name(s) <sup>+</sup>	Region of use for diabetes <sup>#</sup>	Experimental evidence for its use in diabetes management	Other medicinal uses	Plant part (s) used	Traditional preparation method	Identified active constituent(s)	Other relevant phytoconstituents identified in the plant	Interaction/toxicity studies
14	<i>Ananas comosus</i> (L.) Merr.	Bromeliaceae	Pineapple	Ogede oyinbo (I)	SW	extract of the stem bark administered to rats alongside a high-fructose diet prevented the onset of hyperglycaemia (Olatunji et al., 2005); 100–800 mg/kg aqueous and methanol extract of the stem bark decreased blood glucose levels in both fasted normal and STZ-induced diabetic rats dose dependently (Ojewole, 2003); Inhibits $\alpha$ -glucosidase and aldose reductase enzymes (Toyomizu et al., 1993) <sup>§</sup> The ethanolic extract at a dose of 400 mg/kg improved insulin sensitivity in diabetic dyslipidaemic rats; as well as improved glucose uptake in insulin resistant HepG2 cells (Xie et al., 2006) <sup>§</sup>	Inflammation, Anti-parasitic	Leaves, Fruits			(Cardanols), 2-methyl-5-alkyl resorcinol (Toyomizu et al., 1993); Stigmast-4-en-3-ol and Stigmast-4-en-3-one (Alexander-Lindo et al., 2004); Lutein, $\beta$ -carotene, Zeaxanthin, $\alpha$ -tocopherol, $\gamma$ -tocopherol, Thiamin, Stearic acid, Oleic acid and Linoleic acid (Trox et al., 2010)	
15	<i>Anisopus mannii</i> N.E.Br.	Apocynaceae		Sakayau (H), Kashe zaki (H)	NW, NE	100, 200 and 400 mg/kg aqueous leaf extract decreased blood glucose levels in alloxan-induced diabetic mice (Manosroi et al., 2011); Antioxidant effect (Aliyu et al., 2010); 100–400 mg/kg of the aqueous stem extract decreased blood glucose in normal rats (Sani et al., 2009)	Analgesic, Anti-parasitic, Inflammation, Hypertension, Anti-microbial, Infertility	Stem, Leaves, Whole plant	Decoction		Bromelain, Chlorogenic, Caffeic, Coumaroylquinic, P-coumaric and Caffeic acids, Caffeoylglycerols, Coumaroylglycerols, Ferulic acid glucuronide, Hydroferuloylglucose, Ananaflavoside B and C, Ananasate, Dicafeoyl glycerides, Tricin, Feruloyl glycerols (Ma et al., 2007) Anisopusine, Gingerdione, Lupen-3 $\beta$ -yl eicosanoate, Dehydro gingerdione, Ferulic acid (Tsopmo et al., 2009)	
16	<i>Annona muricata</i> L.	Annonaceae	Soursop, Custard apple	Sapi sapi (Y)	SW, SE	100 mg/kg aqueous leaf extract decreased blood glucose, increased serum insulin, decreased $\beta$ -cell damage and possessed antioxidant effects in STZ induced diabetic rats (Adewole and Caxton-Martins, 2006); Methanol extract of the leaves inhibits $\alpha$ -amylase and $\alpha$ -glucosidase enzymes, but less potent than acarbose (Kumar et al., 2011) <sup>§</sup>	Hypertension, Sedative, Cancer, Emetic, Lactagogue, Anti-microbial, Anti-convulsant, Anti-parasitic, Rheumatism, Analgesic, Insecticide	Leaves, Fruit, Seeds, Bark, Root	Infusion, Decoction, Fruit juice		Reticuline, Coclaurine, Anomurine, Anomuricine, Coreximine (Lannuzel et al., 2002); Scyllitol, Oleic, Linoleic and P-coumaric acid, Procyanidins, Stigmasterol (Leboeuf et al., 1980); Annonaine, Asimilobine, Nornuciferine (Hasrat et al., 1997); Acetogenins (Carmen Zafra-Polo et al., 1998); Alkyl esters, Linalool, $\beta$ -caryophyllene, Cadinene, Humulene, Caryophyllene oxide, Phellandrene, Cadinol (Fournier et al., 1999); Gallic acid, Epicatechin, Quercetin and its	Chronic intake of the fruit and infusions of the plant is thought to bring about neurodegeneration in the CNS; attributed to coreximine and reticuline alkaloids present in the plant (Lannuzel et al., 2002), as well as the acetogenin annonacin (Champy et al., 2005)

Table 1 (continued)

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17	<i>Annona senegalensis</i> Pers.	Annonaceae	Wild custard apple	Uburu ocha (I), Abo (Y), Gwander-daji (H), Ogoganto (Es), Ndaweewu (F)	SS, NC, NW, SW	100 mg/kg of the aqueous extract of a herbal preparation ADD-199 containing the roots of <i>Annona senegalensis</i> and three other plants decreased plasma glucose and increased plasma insulin in STZ- induced diabetic mice; as well as increased glucose uptake by isolated diaphragm (Okine et al., 2005) <sup>§</sup> ; Antioxidant effects (Potchoo et al., 2008) <sup>§</sup>	Anti-parasitic, Anti- bacterial, Tumours, Erectile dysfunction, Wound-healing, Snake bites, Convulsions, Hemorrhage	Stem-bark, Root, Leaves	Decoction		glycosides, Catechin, Chlorogenic acid, Argentinine, kaempferol and its glycosides (Nawwar et al., 2012) Acetogenins (Carmen Zafra-Polo et al., 1998); Roemerine, Isocorydine, 8,8-Bisdihydrosiringenin, Syringaresinol (You et al., 1995); Kaurane diterpenes, Quercetin, Sitosterol, Oleic acid, Linoleic acid, Sitosterol (Leboeuf et al., 1980); Rutin, Epicatechin, Catechin, Isoquercetin (Potchoo et al., 2008); Cadinol, $\alpha$ -phellandrene, Z-ocimene, Limonene, $\alpha$ and $\beta$ -pinene, Linalool, Myrcene, Caryophyllenol, 1,8-cineole (Fournier et al., 1999)	Stem bark extract inhibited P-gp mediated Rh-123 efflux (Ezurike et al., 2012); Roemerine interacts with P-gp and enhances vinblastine cytotoxicity (You et al., 1995); ADD-199 did not interact with Cyt P-450 isozymes nor produce any organ toxicity (Nyarko et al., 2005)
18	<i>Anogeissus leiocarpus</i> (DC.) Guill. and Perr.	Combretaceae	Axle wood, Giant fern	Orin-odan or Ayin (Y), Atara (I), Marke (H)	NC, NW, SW	Antioxidant and hepatoprotective effects (Atawodi et al., 2011); 200 mg/kg aqueous extract decreased blood glucose levels after 2 h in alloxan- induced diabetic rats (Etuk and Mohammed, 2009)	Anti-parasitic, Hemorrhoids, Asthma, Anti-microbial, Anti- sickling	Stem-bark	Decoction		Castalagin, Ellagic acid, Flavogallonic acid (Shuaibu et al., 2008); Leiocarpan A and B (Aspinall et al., 1969); Gallic acid, Chlorogenic acid, Protocatechuic acid P-comaric acid (Kone et al., 2012)	Dose-dependent toxicity of the aqueous leaf extract in rat lungs characterised by inflammation and lesions (Agaie et al., 2007)
19	<i>Anthocleista djalensis</i> A. Chev.	Gentianaceae	Cabbage tree	Sapo (Y), Akpakoro or Uvuru (I), Putaa (H)	SS <sup>c</sup> , SE <sup>b</sup> , SW	$\leq 111$ mg/kg ethanolic root extract decreased blood glucose levels in alloxan- induced diabetic rats (Okokon et al., 2012); Alpha amylase inhibitory effects of the hydro-alcoholic extract of the leaves and stem bark as well as hypoglycaemic effect of 1 g/kg of the stem bark in alloxan-induced diabetic rats (Olubomehin et al., 2013)	Anti-microbial, Inflammation, Wound- healing, Anti-parasitic, Fevers, Sexual disorders	Stem-bark, Roots, Leaves	Decoction		Djalonenol, Djalonenosone, Sweroside, Ursolic acid, Sitosterone, Sitosterol, Stigmasterol, Bornesitol, Lichexanthone (Onocha et al., 1995)	Gastrointestinal upsets (Tchacondo et al., 2011)
20	<i>Anthocleista vogelii</i> Planch.	Gentianaceae	Cabbage tree	Kwari (H), Opa oro (Y)	NC, SW	Hypoglycaemic effect of 100– 800 mg/kg aqueous extract in normal and alloxan-induced rodents (Abuh et al., 1990); Hydro-alcoholic extract of the leaves and stem bark produced < 50% alpha amylase inhibitory effects (Olubomehin et al., 2013)	Purgative, Diuretic, Skin infections, Emmenagog, Anti-ulcer, Malaria	Root, Leaves, Stem-bark	Decoction		Sweroside, Vogeloside, Fagaramide (Abuh et al., 1990); Tetraoxygenated xanthones (Chapelle, 1974)	
21	<i>Aristolochia albida</i> Duch.	Aristolochiaceae	Dutchmans pipe, Hill gourd	Duuman duutse (H), Paran funfun (Y)	SW, NE, NW		Anti-parasitic, Anti- venom, Analgesic, Inflammation, Skin infections, Anti-	Leaves, Stem, Roots, Rhizome	Infusion, Decoction		Columbin (Nok et al., 2005); Aristolic acid, Aristolochic acid A, Aristolactam, 6-hydroxy	Risk of AAN (Aristolochic acid nephropathy) (Heinrich et al., 2009)



Table 1 (continued)

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							spasmodic, Aphrodisiac, STDs				aristolochic acid A, Aristolone (Lajide et al., 1993); Aristolochic acids I, II, IV, C and C-beta-D- glucoside, Aristolactam I-beta-D-glucoside Campesterol, Stigmasterol, Sitosterol (Choudhury and Haruna, 1994)	
22	<i>Aristolochia bracteolata</i> Lam.	Aristolochiaceae	Snake wort, Birth wort	Gadau kuka (H)	SS		Skin infections, Anti- helminthic, Anti-venom, Analgesic Stimulant, Insecticide	Leaves Roots, Seeds	Decoction		Aristolochic acid I and II, Aristolactam A (Kumar et al., 2003); Magnoflorine (El Tahir, 1991); N-acetyl normuciferine, Aristo red, β-sitosterol (Chakravarty et al., 1988)	Risk of AAN (Heinrich et al., 2009); Chronic dosing of goats with the aqueous leaf extract resulted in toxic effects culminating in death (Barakati et al., 1983)
23	<i>Aristolochia repens</i> Mill.	Aristolochiaceae		Akoigun (Y)	SW, SS		Hemorrhoids, Rheumatism, Aphrodisiac	Stem bark	Decoction		Aristolochic acids I, II, IV, C and D, Aristolochic acid D- beta-D-glucoside, Aristolactam I-beta-D- glucoside (Michl et al., 2011)	Risk of AAN (Heinrich et al., 2009)
24	<i>Azadirachta indica</i> A.Juss.	Meliaceae	Neem, Indian lilac	Dogonyaro (Y), Ogwu akom (I)	SS, SW	25 mg/ml ethanolic leaf extract increased insulin release from the pancreas (Chattopadhyay, 1999) <sup>8</sup> ; 400 mg/kg hydro-ethanolic extract of the leaves decreased blood glucose in alloxan-induced diabetic rats, and produced a synergistic effect with <i>Vernonia amygdalina</i> (Ebong et al., 2008); 500 mg/kg ethanol extract of the leaves decreased blood glucose levels and improved pancreatic lesions in STZ- induced diabetic rats (Akinola et al., 2010)	Anti-parasitic, Anti- pyretic, Anti-microbial, Anti-ulcer, Jaundice, Ringworm, Liver problems, Hemorrhoids, Inflammation, Wound- healing	Leaves, Seed, Bark, Root, Fruit, Gum	Infusion Decoction		Quercetin, Myricetin and Kaempferol glycosides (Chattopadhyay, 1999); Nimbidin, Azadirachtin, Nimbin, Nimbolide, Sodium nimbidinate, Gedunin, Mahmoodin, Gallic acid, Epicatechin, Catechin, Gallocatechin, Epigallocatechin, Cyclic trisulphide and tetrasulphide, Margolone, Margolonone, Isomargolonone, Gla, GIIa, GIIIa, GIb (Biswas et al., 2002)	Various pharmaco-toxic effects were seen with Neem oil with an LD <sub>50</sub> of 14 and 24 ml/kg in rats and rabbits respectively; and more toxic than edible mustard seed oil suggesting a narrow margin of safety when used therapeutically. (Gandhi et al., 1988)
25	<i>Bauhinia monandra</i> Kurz	Leguminosae	Pink orchid, Napoleon's plume	Abafé (Y)	NW, SW	Antioxidant effects (Argolo et al., 2004); 1 g/kg stem bark extract decreased blood glucose levels in alloxan- induced and glucose loaded diabetic rats (Abo and Jimoh, 2004)	Post-natal hemorrhage, Anti-microbial, Laxative, Inflammation, Pesticidal	Leaves, Stem-bark, Pods, Root	Maceration	Rutin and Quercetin identified as the bioactive constituents for the anti- hyperglycaemic effect in alloxan- induced diabetic rats and insulin stimulatory effect in INS-1 cells (Alade et al., 2011, 2012)	Quercetin, Quercetin-3-O- rutinoside (Aderogba et al., 2006); 3,7-Di-O-α- rhamno pyranosyl quercetin (Menezes et al., 2007); BmoRoL and BmoLL lectins (Souza et al., 2011)	
26	<i>Bauhinia thonningii</i> Schum. Syn:	Leguminosae	Camel's foot	Kalgo (H), Abafé (Y)	NC, NW, SE, SW	Antioxidant effects (Taofeek, 2011); 500 mg/kg aqueous extract of the leaves decreased blood glucose as	Anti-parasitic, Anti- microbial, Malaria, Inflammation, Snake bites, Purgative	Leaves, Roots, Stem- bark	Decoction	D-3-O-methyl chiroinositol isolated from the methanol extract of	Epicatechin, (+)-pinitol, Esters of <i>p</i> -hydroxyphenyl ethanol and <i>p</i> -coumaryl alcohol, Kaur-16-en-19-oic	Co-incubation of 0.01% of the extract in Caco-2 cell monolayers decreased the integrity

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	<i>Piliostigma thonningii</i>					well as improved serum lipid profile in alloxan-induced diabetic rats (Ojezele and Abatan, 2011)				the stem bark decreased blood glucose levels in alloxan-induced diabetic rats dose- dependently (Asuzu and Nwaehujor, 2013)	acid, Labd-13-en-8-Ol-19- oic acid (Baratta et al., 1999); Quercetin, Quercitrin, C-methyl quercetin ethers, C-methyl kaempferol ethers, Piliostigmin (Ibewuikwe et al., 1997); Kaurane diterpenes (Martin et al., 1997); Griffonilide, Rhamnetin, Carotenoids (Okwute et al., 1986) Quercetin-3-O-glucoside, Quercetin-3-O-rutinoside, Kaempferol-7-O- rhamonoside, Kaempferol- 3-O-glucoside (Aderogba et al., 2008); Quercetin, Isoquercetin, Lectins, Protocatechuic acid (Anju et al., 2011) Hyperoside, Isoquercitrin, Quercetin, Quercitrin, P-coumaric acid, Ferulic acid, Rutin, Kaempferol (Compaoré et al., 2011); Benzopyrandiol and triol derivatives (Maillard et al., 1991) Polyacetylenic compounds, Pyrocatechin, Vanillin, P-hydroxybenzoic acid, Gallic acid, Salicylic acid, Protocatechuic acid, P-coumaric acid, Ferulic acid, Caffeic acid, Caffeoyl quinic acids, Eugenol, Esculetin, Chlorogenic acid, Sulfuretin, Chalcones, Apigenin and its glycosides, Luteolin and its glycosides, Quercetin and its glycosides, Kaempferol glycoside, Caryophyllene, Humulene, Lupeol, $\beta$ - sitosterol, Campesterol, $\beta$ - amyrin, Friedelin, $\alpha$ - tocopherol, Centaureidin, Centaurein (Lima Silva et al., 2011) Apocarotenoids, Norbixin, Bixin, Geranylgeranyl and its acetate, octadecanoate, and formiate, Farnesyl acetone (Gutierrez et al., 2011); $\beta$ -tocopherol, Vitamin E (Ponnusamy et	of the monolayer and the secretory transport of Cyclosporin A (CSA) indicating possible inhibition of P-gp (Deferme et al., 2003)
27	<i>Bauhinia tomentosa</i> L.	Leguminosae	Yellowbell orchid, Camel foot tree	Jinga (H), Abafe-pupa (Y)	SW	Antioxidant effects (Aderogba et al., 2008); 500 mg/kg ethanol root extract decreased blood glucose in both normal glucose-loaded rats and alloxan induced diabetic rats (Kaur et al., 2011) <sup>§</sup>	Anti-microbial, Diuretic, Vermifuge, Aphrodisiac, Anti-tumours	Roots, Leaves, Flower				
28	<i>Bauhinia rufescens</i> Lam.	Leguminosae		Jirga (F), Matsatsagi (H)	NW, NE	Antioxidant effects (Aliyu et al., 2009; Compaoré et al., 2011); Dose dependent (200– 400 mg/kg) decrease in blood glucose levels by methanol extract of the leaves in alloxan-induced diabetic rats (Aguh et al., 2013)	Anti-infective, Anti- parasitic, Wound healing, Fibrosis, Inflammation	Stem-bark, Root, Fruit	Maceration			
29	<i>Bidens pilosa</i> L.	Compositae	Spanish needle, Needle grass, Black jack	Abere-oloko (Y)	SW	Acetylenic glucosides decreased blood glucose in C57BL/Ks-db/db mice, a type 2 diabetes model (Ubillas et al., 2000) <sup>§</sup>	Anti-cancer, Anti- pyretic, Anti-microbial, Inflammation, Diuretic, Anti-parasitic, Colic, Wound ulcers, Hemorrhoids, Malaria	Seeds, Leaves, Roots, Aerial parts	Decoction, Infusion	Acetylenic glucosides: 3- $\beta$ -D- glucopyranosyl-1- hydroxy-6(E)- tetradecene- 8,10,12-triynone and 2- $\beta$ -D- glucopyranosyl-1- hydroxy-6(E)- tetradecene-7,9,11- triynone (Ubillas et al., 2000)		
30	<i>Bixa orellana</i> L.	Bixaceae	Lipstick tree, Bixa plant, Annatto, Achiote	Osun-buke (Y), Aje (Y), Uhie (I)	NE, SW, SE	80 mg/kg of the seed coat extract decreased blood glucose levels and increased plasma insulin levels and insulin binding to blood corpuscles in normoglycaemic dogs	Anti-microbial, Anti- parasitic, Skin infections, Anti-tumour, Analgesic, Anti-pyretic, Jaundice, Gonorrhea, Purgative, Snake bites	Leaves, Seeds	Decoction	Aldose reductase inhibitory effects of isoscuteallarein isolated from the leaf extract (Terashima et al., 1991)		The carotenoid Bixin, isolated from the seed coat extract has been shown to induce Cyt P450 enzymes in the liver, kidney and lungs (Jewell and O'Brien,

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						(Russell et al., 2005) <sup>§</sup> ; Methanol extract of the leaves (49 µg/ml) produced inhibitory effects against human pancreatic amylase enzyme (Ponnusamy et al., 2011) <sup>§</sup>					al., 2011); Stigmasterol, Polyprenol, Sitosterol, Ishwarane, Phytol (Raga et al., 2011); Capric, Palmitic, Stearic, Oleic and Linoleic acids (Silva et al., 2008); Gallic acid, Pyrogallol, Isoscutellarein (Terashima et al., 1991); β-carotene, Cryptoxanthin, Lutein, Zeaxanthin, Methyl bixin (Tirimanna, 1981)	1999); Bixin as well as other constituents of annatto dye from the seed extract play an important role in the induction of Cyp 1A and 2B enzymes in rats (De- Oliveira et al., 2003); Seed constituents have also been found to possess opposing hyperglycaemic effects (Fernandes et al., 2002; Gutierrez et al., 2011)
31	<i>Blighia sapida</i> K. D.Koenig	Sapindaceae	Akee apple, Breadfruit tree	Okpu ulla (I), Ishin (Y), Gwanja-kusa (H), Ila (Nu)	SW, NC	Aqueous root bark extract (100 and 200 mg/kg) decreased blood glucose in normoglycaemic rats (Saidu et al., 2012)	Wound ulcers, Malaria, Anti-parasitic, Migraine, Laxative, Diuretic, Epilepsy, Liver diseases, Anti-emetic, Snake bites	Root, Bark, Fruits, Leaves		Hypoglycaemic effect of hypoglycin A and B from the fruit was observed in rabbits, monkeys, rats and mice but not cats, dogs and pigeons with lethality at doses > 50 mg and 150 mg/kg for hypoglycin A and B respectively in mice (Chen et al., 1957)	Hypoglycin A, Hypoglycin B (Hassall et al., 1954); Glycyl-L-alanine, γ-L- glutamyl-trans-α-L- (carboxy cyclopropyl) glycine, Glycylglycine, Diglycylglycine (Fowden and Smith, 1969); Blighinone, Stigmasterol and its fructoside, Oleanolic acid, Hederagenin and its glucosides (Garg and Mitra, 1967)	Hypoglycin A and B in the unripe fruit, although responsible for the hypoglycemic effect can lead to death due to severe fatty acid degeneration and glycogenolysis (Hassall et al., 1954; Sherratt, 1986)
32	<i>Bridelia ferruginea</i> Benth.	Phyllanthaceae		Ira or Iralodan (Y), Kirni or Kizni (H), Ola (I)	SW, SE	100 and 200 mg/kg aqueous and methanol extracts of the leaves decreased blood glucose levels in normal rats and alloxan-induced rats when pre-treated; Also daily intake of 15 mg of the extract as an infusion lowered blood glucose levels of type-2 diabetic patients in a clinical study (Iwu, 1983); Radical scavenging effects (Cimanga et al., 2001); Administration of 250 mg/kg ethanol extract of the root for 4 weeks improved glucose tolerance in high-fructose fed Wistar rats (Bakoma et al., 2011)	Inflammation, Oral thrush, Anti-parasitic, Anti-microbial, Hemorrhoids, Anti- tumour	Leaves, Stem bark, Root	Infusion, Decoction	Hypoglycaemic effect of a mixture of quercetin-3- neohesperidoside, Quercitrin, Quercetin-3- glucoside and Myricetin-3- rhamnoside isolated from the hydro-alcoholic extract of the leaves in fasted rabbits (Addae-Mensah and Munenge, 1989)	Myricetin-3-rhamnoside, Quercetin-3-glucoside, Quercitrin, Quercetin-3- neohesperidoside (Addae- Mensah and Achenbach, 1985); Kaempferol, Vitexin, Apigenin (Iwu, 1983); β-peltatin-5-O-β-D- glucopyranoside and its 5-demethoxy derivative (Rashid et al., 2000); 3-O- methyl quercetin, Rutisin, Myricetin, Ferrugin, Tetra- O-methyl myricetin, Gallocatechin-(4-O-7)- epigallocatechin (Cimanga et al., 2001)	Inhibited P-gp mediated Rh-123 efflux in Caco-2 cells (Ezurike et al., 2012); No observed acute or chronic toxicity in rats after 6 months intake or high doses up to 5 g/kg. However aqueous extract of the leaves prolonged pentobarbitone induced sleeping time, which might indicate possible interaction with Cyp enzymes (Owiredo et al., 2011)
33	<i>Bridelia micrantha</i> (Hochst.) Baill.	Phyllanthaceae	Sweet berry, Coastal golden leaf	Iranje, Ogaofia (I), Ugoagu (I)	SW, SE	250 mg/kg of the methanol extract of the leaves decreased blood glucose in alloxan-induced diabetic rats and produced good antioxidant effects (Adika et al., 2011)	Oral gargle, Anti- microbial, Jaundice, Dysentery	Leaves, Stem bark	Decoction		Delphinidin, Gallic acid, Caffeic acid, Ellagic acid, Friedelin, Epifriedelinol Taraxerol, Taraxerone (Pegel and Rogers, 1968); Camphene, α-pinene, 1,8- cineole, Camphor, Linalool, 1-α-terpineol, α- caryophyllene oxide, 5-β- pregnene, Quinoline (Green et al., 2011)	

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34	<i>Bryophyllum pinnatum</i> (Lam.) Oken	Crassulaceae	Africa never die, Life plant, Resurrection plant	Ewe abamoda (Y)	SW	400 mg/kg of the aqueous extract of the fresh leaves produced hypoglycaemia in both normal and STZ- induced diabetic rats (Ojewole, 2005); Hypoglycemic effect of 500 mg/kg aqueous extract of the leaves in normal fasted glucose-loaded and STZ- induced diabetic rats (Ogbonnia et al., 2008c); <i>In vitro</i> antioxidant effects (Gupta and Banerjee, 2011) <sup>§</sup>	Hypertension, Analgesic, Inflammation, Wound ulcers, Anti-parasitic, Insect bites, Anti-cancer, Cough, Diarrhoea, Sedative, Diuretic, Anti- microbial, Convulsions	Leaves, Flower	Juice extract		Syringic acid, Caffeic acid, 4-hydroxy-3-methoxy cinnamic acid, 4-hydroxy benzoic acid, Hydroxy cinnamic acid, P-coumaric acid, Protocatechuic acid, Phosphoenolpyruvate, Ferulic acid, Astragalin, Friedelin, Luteolin, Quercetin glycosides, Epigallocatechin-3-O- syringate, Kaempferol glycosides, Isorhamnetin glycosides, Myricetin glycosides, $\alpha$ - and $\beta$ - amyrin and their acetates, Glutininol, Bryophollone, Bryophynol, Bryophyllol, Bryophyllin A and B, Bryotoxin A, B and C; Bryophollenone, Patuletin and glycosides Taraxasterol, Stigmasterol, $\beta$ -sitosterol, Stigmasta- dienol (Afzal et al., 2012)	Risk of cardiac glycoside poisoning due to the bufadienolides Bryotoxin A, B, C (McKenzie et al., 1987); Significant decrease in serum ALT levels in rats after daily oral dosing of 2 g/kg aqueous extract of the leaves (Ozolua et al., 2010)
35	<i>Calotropis procera</i> (Aiton) Dryand.	Apocynaceae	Sodom apple, Giant milkweed, Swallow wort, Mudar	Bomu-bomu (Y), Tumfafiya (H)	SW, NW	400 mg/kg dried latex decreased blood glucose in alloxan-induced diabetic rats, increased hepatic glycogen content and produced antioxidant effects (Roy et al., 2005) <sup>§</sup> ; 250 mg/kg of different solvent extracts of the root decreased blood glucose levels in STZ-induced diabetic rats (Bhaskar and Ajay, 2009) <sup>§</sup> ; Antioxidant effects (Olaleye and Rocha, 2007)	Inflammation, Hypertension, Anti- microbial, Anti- parasitic, Purgative, Convulsions, Abortifacient, Anti- cancer, Skin infections, Hemorrhoids, Anti- pyretic, Asthma, Leprosy	Leaves, Latex, Root, Stem bark, Flower	Maceration, Poultice		Calotroposide, Calotropin, Calotoxin, Calotoxoside, Calactin, Calotropain, Calotropia H genin, Proceroside, Uscharin, Uscharidin, Voruscharin, Amyrin (Oliver-Bever, 1986); Calotropterpenyl, Calotropursenyl acetate, Calotropfriedelenyl acetate, 2-propenyl-2'- hydroxy ethyl carbonate, Calotropin FI, FII, DI and DII, Uzarigenin, Ascleposide, Coroglaucigenin, Procerain (Juncker et al., 2009); Flavone-4'-O- $\beta$ -glycoside, Epoxy dihydroxy methoxy cardenolide, $\beta$ - anhydroepidigitoxigenin and its glycoside (Shaker et al., 2010); Calotropoceryl acetate A and B, Calotropoceron, Calotropoceryl A, Pseudo- taraxasterol acetate, Taraxasterol, Stigmasterol, (E)-octadec-7-enoic acid (Ibrahim et al., 2012); CP-P (Apolipoprotein A-1) (Samy et al., 2012)	Cardenolides present in the plant are capable of causing death in mammals at high concentration thus caution should be exerted when extracts of the plant are being ingested (Juncker et al., 2009)

Table 1 (continued)

S/ no.	Plant name	Family	Common name	Local Nigerian name(s) <sup>a</sup>	Region of use for diabetes <sup>#</sup>	Experimental evidence for its use in diabetes management	Other medicinal uses	Plant part (s) used	Traditional preparation method	Identified active constituent(s)	Other relevant phytoconstituents identified in the plant	Interaction/toxicity studies
36	<i>Capsicum annum</i> L., Syn: <i>Capsicum</i> <i>frutescens</i> L.	Solanaceae	Chilli, Bird pepper	Ata or Ata wewe (Y), Ose (I), Barkono (H), Asin (Es)	SW, SE	Alpha glucosidase and $\alpha$ - amylase inhibitory activities and antioxidant effects (Oboh et al., 2011; Kwon et al., 2007); Incorporation of 2% of the fruit powder in a high fat diet given to STZ-induced diabetic rats increased serum insulin levels (Islam and Choi, 2008) <sup>§</sup> ; 100 mg/l fruit extracts possessed PPAR alpha and gamma agonistic activity (Rau et al., 2006) <sup>§</sup>	Analgesic, Antimicrobial, Inflammation, Hemorrhoids, Fevers, Dysentery, Malaria, Carminative, Stimulant	Fruit	Decoction		Capsaicinoids (Schweiggert et al., 2006); Myricetin, Kaempferol, Apigenin, Luteolin, Quercetin (Miean and Mohamed, 2001); CAY-1 (Stergiopoulou et al., 2008); Alpha tocopherol (Ching and Mohamed, 2001); Ortho hydroxyl N-benzyl 16-Methyl 11,14- diene octadecamide, 9, 12- diene-octadecanoic acid (Dastagir et al., 2012); Capsianocide VIII, IX, L, III, V, I and its methyl ester, Oxylipin, Capsidiol, Phosphatidylcholine, Loliolide, Blumenol C glucoside, 3-O-(9,12,15- octadecatrienoyl) glyceryl- $\beta$ -D-galactopyranoside (De Marino et al., 2006)	
37	<i>Carica papaya</i> L.	Caricaceae	Pawpaw	Ibepe (Y), Okworo bekee or Okwere (I), Gwanda (H)	NW, SS, SW	100–400 mg/kg of the aqueous seed extract decreased blood glucose and improved serum lipid levels in normal rats (Adeneye and Olagunju, 2009); 400 mg/kg aqueous extract of the leaves decreased blood glucose in alloxan-induced diabetic rats (Maniyar and Bhixavatimath, 2012) <sup>§</sup> ; Administration of 602 g of the fruit (equivalent to 50 g carbohydrate) to type 2 diabetic patients produced an increase in serum insulin levels in the patients (Fatema et al., 2003) <sup>§</sup> ; Antioxidant effects of different parts of the unripe fruit (Oboh et al., 2013)	Anti-microbial, Anti- parasitic, Dyspepsia, Hemorrhoids, Hypertension, STDs, Purgative, Wound healing, Antivenin, Sickle cell anemia, Abortifacient, Anti- fertility, Cancer, Mental disorder, Malaria, Convulsion	Leaves, Fruit pulp, Seed, Latex	Infusion Decoction, Vegetable, Juice extract		Caffeoyl and Protocatechuic acid hexoside, Gallic acid deoxyhexoside, Caffeoyl hexose-deoxyhexose, Ferulic and Caffeic acids, Myricetin, Isoharmnetin, Quercetin, Kaempferol, Rutin, Lycophene, $\beta$ - cryptoxanthin, $\beta$ -carotene, (Rivera-Pastrana et al., 2010); Chlorogenic and P-coumaric acids, 5,7- dimethoxy coumarin (Canini et al., 2007); Papain, Chymopapain A, B and C, Peptidase A and B, Lysozyme, Carpasamine, Dehydrocarpaine I and II, Carpaine, Aryl glucosides, Carposide, Caricin, Choline, Tropaeoline (Krishna et al., 2008)	Aqueous extract of the leaves in alloxan- induced diabetic rats delayed the hypoglycaemic activity of glimepiride but hastened that of metformin (Fakeye et al., 2007); Contraindicated in patients taking warfarin as it increased the INR of a patient (Shaw et al., 1997); Aqueous extract of the leaves inhibited P-gp efflux activity in Caco-2 cells (Oga et al., 2012)
38	<i>Cassia fistula</i> L.	Leguminosae	Indian laburnum, Golden shower	Aidantoro (Y)	SW	<i>In vitro</i> antioxidant effects (Luximon-Ramma et al., 2002; Manonmani et al., 2005); Hexane extract of the stem bark produced a dose dependent decrease in alloxan-induced diabetic rats (Nirmala et al., 2008); Ethanol and ethyl acetate extract of the bark decreased blood glucose levels in alloxan-induced diabetic rats	Liver disorders, Anti- microbial, Purgative, Astringent, Hemorrhoids, Rheumatism, Ulcers, Jaundice	Seeds, Leaves, Pods, Stem-bark		Catechin isolated from the stem bark decreased plasma glucose levels and increased the activity of glucose metabolizing enzymes in STZ- induced diabetic raats (Daisy et al., 2010)	Fistucacidin, Kaempferol, Rhein, Leucoperlagonidin derivatives, Sennoside A and B, Epiafzelechin and its 3-O- $\beta$ -D- glucopyranoside, Epicatechin, Catechin, Procyanidin B2, Rhamnetin -3-O- gentibioside, Physcion, Chrysophanol, Fistulin, Fistulic acid, 3-formyl-1-	



Table 1 (continued)

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						(Malpani and Manjunath, 2012)					hydroxy-8-methoxy anthraquinone, 3 $\beta$ -hydroxy 17-norpimar -8 (9)-en-15-one (Bahorun et al., 2005); 1,8-dihydroxy-6-methoxy-3-methyl anthraquinone, Tetrahydroxy dimethoxy flavone-3-O- $\alpha$ -arabino pyranoside, Trihydroxy trimethoxy flavone-3-O- $\alpha$ -L-rhamnosyl (1 $\rightarrow$ 2)-O- $\beta$ -D-glucopyranoside, $\beta$ -Sitosterol, Hexacosanol, Lupeol (Kanth et al., 2012); Aurantiamide acetate, Betulinic acid, Xanthone glycoside, Cyclopropenoid fatty acids, Biochanin A, Phytol, Lectins CSL-1, 2 and 3, Furfural derivatives, Fatty acids, Citreosein, Scopoletin, Chromones and Benzyl derivatives (Danish et al., 2011)	
39	<i>Cassia sieberiana</i> DC.	Leguminosae	African laburnum, Drumstick tree	Ukosei (Es), Margaa (H), Margaje (F), Aridan-tooro (Y)	NC, NW, NE, SS,	<i>In vitro</i> antioxidant effects (Awah et al., 2012)	Veterinary, Antimicrobial, Anti-parasitic, Impotence, Convulsion, Inflammation, Analgesic, Malaria, Dys-menorrhea	Root, Leaves, Stem-bark	Decoction		Epiafzelechin (Kpegba et al., 2011); Myricetin and Quercetin 3-O-rhamnoside (Asase et al., 2008); Leucopelargonol, Epicatechol, $\beta$ -sitosterol, Stigmasterol (Tamboura et al., 2005)	Traditional use of the plant is associated with GIT side effects (Maiga et al., 2005); Liver and kidney toxicities of aqueous extracts of various parts of the plant (Toma et al., 2009; Obidah et al., 2009)
40	<i>Cassythia filiformis</i> L., Syn: <i>Cassythia americana</i>	Lauraceae	Love vine, Woevine	Rumfar-gada (H), Sulunwahi (F), Otetebilete (Id)	SE, NC	Administration of 600 mg/kg methanol extract of the stem bark to alloxan-induced diabetic mice decreased blood glucose levels by 46.8% (Ezeigbo and Asuzu, 2010) <i>In vitro</i> antioxidant effects (Mythili et al., 2011) <sup>§</sup>	Anti-parasitic, Uterotonic, Hypertension, Diuretic, Aphrodisiac, Hemorrhoids, Anti-cancer, Anticoagulant, Hemorrhage	Whole plant	Decoction, Dried parts are chewed before meals		Cassythidine, Cassyfiline (Cassythine) and O-methyl cassyfiline, Cassamedine, Neolitsine, Cassameridine, Actinodaphnine and N-methyl actinodaphnine, Cassythicine, Cassythidine, Dicentrine, Bulbocapnine, Nornuciferine, Launobine (Cava et al., 1968); Cathafile, Cathaformine, Lysicamine, Cassyformine, Predicentrine, Filiformine, Isoboldine, Thaliminine, Stepfarine, Pronuciferine, Ocoteine, Syringaresinol, Diasyringaresinol, Yangambin, O-methyl flavinatine, Isovanillin, Vanillin, $\beta$ -sitosterol and Stigmasterol and their D-glucosides (Chang et al., 1998); Isorhamnetin,	250 mg/kg aqueous extract of the whole plant increased cholesterol levels in mice and decreased plasma ALP levels (Babayi et al., 2007) Non-selective cytotoxicity to both cancer and non-cancer cell lines (Stévigny et al., 2002)

Table 1 (continued)

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41	<i>Catharanthus roseus</i> (L.) G.Don	Apocynaceae	Madagascar periwinkle			250 mg/kg methanol extract of the leaves decreased blood glucose levels in alloxan-induced diabetic rats and increased the hypoglycaemic effect of metformin but not glibenclamide (Ohadoma and Michael 2011); Juice extract of the fresh leaves of the plant gave a dose dependent (0.5–1 ml/kg) decrease in blood glucose levels in normal and alloxan-induced diabetic rats (Nammi et al., 2003) <sup>§</sup> ; 500 mg/kg dichloro-methane methanol (1:1) extract of the aerial parts showed a prophylactic action against STZ-induced hyperglycaemia in rats and increased the activity of some glucose metabolizing enzymes (Singh et al., 2001) <sup>§</sup>	Cancer, Malaria, Insect stings, Sore throat, Antibiotic, Diuretic, Expectorant, Wound healing, Hemorrhage, Hypertension	Whole plant, Leaves, Flower, Roots	Decoction		Quercetin and Kaempferol glycosides; Isorhamnetin, Cassythic acid, O-methyl cassythine, Isofiliformine, Phenylalcohol glycoside, Salutaridine, Nicotinic acid (Tsai et al., 2008) Hexamethyl-15-hydroxy methylene- <i>n</i> -octacosatriene-10,18-diol-10- $\beta$ -D-glucopyranoside, 3-Epibetulinic acid, <i>n</i> -pentadecanoyl octa-dec-19-enoate, $\beta$ -Sitosterol (Chung et al., 2007); 3- <i>O</i> -glucosides and 3- <i>O</i> -(6- <i>O</i> - <i>p</i> -coumaroyl) glucosides of Hirsutin, Malvidin and Petunidin (Piovan and Filippini, 2007); Benzoic acid derivatives, Vanillic, Gallic, Cinnamic, <i>o</i> - and <i>p</i> -Coumaric, Caffeic and Ferulic acids; Hydroxy tyrosol, kaempferol, Quercetin, Syringetin glycosides (Mustafa and Verpoorte, 2007); Ursolic and Oleanolic acids (Usia et al., 2005); Ajmalicine, Serpentine, Lochnerine, Tetrahydroalstonine, Reserpine, Akuammine, Vinblastine, Vindoline, Perivine, Leurosine, Leurosidine, Virosine, Catharanthine, Vindoline, Lochnericine, Pleurosine, Vincarodine, Catharine, Leurocristine (Vincristine), Sitsirikine, Carosine (Svoboda et al., 1962) Eleagnine, Anacardic acid, Ascorbic acid (Idowu et al., 2006); Myricetin-3-rhamnoside (Adebayo et al., 2011)	Potent inhibitory effects on Cyp 2D6 of human liver microsomes of ajmalicine and serpentine isolated from the aerial parts (Usia et al., 2005); The vinca alkaloids are metabolized by Cyp3A4 and 3A5 enzymes; while vincristine and vinblastine have been identified as P-gp substrates in canine renal cells (Levêque and Jehl, 2007)
42	<i>Chrysophyllum albidum</i> G.Don	Sapotaceae	African star apple, Cherry	Agbalumo (Y), Udala (I)	SE, SW	100 and 200 mg/kg hydro-ethanol extract of the seed cotyledon given to alloxan-induced diabetic mice for 7 days decreased serum glucose levels (Olorunnisola et al., 2008) <i>In vitro</i> antioxidant effects (Guimarães et al., 2010) <sup>§</sup>	Cancer, Miscarriage, Hemorrhoids, Asthma, Analgesic, Inflammation, Anti-microbial, Anti-parasitic	Seeds, Stem-bark, Leaves, Fruit, Root	Decoction			
43	<i>Citrus aurantiifolia</i> (Christm.) Swingle	Rutaceae	Lime	Osan wewe (Y), Oromankilishi (I), Igbo-pinigue (Es),	SW	<i>In vitro</i> antioxidant effects (Guimarães et al., 2010) <sup>§</sup>	Worm expeller, Weight loss, Anti-microbial, Anti-cancer, Anti-parasitic, Colds, Arthritis	Fruit	Juice extract		$\alpha$ - and $\beta$ -pinene, P-cymene, Limonene and its oxide, Linalool and its oxide, Citral, $\alpha$ - and $\beta$ -terpineol, Myrtenol (Asnaashari et al., 2010); Isoswertisin, 6- <i>O</i> - $\alpha$ -	Bergamottin and other furanocoumarins found in citrus fruits have been identified as inducers and inhibitors of Cyt P450 enzymes (Baumgart et al., 2005)

Table 1 (continued)

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44	<i>Citrus aurantium</i> L.	Rutaceae	Sour orange, Seville orange	Osan ganganin or, Ijaganyin (Y), Oloma oyibo (I), Babban lemu (H), Ntom (Ibibio)	SS	875 mg of a mix of extracts of the fruit and <i>Rauvolfia</i> <i>vomitaria</i> foliage (RC tea) decreased serum glucose levels in diabetes type 2 model db/db mice and also decreased tissue lipid accumulation (Campbell et al., 2006); RC tea given daily for 4 months to type-2 diabetic patients decreased fasting and post prandial plasma glucose levels especially in patients with HbA1c levels < 7.3% (Campbell-Tofte et al., 2011)	Weight loss, GIT problems, Malaria, Fibroids, Cancer, Cough	Fruit, Leaves, Root, Stem- bark, Stem- twigs	Juice extract, Decoction		arabinopyranosides of vitexin and isovitexin (Veitch and Grayer, 2011); Bergamottin, Limettin, Bergapten, 5-geranyloxy- 7-methoxycoumarin, Isopimpinellin, 3-methyl- 1,2-cyclopentadione, 1-methoxy-cyclohexene, Corylone, Umbelliferone, 5,8-dimethoxysoralen, Hexenone, Caryophyllene oxide, Palmitic, Linoleic, Oleic acids, Bergamotene (Sandoval-Montemayor et al., 2012); Imperatorin, Kaempferol, Myricetin, $\beta$ - sitosterol, Rutin, 4,5,7- trihydroxy-3,6-dimethoxy flavones (Shalaby et al., 2011)	Bergapten and 6,7- dihydroxybergamottin inhibit Cyt P450 enzymes (Malhotra et al., 2001); Risk of cardio-toxicity due to synephrine (Calapai et al., 1999)
45	<i>Citrus sinensis</i> (L.) Osbeck	Rutaceae	Orange	Osan mimu (Y), Oroma (I), Lemun misra (F), Alimo (Es)	SW <sup>a</sup>	Antioxidant effects (Guimarães et al., 2010) <sup>§</sup> ; Free and bound phenolics extracted from the dried fruit peel exhibited potent dose- dependent $\alpha$ -amylase and $\alpha$ - glucosidase inhibitory effects (Obob and Ademosun, 2011)		Fruit, Seed	Juice extract Infusion		Psoralene, Xanthotoxin, Bergapten, Imperatorin, Mamesin, Umbelliferone, Quercetin and its glycoside, 4,5,7- trihydroxy-3,6-dimethoxy flavone, Rutin, Hyperin, Hesperidin, $\beta$ -sitosterol, Stigmasterol (Shalaby et al., 2011)	Bergapten has been shown to induce Cyp 3A4 (Malhotra et al., 2001)
46	<i>Citrullus</i> <i>colocynthis</i> (L.) Schrud.	Cucurbitaceae	Egusi melon, Desert gourd, Bitter apple, Bitter cucumber	Baala, Egusi	NW, SW	Saponin fractions of aqueous extract of the rind decreased plasma glucose at doses $\leq 50$ mg/kg in fasted normoglycaemic and	Constipation, Purgative, Anti-tumour, Abortifacient, Oedema, Infections, Rheumatism	Leaves Fruit, Rind, Seed, Pulp	Infusion, Decoction		Cucurbitacin E, I, J, K and L 2-O- $\beta$ -D-glucopyranosides, 3,4'-dihydroxy-3'- methoxy propiophenone, 3,4'-	Extracts of the plant have been shown to cause severe diarrhoea in animals with mortality at doses

Table 1 (continued)

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						alloxan-induced diabetic rabbits (Abdel-Hassan et al., 2000) <sup>§</sup> ; Plasma glucose levels and pancreatic $\beta$ -cell mass were restored to normal in STZ-induced diabetic rats fed an 8% colocynth oil diet (Sebbagh et al., 2009) <sup>§</sup> ; Antioxidant effects (Kumar et al., 2008)					dihydroxypropiofenone, Colocynthisides A and B, Khekadengoside E, Hexano cucurbitacin I 2-O- $\beta$ -D-glucopyranoside, Helicid, Isoviteixin, Isosaponarin, Isoorientin-3'-O-methyl ether, Benzyl and 4-hydroxybenzyl $\beta$ -D-glucopyranoside, 4-( $\beta$ -D-glucopyranosyloxy) benzyl alcohol (Yoshikawa et al., 2007); Isoorientin, 8-O and 6-O- <i>p</i> -hydroxybenzoyl isovitexin and its glucoside (Maatooq et al., 1997); Oleic, Linoleic, Linolenic, Arachidonic, Palmitate, Stearic and Myristic acids (Sebbagh et al., 2009); 2-(nonan-8-one)-(1H)-4-quinolone, 2-(nonan-8-one) 4-methoxy-quinoline, (2S)-3,4-methylenedioxy-5,7-dimethoxyflavan, Hispidulin 7-(6-E- $\beta$ -coumaroyl- $\beta$ -D-glucopyranoside (Salama, 2012)	$\geq 200$ mg/kg (Shafaei et al., 2012; Khoshvaghti and Hamidi, 2012); Possible inhibition of Cyp P450 enzymes when ethanolic extracts of the fruit were co-incubated with rat liver microsomes (Barth et al., 2002)
47	<i>Citrullus lanatus</i> (Thunb.) Mats. and Nakai	Cucurbitaceae	Water melon, Kalahari melon	Egusi bara (Y), Guna (H)		50 mg/kg globulin proteins extracted from the seeds decreased blood glucose levels when pre-administered to normal high glucose fed rats (Teugwa et al., 2013a) <sup>§</sup> ; Antioxidant effects (Tili et al., 2011)	Laxative, Wound ulcers, Anti-bacterial, Tumours	Leaves, Seeds, Fruit pulp	Decoction		Cucurbitacin E (Abdelwahab et al., 2011); Lycophene, Phytofluene, Neurosporene, $\zeta$ - and $\beta$ -carotene, Lutein, Phytoene (Perkins-Veazie et al., 2006); Protocatechuic acid glucosides, Phloroglucinol glucuronide, Ferulic acid hexosides, Isorhamnetin, Citrulline, Salicylic acid-O-hexoside, <i>p</i> -coumaric acid glucoside, Vanillin hexosides, Rutin, Salicin-2-benzoate, Sinapic acid glucoside, Feruloyl sugars, Caffeoylshikimic acids, Caffeoylhexose, Luteolin, Calodendroside; Naringenin, Chrysoeriol Apigenin, Kaempferol, Taxifolin, Saligenin and Isolariciresinol glucosides; Hydroquinone, Isoviteixin, Aviprins, Shikonine, Icariside, Leachianol G, Glehlinoside C, Ajugol,	

Table 1 (continued)

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48	<i>Cola acuminata</i> (P.Beauv.) Schott and Endl.	Malvaceae	Kolanut	Obi agada (Y), Orji (I)	SW	Antioxidant effects (Atawodi et al., 2007) 500 mg/kg of the methanol extract of the stem bark decreased blood glucose levels in alloxan induced diabetic rats after 21 days (Adediwura et al., 2011)	Stimulant, Appetite suppressants, Aphrodisiac, Respiratory infections, Hypertension, Anti- parasitic	Nuts, Stem- bark, Leaves	Decoction, Juice extract		Dihydrophilonotisflavone, Catalposide, Obtusoside, Picrosides, Quercitrin, Coumarin, Cimifugin, (Abu-Reidah et al., 2013) Procyanidin B1 and B2, Catechin, Epicatechin, Caffeine (Atawodi et al., 2007); Theobromine (Niemenak et al., 2008); Chlorogenic, Quinnic and Tannic acids (Odebode, 1996)	
49	<i>Corchorus olitorius</i> L.	Malvaceae	Long fruited jute, Jew's mallow	Ewedu (Y), Ulogburi (I)	SW	Methanol extract of the leaves inhibited both $\alpha$ - amylase and $\alpha$ -glucosidase enzymes (Oboh et al., 2012a) Antioxidant effects (Azuma et al., 1999)	Purgative, Diuretic, Tumours, Analgesic, Cystitis, Measles	Leaves, Seeds	Decoction		3,5-Dicaffeoylquinic acid, Quercetin-3-galactoside, Quercetin-3-glucoside, Quercetin-3-(6-malonyl glucoside), Quercetin-3- (6-malonyl galactoside), Ascorbic acid, $\alpha$ - tocopherol (Azuma et al., 1999); Kaempferol glycosides, Rutin, Isoquercitrin (Sakakibara et al., 2003); Dicaffeoyl quinic acids, Caffeoyl and Dicaffeoyl quinic derivatives, Hyperoside, Chlorogenic acid, Isoquercitrin, Quercetin derivative (Ola et al., 2009); Corchorusides A and B, Capsugenin-25,30- O- $\beta$ -diglucopyranoside (Phuwapraisirisan et al., 2009); Caffeic acid and Isorhamnetin (Oboh et al., 2012a)	Ethanol extract of the aerial parts of the plant inhibited Cyt P450 3A4 and 3A7 (Agbonon et al., 2010)
50	<i>Croton lobatus</i> L.	Euphorbiaceae	Lobed croton, Cascarilla	Eru Alamo (Y)	SW		Wound ulcers, Purgative, Malaria, Dysentery	Fruit, Stems, Leaves, Seed			4,5-O-dicaffeoylquinic, acid Tiliroside, Isovitexin, Vitexin, Chlorogenic acid (Lagnika et al., 2009); Geranylgeraniol, Betulinic acid, Cholestan-3-one, 9,12,15-octadecatrienoic acid methyl ester, 3-(4- methoxy phenyl)-2- phenyl acrylic acid, Tetramethyl tetraentetracosanoic acid, Octadecadienoic acid, Tetramethyl-hexadeca tetraenyl ester, Lobaceride, Cholestan-5,7-dien-3-ol, Ergosterol, 3-hydroxy- choles-5-en-7-one, N-(2- hydroxy-1-phenyl-propyl)	



Table 1 (continued)

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51	<i>Cucumeropsis mannii</i> Naudin	Cucurbitaceae	White melon, African melon	Egusi-itoo (Y), Ogiri (I)	SW	50 mg/kg of globulin proteins extracted from the seed when pre-administered to high glucose fed rats did not cause a significant decrease in blood glucose levels (Teugwa et al., 2013a) <sup>§</sup> ; Antioxidant effects (Agbor et al., 2005)	Anti-microbial, Indigestion, Infant colic	Seed, Fruit	Juice extract, Powdered seeds		benzamide (Chabert et al., 2006) Linoleic acid, Oleic acid, Linolenic acid, Myristic acid, Palmitoleic acid, Palmitic acid, Aracchidic acid, Stearic acid (Kapseu et al., 1993)	
52	<i>Curculigo pilosa</i> (Schumach. and Thonn.) Engl.	Hypoxidaceae	Golden eye grass, Donkey's ear	Epakun	SW	Antioxidant effects (Sofidiya et al., 2011)	Anti-microbial, Epilepsy, Infertility, Sick cell, Purgative, STDs	Rhizome, Fruit	Decoction		Piloside A and B, Curculigoside, Curculigine, Nyasicoside, Pilosidine (Palazzino et al., 2000); B-amylase (Dicko et al., 1999); Nyasicoside, Pilosidine, Curculigine (Cometa et al., 2001)	
53	<i>Curcuma longa</i> L.	Zingiberaceae	Turmeric	Atale pupa	SW, NC	Ethanol extract of the rhizome incorporated in the diet of type 2 diabetic KK-A <sup>y</sup> / Ta mice as 0.2–1 g/100 g produced a hypoglycaemic effect compared to control and showed PPAR <sub>γ</sub> binding activity (Kuroda et al., 2005) <sup>§</sup> ; Antioxidant effects (Selvam et al., 1995) <sup>§</sup> ; Plasma insulin levels of healthy subjects were significantly increased 2 h after ingestion of 6g turmeric powder (Wickenberg et al., 2010) <sup>§</sup>	Peptic ulcer, Inflammation, Anti- microbial, Cancer, Malaria, Pesticide, Hypertension, Jaundice, Depression	Rhizome, Leaves, Flower, Roots	Decoction		Curcumin, Bisdemethoxy curcumin, Demethoxy curcumin and Ar- turmerone (Kuroda et al., 2005; Roth et al., 1998); Tetrahydrocurcumin (Pari and Murugan, 2007); α and β-Pinene, Myrcene, α, β and sesqui-Phelandrene, p-Cymene, 1,8-Cineole, α and γ-Terpinene, Ocimene, p-Methylacetophenone, α- Terpinoline, Terpineol, Thymol, Linalool, ar- and γ-Curcumene, Carvacrol, α-Zingiberene, ar-Tumerone, Dehydrocurcumene, Bisabolone (Leela et al., 2002); Vanillin, Vanillic acid, Ferulic acid and Ferulic aldehyde (Appiah- Opong et al., 2007)	Methanol extracts of the rhizome inhibits CYP 3A4 activity in Caco-2 cells (Hou et al., 2007); Curcumin and its decomposition products inhibited CYP 1A2, 3A4, 2D6, 2C9 and 2B6 enzymes in <i>Escherichia coli</i> transfected with human plasmid cDNA (Appiah- Opong et al., 2007); Methanol extract of the rhizome enhances P-gp efflux activity but curcumin inhibits it (Hou et al., 2008)
54	<i>Cymbopogon citratatus</i> (DC.) Stapf	Poaceae	Lemon grass	Koriko-oba (Y), Nche awula (I), Ihumibo (Es)	SW, SE	Aqueous extract of the leaves produced a dose dependent (125–500 mg/kg) decrease in fasting plasma glucose levels after oral administration to normal rats for 42days (Adeneye and Agbaje, 2007); Antioxidant effects (Cheel et al., 2005)	Oral thrush, Inflammation, Athlete's foot, Fever, Cough, Malaria, Jaundice, Cancer, Infections, Diuretic, Hypertension, Obesity, Sedative, Insecticidal, Aroma- therapy	Leaves	Decoction, Infusion, Juice extract	Geraniol, myrcene and citral were identified as aldose reductase inhibitors based on an in-silico approach (Vyshali et al., 2011)	Isoorientin, Isoscoparin, Swertiajaponin, Isoorientin 2'-O- rhamnoside, Orientin, Chlorogenic acid, Caffeic acid (Cheel et al., 2005); p-Coumaric acid, Myrcene, Limonene, α-Ocimene, α- Pinene, α-Caryophyllene, Phellandrene, Methyl heptenone, Cimbopogonol, Oxobisabolene, Geraniol, Citral, Anisaldehyde, Cinammonaldehyde, Citronelal, Valeric, Salicylaldehyde, Luteolin	Aqueous extract did not inhibit P-gp efflux activity in Caco-2 cells (Oga et al., 2012)

Table 1 (continued)

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55	<i>Daniellia oliveri</i> (Rolfe) Hutch. and Dalziel	Leguminosae	African balsam	Iya (Y), Maje (H), Ozabwa (I)	SE, NE	100, 200 and 400 mg/kg aqueous leaf extract decreased blood glucose levels in normal and alloxan- induced diabetic mice (Manosroi et al., 2011); 250 mg/kg aqueous extract of a mixture of the root with that of <i>Sacrocephalus latifolius</i> for 21days decreased blood glucose levels and increased the activity of various glucose metabolizing enzymes in alloxan-induced diabetic rats (Iwueke et al., 2010); Antioxidant effects (Muanda et al., 2011)	Analgesic, Inflammation, Anti- infective, Aphrodisiac, Hemorrhoids, Spasms, Fever, Diarrhea, Wound ulcers, Tumours, Sickle cell	Root, Leaves, Stem bark	Maceration		and its 6-C and 7-O- glycosides, Quercetin, Kaempferol, Apigenin, Hydroquinone, Catechol, Citronelol, 1,8-Cineole, Myrcene, Tria and Dotriacontanol, Octa and Hexacosanol, Menthol, Elemicin, Linalool, Fuco- and sitosterol (Negrelle and Gomes, 2007)	
56	<i>Detarium microcarpum</i> Guill. and Perr.	Leguminosae		Taura (H), Ogbogbo (Y), Ofo (I)	NE, SE, NC	200 and 400 mg/kg aqueous bark extract decreased blood glucose levels in normal and alloxan-induced diabetic mice after 3hrs (Manosroi et al., 2011); 100 mg/kg of the gum administered alone or incorporated in a tablet containing 400 mg/kg metformin showed good blood glucose reducing effects in STZ-induced diabetic rats (Adikwu et al., 2004)	Anti-microbial, Anti- parasitic, Molluscicidal, Hemorrhoids, Malaria, Impotence, Sickle cell, Diarrhea	Bark, Seeds, Fruit, Gum, Roots	Decoction, Seed powder		3,4-Epoxyclerodan-13E- en-15-oic acid, 5 $\alpha$ ,8 $\alpha$ (2- oxokovalenic acid), 3,4- dihydroxycycloclerodan-13E- en-15-oic acid, 3,4- dihydroxy clerodan-13Z- en-15-oic acid, 2-oxokolavenic acid, Copalic acid (Cavin et al., 2006); Sitosterol, Lupeol, Stigmasterol, Campesterol, $\gamma$ -quinide, Bornesitol, Pinitol, Myoinisitol (Akah et al., 2012); Myristoleic, Myristic and Linolenic acids (Igwenyi and Akubugwo, 2010); 1-naphthalene acetic-5- carboxy 6octahydro trimethyl acid, 1-naphthalene acetic-7- oxo-octahydro tetramethyl acid (Aquino et al., 1992)	Incorporation of 100 mg/kg of the gum extract into metformin tablets enhanced drug release from the formulation (Adikwu et al., 2004)
57	<i>Ficus exasperata</i> Vahl	Moraceae	Fig tree, Forest sandpaper	Eepin or Opoto (Y), Ogbu (I)	SW <sup>a</sup>	100 mg/kg aqueous extract of the leaves given for 30 days decreased blood glucose levels in obese zucker rats	Analgesic, Arthritis, Hemorrhoids, Hypertension, Arrhythmias,	Leaves, Root, Fruits, Latex	Decoction		Glycerol-1,3-dilinolein, 3- O-glycerol acetate, Pheophorbides-a, -b and their derivatives,	High doses of the ethanol leaf extract can lead to toxic injury in

Table 1 (continued)

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58	<i>Ficus thonningii</i> Blume	Moraceae	Loin cloth or Wild fig, Chinese banyan	Cediya (H)	SW	and spontaneously hypertensive STZ-treated rats (Adewole et al., 2011); and reversed nephrotoxic effects of STZ (Adewole et al., 2012); 250 mg/kg aqueous extract of the leaves in fructose-fed rats improved glycaemic control (Taiwo et al., 2010); $\alpha$ - glucosidase & $\alpha$ -amylase inhibitory effects (Kazeem et al., 2013) Antioxidant effects (Abotsi et al., 2010) 0.5 mg/ml of the acetone extract of the leaves produced about 30% inhibitory effects against $\alpha$ - amylase and $\alpha$ -glucosidase enzymes (Olaokun et al., 2013); Dose dependent blood glucose lowering effects of the ethanol stembark extract in STZ-induced and normal diabetic rats (Musabayane et al., 2007) <sup>§</sup>	Abortifacient, Child birth, Insomnia, Infections, Eczema, Cancer, Fevers, Diarrhea, Ulcer, STDs  Malaria, Pain, Diarrhoea, Purgative, Anti- microbial	Leaves, Stem-bark	Decoction		Pyropheophorbide, N-methyl pyrimidine (Bafor et al., 2013); $\alpha$ - Terpineol, $\alpha$ and $\beta$ -Pinene, Sabinene, $\beta$ -Patchoulene, 1,8-cineole, $\alpha$ -thujopsene, $\beta$ -ocimene, Limonene, Linalool, $\beta$ -caryophyllene, Isocaryophyllene, $\beta$ - bisabolene, $\alpha$ -copaene, Globulol (Oladosu et al., 2009)  Benzaldehyde, $\alpha$ - and $\beta$ - pinene, $\beta$ -caryophyllene, Zingiberene, $\alpha$ - and $\beta$ - eudesmol, $\sigma$ - and $\alpha$ - xylene, Phytol, Caryophyllene and Isocaryophyllene oxide (Ogunwande et al., 2008)	liver and kidneys (Ahmed et al., 2012)  Possible testicular, lung and hepatic toxicities at doses $\geq$ 500 mg/kg (Aniagu et al., 2008)
59	<i>Garcinia kola</i> Heckel-	Clusiaceae	Bitter kola	Orogbo (Y), Agbi-ilu (I), Namiji-goro (H)	SW, SE	100 mg/kg kolaviron decreased blood sugar levels in normal and alloxan induced diabetic mice; as well as inhibited aldose reductase enzyme activity (Iwu et al., 1990a); Hypoglycaemic effect of kolaviron is due to GB1 and GB2 in normal and STZ- induced diabetic rats (Adaramoye and Adeyemi, 2006); Alpha glucosidase inhibitory effect of GB1 (Antia et al., 2010)	Cold symptoms, Anti- microbial, Diarrhea, Dysentery, Liver disorders, Aphrodisiac, Poison antidote, Sickle cell	Fruit Root, Stem-bark, Seed	Maceration	Kolaviron-Mix of GB1, GB2 and kolaflavanone (Iwu et al., 1990a)	Garcinia biflavanone (GB) 1, GB2, kolaflavanone (Cotterill et al., 1978); Apigenin-5,7,4'-trimethyl ether, Apigenin 4'-methyl ether, Amentoflavone, Fisetin (Iwu and Igboko, 1982); Conraunalactone, Kolanone, Cycloartenol, 24-methylene cycloartenol, Manniflavanone, Garcini- flavanone (Iwu et al., 1990b); Lavender lactone, Linalol and its oxides, Methyl heptenone, Benzaldehyde, Phenylacetaldehyde, $\beta$ -Myrcene, $\alpha$ -Terpineol, <i>p</i> -Cymen-9-ol, Geraniol, Geranial, $\beta$ -Caryophyllene, Methyl phenylacetate, $\beta$ -Farnesene, Manoyl oxide (Onayade et al., 1998); Garcinoic acid (Mazzini et al., 2009)  $\beta$ -Caryophyllene, $\alpha$ - and $\beta$ -Pinene, Camphene, 1,8- Cineole, Linalol, $\alpha$ - Terpineol, Benzaldehyde,	Pre-ingestion of the seeds by ten healthy volunteers 30 min prior to the administration of the antibiotic (Esimone et al., 2007); Pharmacokinetics of ciprofloxacin in rabbits was altered when co- administered with the seed extract (Esimone et al., 2002)
60	<i>Gongronema</i> <i>latifolium</i> Benth.	Apocynaceae	Bush buck	Utazi (I), Madumaro or Arokeke (Y), Utasi (Ef)	SE, SW, SS	Ethanol extract of the leaves decreased blood glucose levels in STZ-induced diabetic rats and increased	Anti-microbial, Anti- parasitic, Hypertension, Inflammation, Hepato- protective, GIT	Leaves, Stem, Root	Infusion Maceration, Food vegetable	The anti- hyperglycaemic effects of fractions of the methanol		

Table 1 (continued)

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						activity of glucose metabolizing enzymes (Ugochukwu and Babady, 2003) Hypoglycaemic effect of 100 mg/kg of the methanol extract in alloxan-induced diabetic mice (Ogundipe et al., 2003) Antioxidant effects (Fasakin et al., 2011; Ugochukwu and Babady, 2002) 150 ml of a (1:1:1) decoction mix of the leaves of <i>Vernonia amygdalina</i> , <i>Ocimum gratissimum</i> and <i>Gongronema latifolium</i> decreased baseline blood glucose levels when preadministered to normal subjects 45 min before an OGTT (Ejike et al., 2013)	problems, Chewing stick, Laxative, Ulcer, Analgesic, Fevers			extract of the stem and leaves in glucose loaded rats as well as the <i>In vitro</i> glucose stimulating effects in INS-1 cells led to the isolation of $\alpha$ - and $\beta$ -amyrin cinnamate, lupenyl cinnamate and lupenyl acetate as bioactive constituents (Adebajo et al., 2013)	Aromadendrene and its hydrate, $\alpha$ -Humulene, $\delta$ -Cadinene, Germacrene, $\alpha$ - and $\gamma$ -Eudesmol, (E)- Phytol, Methyl palmitate (Edet et al., 2005); 3-O-[6- deoxy-3-O-methyl- $\beta$ -D- allopyranosyl-(1 $\rightarrow$ 4)- $\beta$ -D- canaropyranosyl-17 $\beta$ - mardenin and 3-O-[6- deoxy-3-O-methyl- $\beta$ -D- allopyranosyl-(1 $\rightarrow$ 4)- $\beta$ -D- oleoandropyranosyl-17 $\beta$ - mardenin, 11-O-acetyl- and 12-O-acetyl-3-O-[6- deoxy-3-O-methyl- $\beta$ -D- allopyranosyl-(1 $\rightarrow$ 4)- $\beta$ - canaropyranosyl]-17 $\beta$ - marsdenin (Schneider et al., 1993) Lupenyl acetate, Lupenyl cinnamate, $\beta$ -Sitosterol, Lupeol (Ekundayo, 1980) $\alpha$ - and $\beta$ -amyrin cinnamate (Adebajo et al., 2013) Gossypol, Condensed tannin (Chan et al., 1978); Quercetin glucosides, Gossypetin glucosides, Cyanidin-3- $\beta$ -glucoside (Chrysanthemin) (Hanny, 1980); Myrcene, $\alpha$ - and $\beta$ - pinene, Limonene, $\beta$ - caryophyllene and its oxide, $\gamma$ -bisabolene, Spathulenol, Gossonorol $\beta$ - bisabolol (Elzen et al., 1985) Gymnemic acids I-XVIII, Gymnemagenin or Genin I and its acetate ( $\beta$ -amyrin derivative), Genins G and J, Genin K acetate, Gymnemasaponins I-V, Gymnemasins A-D, Gymnemanol, Gypenosides XXVIII, XXXVII, LV, LXII and LXIII, Gymnemasides I-VII, Oleanane-type saponins, Gurmarin, Gymnamine, Gymnemosides A-E (Porchezhian and Dobriyal, 2003); Gymnemic acids A-D (Sinsheimer et al., 1970); Choline, Betaine, Adenine,	
61	<i>Gossypium hirsutum</i> L.	Malvaceae	Cotton	Auduga (H); Ela-owu (Y); Eto-oyo (Ibibio); Owu (Ige); Ebe-oru (Bi)	NW	Aqueous extract of the leaves produced a non-significant blood glucose lowering effect of only 17% in alloxan- induced diabetic rats (Etuk and Mohammed, 2009)	Gonorrhea, Dysentery, Sore throat, Malaria, Uterine fibroids	Leaves, Root	Decoction, Maceration			
62	<i>Gymnema sylvestre</i> (Retz.) R. Br. Ex Sm.	Apocynaceae	Cow plant		SE	GS4, a low MW component of the aqueous extract of the leaves decreased blood glucose levels and increased insulin release in rats, Type 1 and 2 diabetic patients (Shanmugasundaram et al., 1990a, 1990b; Baskaran et al., 1990) <sup>§</sup> ; The action of GS4 on insulin release is by increased membrane permeability (Persaud et al., 1999) <sup>§</sup> ; A high MW extract of the leaves OSA <sup>®</sup> increased plasma insulin levels <i>in-vitro</i> and in humans through a direct stimulatory effect (Al- Romiyan et al., 2010) <sup>§</sup> ;	Obesity, Anti-sweetner, Ulcer, Diuretics, Laxatives, Skin infectionsAsthma, Hepato-protective, Inflammation, Snake bites, Anti-microbial, Anti-plasmodial	Leaves, Roots	Infusion			

Table 1 (continued)

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						Antioxidant effects (Kang et al., 2012) <sup>§</sup>					Leucine, Valine, Amino butyric acid, Trimethylamine oxide, Isoleucine (Sinsheimer and McIlhenny, 1967); Nonacosane, Condritol A, Hentriacontane, Tritricontane (Manni and Sinsheimer, 1965) Ikirydinium A, Ursolic acid, Serpentine, Pseudo-akuammigine, Huntrabrine methochloride, Strictosidinic acid (Ajala et al., 2011); Corymine, Isocorymine, Acetylcorymine, Dehydro-isocorymine, Umbellamine, Eripine, Erinin, Erinincin, Abereamines 1–4 (delactonized 14-isopropyl hydroxy isocorymines) (Adejuwon et al., 2012); Segunoside (Ajala and Coker, 2012) Di-(2-ethylhexyl) phthalate, Homoorientin (Sofidiya et al., 2010); Friedelan-3-one, Betulinic acid, Lupeol, $\beta$ -Sitosterol, Stigmasterol, Oleic acid (Igoli and Alexander, 2008); Hymenocardine (Pais et al., 1968)	
63	<i>Hunteria umbellata</i> (K. Schum.) Hallier f.	Apocynaceae		Mkpokiri (I), Erin or Abeere (Y), Osu (Bi)		Aqueous extract of the seed produced a dose-dependent (50–200 mg/kg) hypoglycaemic effect in 3 diabetic models (alloxan, fructose and dexamethasone-induced) (Adeneye and Adeyemi, 2009); Antioxidant effects (Adejuwon et al., 2011); An alkaloidal fraction of the butanol extract decreased the post-absorptive glucose concentration in alloxan-induced rats (Adeneye et al., 2012)	Labour induction, Anti-pyretic, Analgesic, Obesity, Gastric ulcer, Dys-menorrhea, Anti-microbial, Anti-parasitic, Immune booster, Anti-helminthic, STDs, Hypertension	Seeds, Fruit Pulp, Bark, Roots	Maceration, Decoction, Infusion			
64	<i>Hymenocardia acida</i> Tul. (in vivo)	Phyllanthaceae	Heart fruit	Janyaro (H), Enache (Id)	SE, NC, NW	Methanol extract of the leaves decreased blood glucose levels in alloxan-induced diabetic rats at doses between 250 and 1000 mg/kg (Ezeigbo and Asuzu, 2010); Antioxidant effects (Sofidiya et al., 2009)	Anti-microbial, Anti-parasitic, Sickle cell, Ulcers, Diarrhea, Dysentery, Analgesic, Malaria, Tumours, Arthritis, Anti-fertility, Insecticidal	Bark, Fruit, Leaves	Decoction, Maceration, Infusion			
65	<i>Ipomoea batatas</i> (L.) Poir.	Convolvulaceae	Sweet potato	Ji-oyibo or Ekimako (I), Odunkun (Y), Dankali (H)	SW	Aqueous extract of fresh whole plants produced a dose-dependent (100–400 mg/kg) decrease in blood glucose in normal and STZ-induced diabetic rats (Olowu et al., 2011); Daily ingestion of 4 g by type 2 diabetic patients for 3 mths resulted in improved FBG and HbA1c levels (Ludvik et al., 2004) <sup>§</sup> ; Improved glucose tolerance and decreased hyperinsulinemia in obese Zucker fatty rats administered 100 mg/kg/day aqueous extract of the cortex (Shuichi and Abe, 2000) <sup>§</sup>	Anti-proliferative, Anti-microbial, Purgative, Wound ulcers, Analgesic, Hemorrhoids	Whole plant, Leaves, Bark	Juice extract, Infusion	Aldose reductase inhibitory effects of ellagic acid and 3,5-dicaffeoyl quinic acid isolated from extract of the leaves (Terashima et al., 1991); Alpha glucosidase inhibitory effect of an isolated anthocyanin Peonidin-3-O-[2-O-(6-O-E-feruloyl- $\beta$ -D-glucopyranosyl)-6-O-E-caffeoyl- $\beta$ -D-glucopyranoside from the root (Matsui et al., 2002)	Non-, Mono- and Diacylated structures of 3-O-(2-O- $\beta$ -D-glucopyranosyl- $\beta$ -D-glucopyranoside)-5-O- $\beta$ -D-glucosides of Cyanidin and Penoidin (Montilla et al., 2011); Gallic, Gentisic, Caffeic, Chlorogenic, <i>p</i> -Coumaric, Sinapic, Benzoic, Anisic and Cinnamic acids; Catechin, Epicatechin, Kaempferol, Myricetin, Quercetin (Carvalho et al., 2010); 4,5-di-O-caffeoylquanic acid, 3-O-caffeoylquanic acid (Chlorogenic acid), 3,5-di-O-caffeoylquanic acid, 3,4-di-O-caffeoylquanic acid, 3,4,5-tri-O-caffeoylquanic acid, Caffeic acid (Islam et	4-Ipomeanol produces an irreversible inhibition of Cyt 3A4 (Alvarez-Diez and Zheng, 2004)



Table 1 (continued)

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66	<i>Irvingia gabonensis</i> (Aubry-Lecomte ex O'Rorke) Baill.	Irvingiaceae	Dikanut, African mango, Bush mango	Ogbono (I)	SE, SS, SW	Daily intake of a dikanut supplemented diet (4g/day) by type 2 diabetic patients for 1 month resulted in improved lipid profile and decreased blood glucose levels (Adamson et al., 1990) 2 g/kg administered 2 ce daily to STZ-induced diabetic rats decreased blood glucose, and lactate dehydrogenase and pyruvate kinase enzymes (Ozolua et al., 2006)  Overweight volunteers given the seed extract in a randomized double-blinded study had decreased blood glucose, adiponectin, leptin and C-reactive protein levels and improved plasma lipid profile compared to placebo (Ngondi et al., 2009) <sup>§</sup> Antioxidant effects (Donfack et al., 2010; Awah et al., 2012)	Dysentery, Wound ulcers, Liver disorders, Hemorrhage, Anti- microbial, Analgesic	Seeds, Fruit, Leaves, Stem-bark, Root	Decoction		al., 2002); Ellagic acid, Caffeic acid, Scopoletin and 3,5-dicaffeoyl quinic acid (Terashima et al., 1991) 3-Friedelanone, Betulinic acid, Oleanolic acid, Methyl gallate, Trimethyl ellagic acid, Hardwickic acid, 3- $\beta$ -acetoxyursolic acid (Donfack et al., 2010);  Ellagic acid, Mono, Di and Tri-methyl ellagic acid and their glycosides, Galloyl ellagic acids, Ellagitannins, Kaempferol glucoside, Quercetin rhamnoside, Diosmetin (Sun and Chen, 2012)	
67	<i>Jatropha curcas</i> L.	Euphorbiaceae	Pignut plant, Physic nut, Purging nut, Barbados nut	Botuje or Lapalapa (Y), Binida zugu (H), Owulo idu	SW	Antioxidant effects (Igbinsola et al., 2011) 250 and 500 mg/ kg of the hydro-ethanolic extract of the leaves decreased blood glucose levels in alloxan-induced diabetic rats (Mishra et al., 2010) <sup>§</sup> 100 mg/l ethanol extract of the stipe showed PPAR $\alpha$ , $\gamma$ and $\delta$ activities (Rau et al., 2006) <sup>§</sup> 250 and 450 mg/kg of the aqueous extract of the roots decreased fasting blood glucose levels in alloxan induced diabetic rats (Aladodo et al., 2013)	Purgative, Cancer, Abortifacient, Diuretic, Hemostatic, Anti- pyretic, Inflammation, Convulsions, Wound healing, Anti-microbial, Insecticidal, Jaundice, STDs, Anti-parasitic, Skin diseases, Molluscicidal, Chewing stick, Irregular menses, Sciatica, Paralysis	Seeds, Leaves, Root Latex, Stem- bark			Curcacycline A (van den Berg et al., 1995); Esterases, Lipase (Staubmann et al., 1999); Curcin, Curcain (Osoniyi and Onajobi, 2003); Scopoletin, Coumaroyl oleanolic acid, Methoxyanthraquinone, Heudelotone, Tetradecyl ferulate, Podocarpatriene and Podocarpatrienone (Ravindranath et al., 2004);  Phospholipase D (Liu et al., 2010); Eicosadienoic, Oleic, Linoleic, Palmitic, Stearic and Eicosenoic acids; 12-deoxy-16- hydroxy phorbol, Riolozatrine, Jatrophol, Jatropholones A and B, Acetoxyjatropholone, Jatropherol 1, 2 and 3; Curcosones A-E, Palmarumycin, Caniojane, Heudelotone, Nobilitin,	Ingestion of the seeds caused severe vomiting and dehydration in children; and hemorrhage of the liver, lungs and stomach resulting in death at high doses in mice (Abdu-Aguye et al., 1986)  Administration of 10 mg of the methanol extract of the seeds daily to rats resulted in changes in their hematological indices (Oluwole and Bolarinwa, 1997) Ethanol extract of the root bark of the plant inhibited Cyt P450 3A4 and 3A7 enzymes (Agbonon et al., 2010)

Table 1 (continued)

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68	<i>Khaya ivorensis</i> A.Chev.	Meliaceae	African, Lagos or Red mahogany	Oganwo (Y), Ono (I)	SW, SS, NC		Arthritis, Fevers, Anti- parasitic, Jaundice, SC anemia, Anti-tumour, Wound healing	Stem bark, Leaves	Maceration, Decoction, Infusion		Spirocurcasone, Ellagic acid, Jatrophalactam, Jatrogrossidione derivatives, $\beta$ -amyrin, Jatrophalactone, Caffeoyl aldehyde, Syringaldehyde, Jatrophadiketone, Uracil, $\beta$ -sitosterol, Jatrophalane, Taraxasterol, Stigmasterol, Daucasterol, Pyrrolidine, Curcamide, Tomentin, Coumarin compounds (Abdelgadir and Van Staden, 2013) 1-O-deacetyl-6deoxy khananolide E, 1-O- deacetyl-2 $\alpha$ -hydroxy khananolide E, 3-acetyl- khanalactone, 11 $\alpha$ - acetoxo-2 $\alpha$ -hydroxy-6- deoxy- destigloylswietenine acetate, Swiemahogin, Khayalactol, Seneganolide, Khananolide A and B, Khananoside (Zhang et al., 2009a); Methyl angolensate, and its 6-hydroxy derivative, 3-deacetylkhivorin, 3,7- dideacetylkhivorin, 1,3,7- trideacetylkhivorin, 7-deacetylgedunin, 7-deacetoxo-7- oxogedunin, Swietenine, 3-O-detigloyl-3-O- acetylswietenine, 3-O- acetylswietenolide (Abdelgaleil et al., 2001); Proceranolide and its n-butyric derivative (Vanucci et al., 1992); Khivorin, Sitosterol, 3-deacetyl khivorin, 7-deacetyl khivorin, Methyl 6-hydroxyangolensate, Swietenolide acetate, Fissinolide, Methyl ivorensate, Esters of 6-deoxyswietenolide (Adesogan and Taylor, 1970) Rutin, Catechin, Quercetin rhamnoside, Procyanidins (Atawodi et al., 2009); 3 $\alpha$ ,7 $\alpha$ -dideacetylkhivorin, 1-O-acetylkhayanolide B	A herbal tonic containing a mix of extracts of the stem barks of <i>Khaya ivorensis</i> , <i>Mitragyna stipulosa</i> and <i>Kigela africana</i> modulated the activity of fat liver Cyt P450 enzymes (Martey et al., 2009) Aqueous extract of the stem bark modulates P-gp mediated efflux of Rhodamine-123 (Ezuruike et al., 2012)
69	<i>Khaya senegalensis</i> (Desv.) A.Juss.	Meliaceae	Dry-zone or African mahogany	Oganwo (Y), Ono (I), Madachi (H), Okpen (Es), Ago (Ig)	SW, SS, NC, NW	An extract of the bark in buffer solution produced moderate inhibition of $\alpha$ - amylase activity <i>in-vitro</i> (Funke and Melzig, 2006)	Fevers, Sickle Cell, Anti- parasitic, Anti- microbial, Anti-tumour, Hypertension, Insecticidal	Stem bark, Leaves, Seeds	Infusion, Maceration, Decoction			

Table 1 (continued)

S/ no.	Plant name	Family	Common name	Local Nigerian name(s)	Region of use for diabetes <sup>#</sup>	Experimental evidence for its use in diabetes management	Other medicinal uses	Plant part (s) used	Traditional preparation method	Identified active constituent(s)	Other relevant phytoconstituents identified in the plant	Interaction/toxicity studies
						200 mg/kg aqueous extract of the bark produced only a 4% decrease in blood glucose levels after 2 h (Etuk and Mohammed, 2009); while the oil extract of the seeds decreased blood glucose levels by 20% after 2 h, which increased to 60% after 8hrs (Momoh and Muhammed, 2011), both in alloxan-induced diabetic rats. Antioxidant effects (Atawodi et al., 2009)					(Zhang et al., 2007); Khayanolides D and E, Khayanoside (Nakatani et al., 2002); Khayanolides A, B and C, Seneganolide, Methyl angolensate and its 6-hydroxy and 6-acetoxy derivatives (Abdelgaleil et al., 2001); Fissinolide, 2,6-dihydroxy fissinolide, Methyl-3 $\beta$ -acetoxy-6-hydroxy-1-oxomeliac-14-enoate (Khalid et al., 1998); 2-hydroxy mexicanolide, 6-deoxy destigloyl swietenine, 2,3-dihydroxy-3-deoxymexicanolide, Mexicanolide, 3 $\beta$ -hydroxy-3-deoxymexicanolide, 3 $\beta$ -hydroxy-3-deoxycarapin, 3-acetyl-7-keto khivorin, 3-deacetyl khivorin (Govindachari and Kumari, 1998); Methyl 1 $\alpha$ -acetoxy tri hydroxyl-2 $\alpha$ -methoxy-2 $\beta$ , 14 $\beta$ -epoxy tricyclomeliac-7-oate, Methyl 1 $\alpha$ -acetoxy tetra hydroxyl-3-oxo-tricyclomeliac-7-oate, Scopoletin, $\beta$ -quercitrin (Olmo et al., 1997)	
70	<i>Lawsonia inermis</i> L.	Lythraceae	Henna plant, Mehndi, Egyptian's priest	Laali (Y), Lelle (H)	SW	Alpha glucosidase inhibitory effects of the ethanol extract of the leaves (Prashanth et al., 2001) <sup>§</sup> Increased activity of <i>in-vivo</i> antioxidant enzymes (Dasgupta et al., 2003) <sup>§</sup> Daily administration of graded doses (100–800 mg/kg) of the ethanol extract of the leaves for 2 weeks decreased blood sugar levels in alloxan-induced diabetic rats (Inawati and Winarno, 2008) <sup>§</sup> <i>In vitro</i> antioxidant effects of isolated constituents of the plant (Hsouna et al., 2011) <sup>§</sup>	Wound infection, Anti-microbial, Anti-parasitic, Jaundice, Nervous disorder, Arthritis, Analgesic, Ulcers, Diarrhea, Anti-pyretic, Hepato-protective, Leucorrhoea, Excessive ejaculation, Emmenagog, Skin diseases, STDs, Abortifacient, Sick cell, Tumours, Tuberculosis, Splenomegaly, Menorrhagia	Leaves	Decoction	Lawsonic acid isolated from the ethanol extract of the aerial parts inhibited the formation of glycated protein <i>In vitro</i> (Sultana et al., 2009)	$\beta$ -Sitosterol glucoside, Gallic acid, Coumarins, Xanthones, Lawsoniaside, Laliolide, Luteolin glucosides, 1,2-dihydroxy-4-glucosyloxy naphthalene (Takeda and Fatope, 1988); Vomifoliol, Lawsonicin, Lawsonadeem (Siddiqui et al., 2003); Isoplumbagin, Hexenol, Linalool, $\beta$ -Ionone, $\alpha$ - and $\gamma$ -Terpineol, Terpinolene, $\delta$ -3-Carene, Benzaldehyde, Isocaryophyllene, Methyl salicylate, Naphthalene, Eugenol, Germacrene D, Farnesene, Bisabolene, $\beta$ -Elemene, Isophytol, $\delta$ -Cadinene, Cadalene, Geranyl isobutyrate, Methyl cinnamate (Oyedeki et al., 2005);	Administration of henna leaf extract to mice for 21days resulted in increased activity of cytochrome b <sub>5</sub> reductase enzyme and the phase 2 enzymes GST and DDT (Dasgupta et al., 2003) Topical application to skin lesions in G6PD deficient patients resulted in hemolytic anemia (Kök et al., 2004)

Table 1 (continued)

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71	<i>Mangifera indica</i> L.	Anacardiaceae	Mango	Mangoro	SS, SE	1 g/kg of the aqueous extract of the leaves decreased blood glucose levels in normal and glucose loaded mice, but not in STZ-induced diabetic mice (Aderibigbe et al., 2001) Alpha glucosidase inhibitory effects of the ethanol extract of the bark (Prashanth et al., 2001) <sup>§</sup> 200 mg/kg aqueous extract of the leaves decreased blood glucose levels in alloxan-induced diabetic rats (Etuk and Mohammed, 2009) Dipeptidyl peptidase IV inhibitory activity of the methanol extract of the leaves (Yogisha and Raveesha, 2010) <sup>§</sup> Antioxidant effects (Badmus et al., 2011)	Malaria, Analgesic, Inflammation, Anti-microbial, Anti-helminthic, Diarrhoea, Menorrhagia, Hypertension, Insomnia, Asthma, Scabies, STDs, Anemia, Malaria	Leaves Stem-bark, Kernel, Fruits	Decoction		Mannitol, Hennaannic acid, Lawsone (2-hydroxy 1,4-naphthoquinone), Behenic, Oleic, Linolenic, Arachidic, Palmitic and Stearic acids, Laxanthone I, II and III, Apigenin glycosides, Stigmasterol, Acacetin, Cosmoisin, <i>p</i> -Coumaric acid, Fraxetin, Hennadiol, Scopoletin, Esculetin, Apiin, Lupeol, Betulin, Betulinic acid, Lawsoshamim, 2-methoxy-3-methyl naphthaquinone, 24 $\beta$ -ethyl cholest-4-enol, Esters of Lawnermis acid (Chaudhary et al., 2010) Trihydroxy acetophenone and naphthalene glucopyranosides (Hsouna et al., 2011) Tannic acid, Gallic acid, Epicatechin, Ellagic acid, Gallocatechin, <i>n</i> -butyl cyanidin (Arogba, 2000); 3,4-dihydroxy benzoic acid, Benzoic acid, Methyl gallate, Propyl gallate, Mangiferin, Catechin, Benzoic acid propyl ester (Núñez Sellés et al., 2002) Violaxanthin dibutyrate, $\beta$ -Carotene, 9- <i>cis</i> - and <i>trans</i> -violaxanthin, Luteoxanthin, Mutatoxanthin, Neochrom, Xanthophyll palmitic and myristic acid esters (Pott et al., 2003); Isomangiferin, Quercetin and its glycosides, Kaempferol-3- <i>O</i> -glucoside, Rhamnetin-3- <i>O</i> -glycoside, Mangiferin and Isomangiferin gallate (Schieber et al., 2003; Berardini et al., 2005) $\beta$ -Sitosterol glucoside, Stigmast-4-en-3-one, Galactosyl diacylglyceride, Galactocerebroside, Scopoletin, Isoscopoletin, Scoparone, Esculetin, Ayapin, Umbelliferone, Scopolin, Esculin, $\beta$ -Carotene (Bayoumi et al.,	Stem bark extract of the plant, mangiferin and its metabolite norathyriol as well as quercetin, constituents of the plant showed dose-dependent modulation of P-gp activity in HK-2 and Caco-2 cell lines (Chieli et al., 2009) The stem bark extract also showed inhibitory effects for Cyp1A, 2D and 3A4 enzymes of human liver microsomes (Rodeiro et al., 2009) Although intake of a cassava tuber rich diet has been implicated in the aetiology of pancreatic diabetes (Kamalu, 1991); experiments have shown that it only aggravates diabetes in
72	<i>Manihot esculenta</i> Crantz, Syn: <i>Manihot utilissima</i> Pohl	Euphorbiaceae	Cassava, Tapioca	Gbaguda or Ege (Y), Akpu or Abacha (I), Rogo (H)	SE, SW	Increased intake of cassava leaves in diet decreases the risk of metabolic syndrome in Type-2 diabetic patients (Mvitu Muaka et al., 2010) <sup>§</sup> Antioxidant effects of the aqueous extract of the leaves (Tsumbu et al., 2011) <sup>§</sup>	Arthritis, Gonorrhea, Burns, Ulcer	LeavesTubers	Decoction			

Table 1 (continued)

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73	<i>Momordica charantia</i> L.	Cucurbitaceae	African cucumber, Bitter melon, Bitter guord, Bitter squash, Karela	Ejirin (Y), Ebe isiugwu (Bi), Urakhanye (Es), Daddagu (H)	SW, SS, NW	Daily administration of 10 ml/kg of the fruit juice extract to STZ-induced diabetic rats for 10wks decreased blood glucose levels and increased plasma insulin levels and the number of insulin positive islet cells. There was decreased glucose uptake by the brush border vessicles of the jejunum in extract treated rats compared to control. <i>In vitro</i> , 5 µg/ml of the extract increased glucose transport into L6 myotubes (Ahmed et al., 2004) Several clinical studies in type-2 diabetic patients given extracts of the plant produced hypoglycaemic effects (Leung et al., 2009) <sup>§</sup>	Anti-fertility, Malaria, Anti-helminthic, Anti- microbial, Insecticidal, Weight loss, Abortifacient, Skin infections, Inflammation, Purgative, Dysentry, Fevers, Burns, Colic	Fruit, Leaves, Root, Seeds	Decoction, Juice extract		2010); Cyanidin and Delphinidin 3-O-(6''-O-α- rhamno pyranosyl-β- glucopyranoside) (Byamukama et al., 2009); Rutin, Kaempferol-3-O- and 4'-O-rutinoside, Ferulic acid, Amentoflavone (Ola et al., 2009); Caproic, Caprylic, Capric, Lauric, Myristic, Palmitic, Oleic, Linoleic, Arachidic, Behenic and Lignoceric acids (Raja and Ramakrishna, 1990); Linamarin, Lotaustralin (Ogunsua, 1980) Esters, Alcohols and Sugars of Cucurbitane triterpenoids, Kuguacins, Charantosides, Trinorcucurbitacin, Penta- norcucurbitacins, Octa- norcucurbitacin (Lee et al., 2009); Momorcharins, Momordin, Momordolol, Charantins, Momordenol, Momordicilin, Charine, Momordicosides, Momordicines, Diosgenin, Cryptoxanthin, Vicine, Cucurbitins, Cucurbitacins, Cucurbitanes, Erythrodiol, Cycloartenols, Gentisic, Elaeostearic, Galacturonic and Pipecolic acids; MAP 30, Goyaglycosides, Goyasaponins, P-insulin polypeptide, Ascorbigen, Multiflorinols, Luteolin, Lauric, Myristic, Palmitic, Stearic, Palmitoleic, Oleic, Linoleic and Linolenic acids (Paul and Raychaudhuri, 2010)	low-protein diets (Yessoufou et al., 2006; Manwa et al., 2010) Risk of toxic effects on organs due to high cyanide content (Soto- Blanco and Górniak, 2010)  Aqueous extract of the leaves inhibited GST enzyme in both rat and human liver cytosols and recombinant GSTs; as well as the activity of Cyp 2C9 supersomes but not Cyp 1A2, 2D6 and 3A4 (Appiah-Opong et al., 2008) A potentiated hypoglycaemic effect has been observed when extracts of the plant are co- administered with known anti-diabetic drugs (Nivitabishekam et al., 2009)
74	<i>Momordica foetida</i> Schumach.	Cucurbitaceae	Bitter melon	Ebe isiugwu (Bi) Ejinrin-wewe (Y)	SS SS	500 mg/kg aqueous leaf extract decreased blood glucose levels in normal, high glucose fed and alloxan- induced diabetic rats (Osinubi et al., 2008) Antioxidant effects (Acquaviva et al., 2013)	Malaria  Malaria, Ulcer, GIT disorders, Anti- microbial, Anti- helminthic, Hypertension, Abortifacient	Root  Fruit, Leaves, Stem, Flower, Whole plant	Juice extract  Maceration, Decoction	1 mg/kg foetidin isolated from the plant decreased blood glucose levels of normal fasted, but not alloxan-induced rats (Marquis et al., 1977)	5,25-stigmastadiene-ol- glucoside, Foetidin, β- sitosterol glucoside (Marquis et al., 1977); β- Hydroxyfriedel-6(7)-ene- 3-one, Octadecanoic acid, Stigmasterol-β-D- glucoside, Choline chloride (Olaniyi, 1980); Cucurbitacins (Chen et al.,	



Table 1 (continued)

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75	<i>Mondia whiteii</i> (Hook.f.) Skeels	Apocynaceae	White ginger, African ginger	Isirigun or Aghuma or Gbolo- gbolo (Y)	SW	Aqueous extract of the roots did not show any inhibition against pancreatic alpha amylase and lipase enzymes (Etoundi et al., 2010) <sup>§</sup>	Infertility, Erectile dysfunction, Malaria, Gonorrhea, Anti-parasitic, Anti-depressant, Anti-spasmodic, Hemorrhoids, Inflammation, Memory loss, Cancer	Stem, Root	Infusion, Decoction		2005); 3 $\beta$ ,7 $\beta$ -dihydroxyl-cucurbita-5,23,25-trien-19-al, Kaempferol-3-O- $\beta$ -D-glucopyranoside (Odeleye et al., 2009) Isovanillin, 2-hydroxy-4-methoxy benzaldehyde and its -2-O- $\beta$ -D-glucopyranose-(1 $\rightarrow$ 6)-O- $\beta$ -D-xylopyranoside (Koorbanally et al., 2000); Propacin, 5-methoxy propacin, 5-chloropropacin, Squalene, $\beta$ -sitosterol, 3-methoxy-4-hydroxy benzaldehyde, 6-methoxy-7-hydroxycoumarin, 6-methoxy-7,8-dihydroxy coumarin (Patnam et al., 2005); Lolilide (Neergaard et al., 2010); Stigmasterol, 9-Hexacosene (Githinji et al., 2011); $\alpha$ and $\beta$ -amyrin acetate (Watcho et al., 2012)	
76	<i>Morinda citrifolia</i> L.	Rubiaceae	Indian mulberry, Noni		SW	300 mg/kg of a mixture of the aqueous fruit extract alongside that of <i>Coccinia indica</i> decreased blood glucose levels in alloxan-induced diabetic rats (Kumar and Verma, 2011) <sup>§</sup> Administration of 2 ml/kg of the fruit juice extract twice a day to STZ-induced diabetic rats for twenty days resulted in a significant decrease in fasting blood glucose levels by the 5th day post administration (Nayak et al., 2011) <sup>§</sup> Antioxidant effects for the methanol extract of roots and ethyl acetate extract of plant (Zin et al., 2002) <sup>§</sup> Administration of 1ml/150mg body weight of Tahitian noni juice® for 4 weeks resulted in a prophylactic action against alloxan-induced diabetes in rats (Horsfal et al., 2008).	Malaria, Wound healing, Anti-microbial, Anti-helminthic, Inflammation, Immune booster, Colds and Flu, Ulcers, Tumours, Analgesic, Arthritis, Hypertension, Tuberculosis	Fruits, Roots, Stems, Bark, Flower, Leaves	Decoction, Maceration	Hypoglycemic effects of the anthraquinones, damnacanthal-3-O- $\beta$ -D-primeveroside and lucidin 3-O- $\beta$ -D-primeveroside from the butanol fraction of the methanol extract at 100 mg/kg in STZ-induced diabetic mice. (Kamiya et al., 2008)	6-O-( $\beta$ -D-glucopyranosyl)-1-O-octanoyl- $\beta$ -D-glucopyranose and 1-O-hexanoyl- $\beta$ -D-glucopyranose, 3-methylbut-3-enyl 6-O- $\beta$ -D-glucopyranosyl- $\beta$ -D-glucopyranoside (Wang et al., 2000); Citrofolinin A and B, Kaempferol and Quercetin glycosides, Physcion, Ricinoleic, Octanoic, Hexanoic acids (Sang et al., 2001); Scopoletin, L-asperuloside, Alizarin, Asperulosidic, Caproic, Caprylic and Ursolic acids, Acubin, Rubiadin and its 1-methyl ether, Nordamnacanthal, Morindone, Rutin, 1-methoxy-2-formyl-3-hydroxy anthraquinone, Citrifolinolide, Proxeronine (Wang et al., 2002); Morenone-1 and 2, 6,8-dimethoxy-3-methyl anthraquinones 1-O- $\beta$ -rhamnopyranosyl(1 $\rightarrow$ 4) $\beta$ -D-glucopyranoside, 6 $\alpha$ -hydroxyadoxoside, 6 $\beta$ ,7 $\beta$ -epoxy-8-epi-splendoside,	Risk of liver injury/hepatitis (Millonig et al., 2005; Yüce et al., 2006; Mrzljak et al., 2013) Noni juice extract increased the activity of amino-pyrene N-demethylase (APND) and glutathione-S-transferase (GST) enzymes and decreased the activity of uridine diphosphoglucuronosyl transferase (UGT) enzyme of rat liver hepatocytes both <i>In vitro</i> and <i>ex vivo</i> (Mahfoudh et al., 2009) Co-incubation of noni juice and digoxin in Caco-2 monolayers did not change the net digoxin flux indicating no modulation of P-gp by noni juice (Engdal and Nilsen, 2008)

Table 1 (continued)

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77	<i>Morinda lucida</i> Benth.	Rubiaceae	Brimstone tree	Oruwo (Y), Eze ogwu (I)	NC, SW	Administration of the methanol extract of the leaves produced a dose dependent (50–400mg/kg) decrease in plasma glucose levels in both normal and STZ-induced diabetic rats (Olajide et al., 1999)	Malaria, Anti-microbial, Anti-parasitic, Anti-helminthic, Analgesic, Laxative, Hypertension, Jaundice, Oligo-menorrhea, Insomnia, Wound ulcers, Diuretic	Leaves, Roots, Stem- bark	Decoction		Borreriagenin, Deacetyl asperuloside, Dehydro methoxygaertneroside, 5,15-dimethyl morindol, Alizarin-1-methyl ether, Anthragallol-1,3-dimethyl ether, Anthragallol-2-methyl ether, 6-hydroxy-anthragallol-1,3-dimethyl ether, Morindone-5-methyl ether, Asuperlosidic acid, Deacetylasperulosidic acid, Morindacin (Kamiya et al., 2005); Ursolic acid, Oleanolic acid (Cimanga et al., 2006) 1-Methylether alizarin, Soranjidiol, Damnacanthal, Nordamnacanthal, Lucidin, Rubiadin, Morindin, Munjistin, Purpuroxanthin, Digitolutein, Oruwalol, Oruwal (Lawal et al., 2012)	Aqueous extract dose dependently (1–20mg/ml) inhibited the P-gp mediated transport of digoxin across monolayers of Caco-2 cells (Oga et al., 2012) Aqueous extract and ethanol extract of the leaves moderately inhibited Cyp3A4 and 3A7 enzymes respectively (Agbonon et al., 2010) 0.5 mg/ml aqueous extract of the leaves inhibited the activity of the recombinant GST M1-1 enzyme by > 70%, but not those of rat and human liver cytosols (Appiah-Opong et al., 2008)
78	<i>Moringa oleifera</i> Lam.	Moringaceae	Drumstick orHorseradish tree, Moringa	Zogale (H), Okwe-oyibo or Okochi egbu (I), Gergedi (Igala), Ewe- igbale or Gbogbo-nise (Y), Konamarade (F)	SE, SW, NW, NC	Aqueous extract of the leaves decreased blood glucose levels in normal, high glucose fed and STZ-induced diabetic rats at doses between 100 and 300 mg/kg (Jaiswal et al., 2009) <sup>§</sup> 200 mg/kg of the leaf powder improved glucose tolerance in both normal wistar and spontaneously type-2 diabetic GK rats (Ndong et al., 2007) <sup>§</sup> Antioxidant effects (Siddhuraju and Becker, 2003) <sup>§</sup>	Antimicrobial, Anti-parasitic, Anti-cancer, Inflammation, Diuretic, Anemia, Hypertension, Aphrodisiac, Anti-pyretic, Purgative, GIT disorders, Immune stimulant, Anti-spasmodic	Leaves, Pods	Infusion, Dried leaves	Isolated benzyl derivatives from the methanol extract of the fruits stimulated insulin release from the pancreatic $\beta$ -cell line INS-1 (Francis et al., 2004)	Quercetin and Kaempferol glycosides, Chlorogenic acid, Rutin (Ndong et al., 2007); Isoquercitrin, Rhamnetin, Vanillin, $\beta$ -sitosterol, $\beta$ -sitostenone, Zeatin, 4-hydroxymellin, Niazirin, Niazicin A, Methyl 2,4-( $\alpha$ -L-rhamnopyranosyl) phenyl acetate, N-[4-( $\beta$ -D-glucopyranosyl)benzyl]-1-O- $\alpha$ -D-glucopyranosyl thiocarboxamide, 4-[( $\beta$ -D-glucopyranosyl)-(1 $\rightarrow$ 3)-( $\alpha$ -L-rhamnopyranosyl) phenylacetoneitrile, 1-O-phenyl- $\alpha$ -L-rhamno pyranoside, Methyl N-(4 [(4'-O-acetyl- $\alpha$ -L-	Aqueous and methanol extracts of the leaves inhibited Cyp3A4 hydroxylation of testosterone in human liver microsomes (Monera et al., 2008) Hydroalcoholic extract of the drumsticks increased the activities of hepatic Cyt P450 and Cyt b <sub>5</sub> enzymes as well as the antioxidant enzymes GST, GPx and GR (Bharali et al., 2003)

Table 1 (continued)

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79	<i>Morus alba</i> L.	Moraceae	White mulberry			Alpha glucosidase inhibitory effects of the aqueous extract of the leaves in Caco-2 cells (Hansawasdi and Kawabata, 2006) <sup>§</sup> The leaf extract showed inhibitory effects against rat and human disaccharidase enzymes of the intestinal mucosa as well as decreased post-prandial glucose levels in sucrose fed rats (Oku et al., 2006) <sup>§</sup> 400 and 600 mg/kg ethanol extract of the leaves decreased blood glucose levels in STZ-induced diabetic rats and increased the number of $\beta$ -cells in the islets of the pancreas (Mohammadi and Naik, 2008) <sup>§</sup> Ingestion of the leaf extract by KK-Ay mice as part of the diet decreased blood glucose levels, improved glucose tolerance and increased plasma insulin levels (Tanabe et al., 2011) <sup>§</sup> Antioxidant effects (Yen et al., 1996) <sup>§</sup>	Anti-helminthic, Laxative, Emollient, Molluscicidal, Anti-microbial	Leaves, Fruit, Bark	Infusion, Decoction, Maceration		rhamnopyranosyl)benzyl] carbamate, Methyl <i>N</i> -4-[( $\alpha$ -L-rhamnopyranosyl)benzyl] carbamate, <i>O</i> -[2'-hydroxy-3'-2'-heptenyl oxy]-propyl undecanoate, methyl <i>p</i> -hydroxybenzoate, Moringine, Moringinine (Anwar et al., 2007) Morusin, Isomorusin, Compound A (Taro et al., 1978); Kuwanons K and L (Nomura et al., 1983); $\beta$ -carotene, $\alpha$ -tocopherol (Yen et al., 1996); Isoquercitrin, Astragalin, Scopolin, Skimmin, Roseoside II, Benzyl <i>D</i> -glucopyranoside (Doi et al., 2001); 1-Deoxynojirimycin or Moranoline and its derivatives, Fagomine, Calystegin B1 and B2, (2R,3R,4R)-2-hydroxy methyl-3,4-dihydroxy pyrrolidine- <i>N</i> -propionamide, 4- <i>O</i> - $\alpha$ - <i>D</i> -galactopyranosyl-calystegin B2, 3 $\beta$ ,6 $\beta$ -dihydroxynortropane (Asano et al., 2001); Morbalbanone, Kuwanon S, Mulberroside C, $\alpha$ -acetyl amylin, Cyclomorusin, Eudraflavone-B hydroperoxide, Oxy dihydromorusin, Lechianone G (Du et al., 2003); Steppogenin-4'- <i>O</i> - $\beta$ - <i>D</i> -glucoside, Mulberroside A, Moracin M (Zhang et al., 2009b)	A sodium chloride extract of the leaves showed an insignificant dose dependent (2–6 mg/ml) inhibition of Cyp 3A4 enzyme activity in human liver microsomes (Pao et al., 2012)
80	<i>Murraya koenigii</i> (L.) Spreng.	Rutaceae	Curry tree, Sweet neem		NW, SW	Methanol extract of the stem and leaves did not significantly decrease blood glucose levels in normal and alloxan-induced diabetic rats; while chloroform extract of the stems and isolated constituents decreased glucose mediated insulin release from INS cells (Adebajo et al., 2005) Hypoglycaemic effect of defatted ethanol extract of the leaves in STZ-induced diabetic rats and Antioxidant	Dysentery, Diarrhoea, Stimulant, Anti-venom, Hypertension, Anti-microbial, Inflammation, Anti-parasitic	Leaves, Seed, Stem	Powdered leaves as spice, Decoction	Administration of mahanimbine isolated from the petroleum ether fraction of the leaves decreased blood glucose levels in STZ-induced diabetic rats and had a dose-dependent $\alpha$ amylase and $\alpha$ glucosidase inhibitory effect (Dineshkumar et	Indicolactone, 2",3"-epoxy indicolactone, Anisolactone (Adebajo et al., 1997); Xanthotoxin, Phellopterin, Isogoserol, Byakangelicol, Gosferol, Isobyakangelicol, Neobyakangelicol, Byakangelicin (Adebajo and Reisch, 2000); Bismurrayafoline, Euchrestine B, Mahanine, Mahaninebicine, <i>O</i> -methyl mahanine, Isomahanine, Bismahane, 8,10-	Methanol extract of the leaves as well as isolated constituents of the plant inhibited Cyt P450 enzymes in rat liver microsomes. They also showed dose-dependent inhibitory effects against Cyp 1A2, 2C9, 2D6 and 3A4 enzymes (Pandit et al., 2012)

Table 1 (continued)

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						effects (Arulselvan and Subramanian, 2007) <sup>§</sup>				al., 2010) At a concentration of 1 mM, mangiferin showed 2-fold increase in glucose utilization in 3T3-L1 cells compared with untreated control (Dinesh Kumar et al., 2013)	tetrahydro dihydro tetramethyl bis(4-methyl-3-pentenyl)-bipyranocarbazole, Bispirayafoline (Tachibana et al., 2003); Mahanimbilol, Grinimbine, Girinimbilol, Murrayanine, Isomahanimbine, Koenimbine, Murrayacine, Murrayaquinone-A, Murrayazolidine, Murrayazoline, Mahanimbine (Adebajo et al., 2005); Mahanimbilyl and Grinimbilyl acetate, Bicyclomahanimbiline (Adebajo et al., 2006); PI, PII, PIII (Ningappa and Srinivas, 2008)	
81	<i>Musa paradisiaca</i> L., Syn: <i>Musa sapientum</i> L.	Musaceae	Plantain Banana	Ogede (Y), Abrika (I), Ayaba (H)	SW	250 mg/kg aqueous and methanol extract of the root decreased blood glucose levels in alloxan (Adewoye et al., 2009) and STZ-induced diabetic rats singly and in combination with the leaves of <i>Coccinia indica</i> (Mallick et al., 2007) <sup>§</sup> ; as well as <i>in vivo</i> antioxidant effects. Dose dependent hypoglycaemic effect of the methanol extract of the mature fruits in normal and STZ-induced diabetic mice (Ojewole and Adewunmi, 2003)	Anemia, Hypertension, Ulcers	Fruit	As a meal, Juice extract		14 $\alpha$ -methyl cyclo-5 $\alpha$ -ergost-24(28)-en-3 $\beta$ -ol (Knapp et al., 1972); $\alpha$ -glucan phosphorylase (Singh and Sanwal, 1975); Cycloeucaenol, 24-methyl cycloartanol, 31-nor cyclo laudenone, Trimethyl-5 $\alpha$ -cholesta-dien-3 $\beta$ -ol (Dutta et al., 1983); Sitoindoside I, II, III and IV, Sitosterol gentiobioside, Myo-inositol- $\beta$ -D-glucoside, Sitosterol, Campesterol, Cycloartenol, Citrostadienol, Palmitic, Lauric, Myristic, Linoleic, Linolenic and Oleic acids; 24-ethylphenol (Ghosal, 1985); Irenolone, Emenolone (Luis et al., 1993); Leucocyanidin, Leuco-anthocyanidin (Lewis et al., 1999); Polyphenol oxidase (Yang et al., 2000); Rel-(3S,4aR,10bR)-8-hydroxy-3-(4-hydroxy phenyl)-9-methoxy tetra hydro naphthopyran, 1,2-dihydro-trihydroxy-9-(4-methoxy phenyl) phenalene, Hydroxy anogorufone, 2-(4-hydroxyphenyl) naphthalic anhydride, 1,7-bis(4-hydroxy phenyl) hepta-4(E),6(E)-dien-3-one (Jang et al., 2002)	Polyvalent cations present in the plant has been shown to form non-absorbable complexes with quinolone antibiotics, thus affecting their pharmacokinetics if co-administered (Nwafor et al., 2003)

Table 1 (continued)

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82	<i>Ocimum gratissimum</i> L.	Lamiaceae	Scent leaf, African basil, Mint	Nchonwu (I), Efirin (Y), Daidoya (H)	SE, SS, SW <sup>a</sup> , NW	200 mg/kg aqueous extract of the leaves improved glucose tolerance in normal and neonatal STZ-induced diabetic rats (Oguanobi et al., 2012) <i>In vitro</i> antioxidant effects (Akinmoladun et al., 2010) (Awah and Verla 2010) 400 mg/kg methanol extract of the leaves decreased blood glucose levels in normal and alloxan-induced diabetic rats (Aguiyi et al., 2000) 150 ml of a (1:1:1) decoction mix of the leaves of <i>Vernonia amygdalina</i> , <i>Ocimum gratissimum</i> and <i>Gongronema latifolium</i> decreased baseline blood glucose levels in normal subjects when preadministered to normal subjects 45 min before an OGTT (Ejike et al., 2013)	Diarrhoea, Malaria, Anti-microbial, Anti- parasitic, Anxiolytic, Analgesic, Inflammation, Wound healing, Cold symptoms, Hemorrhoids, Insect repellent, Anti- helminthic, Infant colic	Leaves	Infusion, Food vegetable		Oleanolic acid (Njoku et al., 1997); Xanthomicrol, Cirsimaritin, Rutin, Kaempferol 3-O-rutinoside, Luteolin 5-O- and 7-O-glucosides, Vicenin-2, Isothymusin, Apigenin 7-O-glucoside, Vitexin, Isovitexin, Quercetin 3-O-glucoside (Grayer et al., 2000); Thymol, Eugenol, Luteolin, Cirsiliol, $\alpha$ -Camphene, <i>p</i> -Cymene, 1,8-Cineole, Geraniol, $\gamma$ -Caryophyllene, $\gamma$ -terpinene, $\gamma$ -terpineol, Terpinolene, $\alpha$ -Copaene, Methylchavicol, Anisole, $\gamma$ -Selinene, $\gamma$ -Murolene, Spathulenol (Vieira et al., 2001); Caffeic acid, Cichoric acid, Rosmarinic acid, Caffeoyl derivatives, Nevadensin (Ola et al., 2009)	Aqueous and ethanol extract of the leaves caused dose-dependent (400–3200 mg/kg) increase in AST and ALT enzyme levels, markers of hepatotoxicity (Ajibade et al., 2012; Onaolapo and Onaolapo, 2012)
83	<i>Parinari curatellifolia</i> Planch, ex Benth.	Chrysobalanaceae	Mobola plum	Ebere (Y)		Significant blood glucose lowering effects of 250 mg/ kg of the aqueous ethanolic extract of the seeds in alloxan-induced diabetic rats (Ogbonnia et al., 2008b)	Malaria, Dysentery, Epilepsy, Toothache, STDs, Anti-cancer	Seeds, Root- bark			15-Oxozaopatin and its 13-methoxy and 13-hydroxy derivatives (Lee et al., 1996); Quercetin-3-O-arabinoside, Quercetin-3-O-glucosyl galactoside, Quercetin-3-O-rhamnoside, Kaempferol-3,4-di-O-glucoside and glycoside, Kaempferol-3-O-glucoside, Quercetin-3-O-rutinoside, Kaempferol-3-O-rutinoside, Myricetin-3-O-rhamnoside, Myricetin-3-O-galactoside (Coradin et al., 1985)	
84	<i>Parkia biglobosa</i> (Jacq.) G.Don	Leguminosae	African locust beanSoumbala	Iru (Y), Ugba (I), Dawadawa (H)	SW	Diet supplementation with the aqueous and methanolic extract of the seeds (6 g/kg) resulted in > 60% decrease in fasting blood glucose levels in alloxan-induced diabetic rats (Odetola et al., 2006)	Hypertension, Analgesic, Inflammation, Anti- microbial, Snake venom, Fevers, Diarrhoea, Anti- plasmodial, Anti- helminthic	Leaves, Root, Bark	Infusion		Epicatchin, Gallocatchin-O-glucuronide, Catechin-O-gallate-O-glucuronide and other catechin derivatives (Tala et al., 2013); Homogalacturonan, Arabinogalactan, Rhamnogalactans and Xylogalactans (El-Zoubair, 2010); Pyrazine derivatives, Dimethyl disulfide and trisulfide, Limonene, 2-Pentyl furan, Trimethyl oxazole, Indole, Methyl isothiazole, 4,4-Dihydro-2-methyl	

Table 1 (continued)

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85	<i>Persea americana</i> Mill.	Lauraceae	Avocado pear, Alligator pear	Ube bekee or Ube oyibo (I), Igba or Apoka or Ipia (Y), Eben mbakara (Ef), Piya (H)	SE, SS	Administration of 10 mg/kg aqueous extract of the leaves for 8 weeks decreased plasma glucose levels of rats fed a high-cholesterol diet (Brai et al., 2007) Hypoglycaemic effect of the aqueous extract of the seeds in normal and alloxan-induced diabetic rats and protective effect on pancreatic islet cells (Edem et al., 2009)	Anemia, Analgesic, Anti- microbial, Hypertension, High cholesterol, Inflammation, Convulsions, Wound healing, Gastric ulcer, Arthritis, Cough, Insecticidal	Seeds, Leaves, Root, Bark, Fruit			thiazole, Trimethyl pyrazole, (Ouoba et al., 2005); Ferulic acid, Isoferuloyl alkanoyl glycerol, Feruloyl lignoceryl glycerol, Lupeol, Epicatechin-3-O-gallate, Epigallocatechin-3-O- gallate, 4-O-methyl-epi- gallocatechin, Epigallocatechin (Tringali et al., 2000) Epi-dihydrophaseic acid $\beta$ - D-glucoside, Hydroxy abscisic acid $\beta$ -D-glucoside, (del Refugio Ramos et al., 2004); 1,2,4-trihydroxy nonadecane derivatives, 1,2,4-trihydroxy heptadec- 16-ene and heptadec-16- yne derivatives (Abe et al., 2005); Persin ((Z,Z)-1- (acetyloxy)-2-hydroxy- 12,15-heneicosadien-4- one) (Oelrichs et al., 1995) $\alpha$ - and $\beta$ -pinene, Sabinene, $\alpha$ - and $\beta$ -cubebene, $\beta$ - caryophyllene, Valencene, $\alpha$ -humulene, Germacrene D, cis- $\gamma$ - and $\delta$ -cadinene, Caryophyllene oxide, Spathulenol (Ogunbinu et al., 2007) Geraniin, Amariin, Amarulone, Corilagin, 1,6- digalloylglucopyranose, Quercetin-3-O- glucopyranoside, Gallic acid, Rutin, Galocatechin, (Foo, 1993); Amariin acid, 1-O-galloyl-2,4- dehydro hexahydroxy diphenoyl glucopyranose elaecarpusin, Geraniin acid B, Repandusin acid A, Phyllanthusin D (Yeap Foo, 1995); Astragalin, Phyllanthin, Hypo- phyllanthin. Quercetin (Rajeshkumar et al., 2002); Ursolic acid, Oleanolic acid, Dotriacontanyl docosanoate, Triacantanol (Ali et al., 2006)	Ethanol extract of the leaves inhibited the activity of Cyp3A4, 3A5 and 3A7 enzyme supersomes (Agbonon et al., 2010)
86	<i>Phyllanthus amarus</i>	Phyllanthaceae	Pick-a-back, Stone breaker, Carry me seed, Black catnip	Eyin olobe (Y)	SW	Antioxidant effects of constituents (Londhe et al., 2008) $\alpha$ -amylase inhibitory effects (Ali et al., 2006) Aqueous extract of the seeds and leaves showed a dose- dependent (150–600mg/kg) decrease in fasting blood glucose levels of normal rats (Adeneye et al., 2006) Dose dependent (200–1000 mg/ kg) decrease in blood sugar levels by methanol extract in alloxan-induced diabetic rats (Raphael et al., 2002) <sup>§</sup> No evidence of a hypoglycaemic effect was observed with NIDDM patients taking 25 g of the powdered extract daily for 1 week as a substitute to their oral hypoglycaemic drugs (Moshi et al., 2001) <sup>§</sup>	Fevers, Ringworm, Gonorrhoea, Cancer, Anti-viral, Diuretic, Hypertension, Anti- microbial, Diarrhoea, Inflammation, Analgesic, Dropsy, Jaundice, Hepato- protective, Gastric ulcers, Kidney disorders	Whole plant	Decoction			Aqueous and Ethanol extracts of the aerial parts of the plant inhibited the activity of Cyp3A4, 3A5 and 3A7 enzyme supersomes (Agbonon et al., 2010) Aqueous extract of the whole plant inhibited the activity of Cyp 1A2, 2C9, 2D6 and 3A4 plasmids as well as GST enzyme in rat and human liver cytosols (Appiah-Opang et al., 2008) The inhibitory effect on Cyt P450 enzymes was also observed with the methanol extract and confirmed <i>in vivo</i> (Hari Kumar and Kuttan, 2006)
87		Apocynaceae	Akuamma plant	Abere (Y), Osu-igwe,		Hypoglycaemic effect of the glycosidic fraction (250mg/	Hypertension, Anesthesia, Malaria,		Infusion	Akuammicine isolated from the	Pseudo-akuammidine, Akuammiline,	400 mg/kg of the stembark extract

Table 1 (continued)

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	<i>Picralima nitida</i> (Stapf) T.Durand and H.Durand			Mkpokiri or Otosu (I)	SW, SE, NW, NC, SS	kg) of the methanol extract of the leaves in normal and alloxan-induced diabetic rats (Okonta and Aguwa, 2007) 300 mg/kg hydro-ethanol extract of the leaves decreased blood glucose levels in STZ-induced diabetic mice and <i>In vitro</i> antioxidant effects (Teugwa et al., 2013b) <sup>§</sup>	Jaundice, Pneumonia, AsthmaTrypanosomiasis	Stem-bark, Seeds, Root, Fruit rind		chloroform extract of the seeds stimulated glucose uptake in 3T3-L1 adipocytes (Shittu et al., 2010)	Melinisime, Akuammine, Picracine, Akuammidine, Picra-phylline, Akuammigine, Akuammicine (Oliver- Bever, 1986); Alstonine, Picranitidine, Picratidine, Picraline, $\psi$ -akuammigine (Okunji et al., 2005); 10- deoxyakuammine, Burnamine (Shittu et al., 2010); Coumesan glycoside (Jacques et al., 2011)	produced hepato-toxic effects characterized by necrotic damage congestion of hepatic blood vessels (Fakeye et al., 2004) Methanol extract of the fruit rind administered daily for 6 weeks elevated AST, ALT and GSH levels in rats (Kouitcheu Mabeku et al., 2008)
88	<i>Rauvolfia</i> <i>vomitorea</i> Afzel.	Apocynaceae	African or Indian snakeroot	Asofeyeje (Y), Akanta (I), Wadda (H)	SW, SS	875 mg of a mix of extracts of the fruit and <i>Rauvolfia</i> <i>vomitorea</i> foliage (RC tea) decreased serum glucose levels in diabetes type 2 model db/db mice and also decreased tissue lipid accumulation (Campbell et al., 2006) In a pilot clinical study in type-2 diabetic patients, RC tea given daily for 4 months decreased post prandial and fasting plasma glucose levels with greater effects seen in patients with HbA1c levels < 7.3% (Campbell-Tofte et al., 2011)	Mental disorders, Sedative, Hypertension, Snake bites, Skin infections, Anti- parasitic, Oral infections, Rheumatism, Aphrodisiac, Purgative	Root, Stem, Stem-bark, Leaves	Decoction, Maceration, Powdered root	<i>In silico</i> prediction of isosandwichine and ajmaline as potential DPP-IV inhibitors (Guasch et al., 2012)	Lupeol, Ursolic acid, $\beta$ - stigmasterol, Betulinic acid, Sitosterol, Palmitic acid, 3 $\beta$ -hexadecanoyloxy- lupeol (Fannang et al., 2011); Reserpine, Yohimbine, Ajmaline, Ajmalicine, Alstonine, Serpentine Apigenin rhamnoside, Naringin (Campbell-Tofte et al., 2011)	
89	<i>Sarcocephalus</i> <i>latifolius</i> (Sm.) E. A.Bruce, Syn: <i>Nauclea latifolia</i>	Rubiaceae	African peach	Ubulu inu (I)	SE, NW	200 mg/kg aqueous extract of the leaves decreased blood glucose levels in alloxan- induced diabetic rats but not normal rats (Gidado et al., 2005) Anti-hyperglycaemic effect of 200 mg/kg ethanol extract of the leaves preadministered to rats prior to the oral or intraperitoneal administration of 2 g/kg glucose and alpha glucosidase inhibitory effects (Gidado et al., 2012) Hypoglycaemic effect in alloxan-induced diabetic rats and increased activity of glucose metabolising enzymes (Iwueke and Nwodo, 2008) <i>In vitro</i> antioxidant effects (Awah et al., 2012)	Malaria, Anti-parasitic, Anti-infective, Hypertension, Jaundice, Infertility	Root, Bark, Leaves	Maceration		Strictosamide, 21-O- methyl strictosamide aglycone, 21-O-ethyl strictosamide aglycone, Angustine, Nauclefine, Angustidine, Angustoline, 19-O-ethyl angustoline, Naucleidinal, 19-epi- naucleidinal, Quinovic acid-3 $\beta$ -O- $\alpha$ -L-rhamno pyranoside, Quinovic acid- 3 $\beta$ -O- $\beta$ -D-fucopyranoside, Scopoletin, $\beta$ -Sitosterol (Abreu and Pereira, 2001); Penta-O-benzoyl- $\alpha$ -D- fructo furanose, Penta-O- benzoyl- $\beta$ -D-fructo furanose, Penta-O- benzoyl- $\beta$ -D-fructo pyranose, Tetra-O- benzoyl- $\beta$ -D-fructo pyranose, $\alpha$ - and $\beta$ -D- pyranose forms of glucose, xylose and arabinose perbenzoates, Glycerol and D-Erythriol	Strictosamide binds to human serum albumin, which could in turn affect the bio- availability of highly protein bound drugs if co-administered (Pu et al., 2013)



Table 1 (continued)

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90	<i>Scoparia dulcis</i> L.	Plantaginaceae	Sweet broomweed	Roma-fada (H), Aiya (I), Mesen- mesen gogoro (Y)Ndiyang (Ef) Bibimbelemono (Ij)	NC	Administration of the aqueous extract of the leaves for 45 days produced a dose dependent (150–450 mg/kg) decrease in glucose levels after an OGTT; as well as a hypoglycaemic effect in alloxan-induced diabetic rats. (Pari and Venkateswaran, 2002) <sup>§</sup> 200 mg/kg aqueous extract of the whole plant also produced a hypoglycaemic effect in STZ-induced diabetic rats, increased plasma insulin levels and protected against diabetes induced oxidative stress (Latha and Pari, 2004; Latha et al., 2004) <sup>§</sup> A flavonoid rich fraction of the aqueous extract of the aerial plant increased glucose uptake in cells possibly by increasing expression and translocation of the GLUT4 receptor (Beh et al., 2010) <sup>§</sup>	Anti-infective, HIV, Abortifacient, Sick cell, InflammationAnalgesic, Anti-tumour, Bronchitis, Hypertension, Gastric disorders, Sedative	Leaves, Whole plant	Infusion, Decoction		perbenzoates, Tetra-O- benzoy-fructo furanoside (Abreu et al., 2001); Betulinic acid (Yinusa et al., 2012) Scoparol (3'-O-methyl luteolin), Scoparoside (glycosyl scopanol), Amellin (Oliver-Bever, 1986); Scoparic acid A, B and C, Scopadulcic acid A and B (Hayashi et al., 1988)	
91	<i>Securidaca longipedunculata</i> Fresen	Polygalaceae	Violet tree, Rhodesian violet	Ipeta (Y), Sanya or Uwar magunguna (H), Ezeogwu (I)	SW, NE, SE	An extract of the root in buffer solution produced slight inhibition of $\alpha$ -amylase activity <i>in-vitro</i> (Funke and Melzig, 2006) Dose- dependent (50–800 mg/kg) hypoglycaemic effect of the aqueous root bark extract in normal and STZ-induced diabetic rats (Ojewole, 2008)	Erectile dysfunction, Arthritis, Tumours, Cough, Inflammation, Anti-pyretic, Analgesic, Pesticide, Anti- microbial, Convulsions	Root, Stem- bark Leaves, Seeds	Decoction, Tinctures, Infusions, Powders		Scopadulin (Hayashi et al., 1990); Scoparinol, Dulcinol, Benzoxazolinone, Betulinic acid, scutellarin, Sorbifolin (Ahmed and Jakupovic, 1990); Scopadulciol, Glutininol, Acacetin, 6-methoxy benzoxazoline (Hayashi et al., 1991); Adrenaline, Noradrenaline (Freire et al., 1996); Iso-dulcinol, Dulcidiol, 4- <i>epi</i> - scopadulcic acid B, Scopanlal, Scopadiol (Ahsan et al., 2003); $\beta$ - sitosterol- $\beta$ -D-gluc; side, Friedelan-3-one, Hispidulin (4,5,7- trihydroxy-6-methoxy flavone) (Osei-Safo et al., 2009); Luteolin, P-coumarin, Apigenin, Quercetin (Beh et al., 2010); Dulcinodal, Dulcinodiol, Scopadiol decanoate, (Ahsan et al., 2012) Benzyl salicylate, Methyl paraben, Methyl vanillate, Methyl 2,6-dihydroxy benzoate, Lumiflavin (Costa et al., 1992); Methyl salicylate (Methyl-2- hydroxy benzoate), Methyl-2-hydroxy-6- methoxybenzoate, Benzyl- 2-hydroxy-6-methoxy benzoate (Jayasekara et al., 2002); Securidaca xanthone (1,5-dihydroxy- 2,3,6,7,8-penta	Nephrotoxic and hepatotoxic effects in rats administered 2 mg/ kg aqueous extract intra-peritoneally for 14 days (Dapar et al., 2007) Elevated levels of serum alkaline and acid phosphatase levels as well as decreased levels of antioxidant enzymes such as GSH and SOD in the liver and kidney (Ajiboye et al., 2010)

Table 1 (continued)

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92	<i>Secamone afzelii</i> (Roem. and Schult.) K.Schum.	Apocynaceae	Secamone, Ringworm plant	Ailu (Y)	SW	<i>In vitro</i> antioxidant effects (Mensah et al., 2004)	Hemorrhoids, Anti- microbial, Purgative, Dysentery, Colic, Wound healing, Aphrodisiac, Measles, STDs	Leaves, Pods, Stems, Whole plant	Maceration		methoxyxanthone), 2-hydroxy-1,7-dimethoxy xanthone, 1,6-dihydroxy xanthone, 6-methoxy salicylic acid and its methyl ester, $\beta$ -D-(6- sinapoyl)- glucopyranoside, $\beta$ -D-(3- sinapoyl)-fructofuranosyl- $\alpha$ -D-(6-sinapoyl)-gluco pyranoside (Meli Lannang et al., 2006); Methyl salicylate, $\alpha$ - and $\beta$ -pinene, 1,8-cineole, $\alpha$ -cadinol, p-cymene, ethyl salicylate (Adebayo et al., 2007); 1,4- dihydroxy-7-methoxy xanthone, Senegenic acid, Senegenin, Elymoclavine, Dehydroelymoclavine, 4,5- di-O-caffeic acid, 3,4,5-tri- O-caffeoyl quinic acid, Sinapic acid (Meyer et al., 2008); Securidacaside A and B (Stevenson et al., 2009); Gallic acid, Chlorogenic acid, Caffeic acid, Epicatechin, P-coumaric acid, Rutin, Quercetin, Cinnamic acid, Apigenin (Muanda et al., 2010) Alpha tocopherol (Mensah et al., 2004); Caffeic, Gentysic, Ferulic, Chlorogenic, $\alpha$ -resorcylic, Syringic, Protocatechuic, Homoprotocatechuic, p-hydroxyphenylacetic, p-hydroxybenzoic, Synapic, Vanillic, Coumaric, O-hydroxyphenylacetic and Salicylic acids (Nowak and Kawka, 1998)	
93	<i>Senna alata</i> (L.) Roxb., Syn. <i>Cassia</i> <i>alata</i> (L.)	Leguminosae	Ringworm plant, Candle bush	Asunwon oyibo (Y)	SW	De-fatted methanol extract of the leaves gave a slight dose- dependent (100–400 mg/kg) decrease in blood glucose levels in STZ-induced diabetic rats but not in normal rats (Palanichamy et al., 1988) <sup>§</sup>	Purgative, Ringworm, Eczema, Pruritus, Snake bites, Analgesic, Constipation, Hypertension, Anti- infective, Inflammation	Leaves, Flower, Root, Stem, Bark	Decoction, Juice extract	Alpha glucosidase inhibitory effects of the flavonoids kaempferol and its 3-O-gentiobioside isolated from the methanol extract of the leaves (Varghese et al., 2013)	Linalool, $\alpha$ -terpineol, Borneol, Pentadecanal, $\beta$ - sitosterol, Stigmasterol, Daucosterol, Alarone, 2,6- dimethoxy benzoquinone, Dalbergin, 2,3,7 tri-O- methyl ellagic acid, Torachryson, Alatonal, p- hydroxybenzoic acid, Adenine, Cassiaxanthone, Sennosides, Kaempferol, its 3-O-gentiobioside and	0.5 mg/ml aqueous extract of the leaves showed > 70% inhibition of GST enzymes in human and rat liver cytosols and recombinant GSTs; as well as inhibited Cyp 1A2, 2D6 and 3A4 supersomes but not 2C9 (Appiah-Openg et al., 2008).

Table 1 (continued)

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94	<i>Senna occidentalis</i> (L.) Synonym, ( <i>Cassia occidentalis</i> )	Leguminosae	Coffee senna	Sanga-sanga or Rai dore (H), Rere (Y), Akede-agbara (I)	NW, SW	<i>In vitro</i> antioxidant effects (Akinmoladun et al., 2010) Incorporation of the dry leaves 6.25% by weight into the diet of STZ-induced diabetic mice did not produce any hypoglycaemic effect after 9 days of treatment (Swanston-Flatt et al., 1989) <sup>§</sup> Hypoglycaemic effect of 200 mg/kg aqueous extract of the leaves was observed in both normal and alloxan-induced diabetic rats, as well as partial restoration of the islet cells of the diabetic rats (Verma et al., 2010) <sup>§</sup>	Inflammation, Anti- pyretic, Analgesic, Purgative, Malaria, Anti- tumour, Anti-microbial, Hepato-protective, Insecticidal, GIT ailments	Leaves, Pods, Seeds	Decoction		3-O- $\beta$ -D-glucopyranoside, Luteolin, Chrysoeriol-7-O- and Rhamnetin-3-O- (2"- O- $\beta$ -D-manno pyranosyl)- $\beta$ -D-allopyranoside, Aloe- emodin and its 8-O- $\beta$ - glucoside, Chrysophanol, Rhein, Physcion and its 1- O-glucoside, Alquinone, Isochrysophanol, Adenine, 1,3,8-trihydroxy-2-methyl anthraquinones (Hennebelle et al., 2009); Naringin, Apigenin (Okpuzor et al., 2009)	Ingestion of the seeds (beans) has been shown to cause acute hepato- myoencephalopathy in children and is also known to be toxic to animals (Vashishtha et al., 2009) Possible risk of renal impairment with chronic administration of anthraquinones glycosides from senna (Vanderperren et al., 2005)
95	<i>Senna singueana</i> (Delile) Lock, Syn: <i>Cassia</i> <i>goratensis</i>	Leguminosae	Golden shower	Runfu (H)		200 mg/kg aqueous extract of the leaves decreased blood glucose levels by 53% in alloxan-induced diabetic rats (Etuk and Mohammed, 2009)	Inflammation, Analgesic, Malaria, Gonorrhea, Heartburn, Convulsions, Constipation, Wound	Root, Leaves	Decoction		Torosachrysone, 7-methyl physcion, Germichrysone, Cassiamin A, Singueanol-I and II, Chrysophanol, Cassiamin A, Lupeol,	

Table 1 (continued)

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96	<i>Solanum aethiopicum</i> L., misnamed <i>Solanum incanum</i> L.	Solanaceae	Garden egg	Osun (Y), Anara (I)	SE, SW	The root and fruit extracts (200 mg/kg) decreased blood glucose levels in both normal and STZ-induced diabetic rats. In addition, the fruit extract decreased weekly food consumption (Musabayane et al., 2006) Administration of 50 g of the leaves to normal volunteers prior to an oral glucose tolerance test produced a decrease in blood glucose levels (Okolie et al., 2009)	ulcers, Snake bites, Skin cancer  Convulsions, Colic, Flatulence, Syphilis, Hypertension, Anti-fungal, STDs, Hepatitis	Leaves, Fruit, Roots	Infusion, Juice extract		Campesterol, $\beta$ -sitosterol, Stigmasterol, Leucopelargonidin (Gebrelibanos, 2012) Diosgenin, Yamogenin (Gbile and Adesina, 1988) Solasodine, Solamargine, Solasonine, Ursolic acid, Carpesterol, $\beta$ -sitosterol, Incanumine, Stigmasterol- $\beta$ -D-glucoside, Khasianine (Lin et al., 1990) Chlorogenic acid, Trans-p-coumaric acid, Astragalin, Kaempferol, Quercetin, Isoquercitrin, Adenosine, Caffeic and Protocatechuic acids, Luteolin-7-O- $\beta$ -D-glucopyranoside, Benzyl O- $\beta$ -D-xylopyranosyl- $\beta$ -D-glucopyranoside, Kaempferol glucosides, Isorhamnetin glucosides, Quercetin glucosides (Lin et al., 2000b) Solavetivone, Lubiminoic acid, Lubimin, Lubiminol, Aethione (Nagaoka et al., 2001) Aethiosides A–C (Tagawa et al., 2003)	
97	<i>Solanum melongena</i> L.	Solanaceae	African Eggplant, Aubergine	Igbagba or Igba ijesu (Y), Mafowo- bomonu (I)	SW, SS	<i>in vivo</i> antioxidant effects (Sudheesh et al., 1999) Low $\alpha$ -amylase but high $\alpha$ -glucosidase inhibitory effects and <i>In vitro</i> antioxidant effects (Nwanna et al., 2013)	Cholesterol, Anti-viral, Sedative, Analgesic, Fevers, Rheumatism, Skin diseases, Digestive tonic	Leaves, Fruit	Soup condiment, Juice extract		Polyphenol oxidase (Fujita and Tono, 1988); Solanidine (Keeler et al., 1990); Delphinidin (Nagase et al., 1998); $\alpha$ -solasoline, $\alpha$ -solamargine (Sánchez-Mata et al., 2010)	Possible inhibitory effect of steroidal alkaloids like solanidine on drug transport due to interaction with multi-drug resistant protein such as P-gp (Lavie et al., 2001)
98	<i>Sorghum bicolor</i> (L.) Moench, ( <i>Sorghum caudatum</i> )	Poaceae	Sorghum	Okababa or Poroporo (Y), Sorgum (I), Jero (H)	SW	<i>In vitro</i> protein glycation inhibitory effects (Farrar et al., 2008) <sup>§</sup> Alpha amylase and $\alpha$ -glucosidase inhibitors (Kim et al., 2011) <sup>§</sup> 250 mg/kg sorghum extract decreased serum glucose and increased serum insulin levels in diabetic but not normal rats (Chung et al., 2011) <sup>§</sup> <i>In vitro</i> antioxidant effects (Afify et al., 2012) Improved insulin sensitivity due to increased expression of PPAR $\gamma$ receptors in rats fed a high fat diet followed by 0.5% and 1% sorghum meal (Park et al., 2012) <sup>§</sup>	Malaria, Fevers, Anemia, Anti-microbial	Leaves, Shaft	Maceration, Infusion		Procyanidin B1, Sinapic acid, Epicatechin gallate, Peonidin, Prodelphinidin, Luteolinidin, Fisetinidin, Pelargonidin, Cyanidin and Apigeninidin derivatives, Gallic, Caffeic, Gentisic, Chlorogenic, Syringic, <i>p</i> -hydroxy benzoic, Ferulic acids, Luteoforol, Apiforol, Luteolin, Naringenin, Eriodictoyl, Taxifolin, Sitosterol, Stigmasterol, Campesterol, Cholesterol (Awika and Rooney, 2004); Benzoic, <i>p</i> - <i>o</i> - and <i>m</i> -coumaric, $\beta$ -resorcylic, Protocatechuic, Veratric, Vanillic, Homogentisic and	

Table 1 (continued)

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99	<i>Sphenocentrum jollyanum</i> Pierre	Menispermaceae		Akerejupon (Y)	SW, SE	<i>In vitro</i> (Nia et al., 2004) and <i>in vivo</i> antioxidant effects (Olorunnisola and Afolayan, 2013) Ethanol extract of the root decreased blood glucose levels in normal high glucose fed and alloxan-induced diabetic rabbits (Mbaka et al., 2009) Pre-administration of the aqueous extract of the roots for 7 days before induction of diabetes with alloxan had a protective effect against elevated sugar level and β-cell degeneration (Mbaka and Adeyemi, 2011)	Hypertension, Cough, Wounds, Fevers, Jaundice, Malaria, Emetic, Purgative, Aphrodisiac, Swollen breasts, Inflammation, Depression, Sickle cell, Anti-microbial, Analgesic, Anti-cancer, Anti-helminthic, Aphrodisiac, Constipation	Root, Seed, Stem-bark, Fruit, Leaves		<i>t</i> -cinnamic acids, Vanillin, Pyrogallol, Resveratrol, Hesperidin, Rutin, Myricetin, Hesperetin, Formononetin, Quercetin, Biochanin A, Naringin (Chung et al., 2011); β- carotene, α-tocopherol, Apigenin, Kaempferol, Hypersoid, Catechin, Christin (Afify et al., 2012) Palmatine, Columbamine (Raji et al., 2006); Columbin, Isocolumbin, Fibleucine (Moody et al., 2006); Isocaryophyllene, α-Pinene, α-Eudesmol, 1,8- cineole (Aboaba and Ekundayo, 2010)	Extract of the leaves decreased the elevated levels of liver AST, ALT and ASP enzymes as well as increased GSH levels in rats infected with plasmodium (Olorunnisola and Afolayan, 2013)	
100	<i>Spondias mombin</i> L.	Anacardiaceae	Hog plum	Iyeye or Olosan (Y), Tsada (H), Ngulungwu or Isikara (I)	SW	Hypoglycaemic effect of the methanol extract (1g/kg) of the leaves and its chloroform fraction was observed in glucose loaded (2 g/kg) and alloxan-induced diabetic rats (Fred-jaiyesimi et al., 2009b) <i>In vitro</i> antioxidant effects (Akinmoladun et al., 2010)	Infertility, Child birth, Abortifacient, Inflammation, GIT disorders, Psychosis, Laxative, Anti-infective, Diuretic, Lactation, Anxiety	Leaves, Fruit	Decoction		Geraniin, Galloyl geranin, Chlorogenic acid, 2-O- caffeoylhydroxycitric acid (Corthout et al., 1992); Pelandjuaic acid, 6-(8'Z, 11'Z-heptadecadienyl)- salicylic acid, 6-(10'Z- heptadecenyl)-salicylic acid, 6-(12'Z-nona- decenyl)-salicylic acid, 6- (15'Z-heneicosenyl)- salicylic acid (Corthout et al., 1994); Anacardic acid derivative (Coates et al., 1994); 3β-olean-12-en-3- yl (9Z)-hexadec-9-enoate, α-sitosterol (Fred- Jaiyesimi et al., 2009a) Ipolamide (Poser et al., 1997); Stachytarphine, β- (3',4')-dihydroxyphenyl)- ethyl-O-α-L- rhamnopyranosyl-(1,3)-β- D-(4-O-caffeoyl)- glucopyranoside (Mohammed et al., 2012a, 2012b)	
101	<i>Stachytarpheta angustifolia</i> (Mill.) Vahl	Verbenaceae		Ncha aji (I), Wutsiya bera (H), Iru alangba (Y)	SE, SW, NW	750 mg/kg aqueous extract decreased blood glucose levels in normal and alloxan- induced diabetic rats (Isah et al., 2007) 250 mg/kg of a herbal mixture (Okudibet <sup>®</sup> ) made up of bark of <i>Alstonia congensis</i> , aerial parts of <i>Stachytarpheta angustifolia</i> and fruits of <i>Xylopia aethiopica</i> administered for 30 days produced a hypoglycaemic effect in	Immune modulatory, Anti-microbial, Diarrhoea, Abortifacient, Skin ulcers, Rheumatism, Cataract, Ear sores, Gonorrhea	Leaves	Maceration			

Table 1 (continued)

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102	<i>Strophanthus hispidus</i> DC.	Apocynaceae	Poison arrow vine, Brown/ hairy strophanthus	Sagere (Y), Aguru-ala or Osisi nke aguru (I), Kwan-kwani (H)	SW, SE, NW, NC	alloxan-induced diabetic rats (Ogbonnia et al., 2010) <i>In- vitro</i> antioxidant effects (Awah et al., 2010) Administration of 2 mg and 5 mg of various extracts of the plant produced a dose dependent decrease in blood glucose levels in normal rabbits (Ojiako and Igwe, 2009)	Cardio-stimulant, Snake bites, Insecticidal, STDs, Inflammation, Constipation	Stem, Root, Leaves	Decoction		Strophanthidin, Cymarín, Cymarol, Strophanthidol, Periplogenin, Emicymarin, (Heftmann et al., 1954); 9-hydroxyoctadec-12- enoic acid, Triglycerides, 2-mono glyceride (Gunstone and Qureshi, 1968)	
103	<i>Syzygium guineense</i> (Willd.) DC.	Myrtaceae	Snake bean treeWater berryWater pear	Malmo (H), Adere (Y), Ori (I), Mho (Ti), Asurahi (F)	SW, NW	The hypoglycaemic effect of the butanol fraction of the aqueous extract of the leaves decreased blood glucose levels in normal and alloxan- induced diabetic rats (Worku, 2009) <sup>§</sup>	Hypertension Cardio- protective, Anti- microbial, Diarrhoea, Inflammation, Immune- modulatory, venom, Anti-cancer	Seed, Stem, Leaves	Decoction		Arjunolic acid, Ursolic acid, Asciatic acid, Terminolic acid, Betulinic acid, Oleanolic acid, 2-hydroxy oleanolic acid, 2-hydroxy ursolic acid, 6-hydroxy asiatic acid, Arjunolic acid 28- $\beta$ -gluco pyranosyl ester, Asiatic acid 28- $\beta$ -glucopyranosyl ester (Djoukeng et al., 2005) Caryophyllene oxide, Benzyl benzoate, $\alpha$ - terpineol, Linalool, $\alpha$ and $\beta$ caryophyllene, $\alpha$ -cadinol, (Noudogbessi et al., 2008) Arabinogalactan-type pectic polysaccharides (Ghildyal et al., 2010)	
104	<i>Tamarindus indica</i> L.	Leguminosae	Tamarind, Indian date	Tsamiya (H), Icheku oyibo (I), Ajagbon (Y), Tamsugu (Nu)	NW	<i>In vitro</i> (Siddhuraju, 2007) and <i>in vivo</i> antioxidant effects (Bhutkar and Bhise, 2011) 800 mg/kg of the aqueous extract of the seed administered for 14 days decreased blood glucose levels and increased serum insulin levels in STZ-induced diabetic rats, resulting in increased glucose metabolism (Maiti et al., 2005) <sup>§</sup> An extract of the leaves in buffer solution produced 90% inhibition of $\alpha$ -amylase activity <i>in-vitro</i> (Funke and Melzig, 2006)	Nutritional, Inflammation, Anti- microbial, Anti- parasitic, Fevers, Laxative, Alcohol detox, Anti-cancer, Anti- obesity, Hepato- protective	Stem-bark, Fruits, Seed	Decoction, Maceration, Powder		Methyl 3,4-dihydroxy benzoate, Epicatechin, 3,4- dihydroxy phenylacetate, 2-hydroxy-3',4'-dihydroxy acetophenone (Tsuda et al., 1994); Methyl salicylate, Eugenol, Vanillin; Lauric, Benzoic, Acetic, Myristic, Oleic, Linoleic, Linolenic and Palmitoleic acids (Wong et al., 1998); Apigenin, Eriodictyol, Narigenin, Procyanidin B <sub>2</sub> , Taxifolin, Procyanidin trimer, tetramer, pentamer and hexamer; Luteolin (Sudjaroen et al., 2005); Apigenin, Vitexin, $\beta$ - sitosterol, (+)-Pinitol, 21- oxobehenic and Eicosanoic acid, Octacosanoyl ferulate, <i>n</i> -hexacosane (Jain et al., 2007); Lupeol,	100 and 200 mg/kg ethanol extract of the bark administered for 45 days increased previously depleted GSH levels in alloxan- induced diabetic rats (Bhutkar and Bhise, 2011) Bioavailability of aspirin increased in healthy adults co- administered a porridge meal containing the fruit extract of tamarind (Mustapha et al., 1996)

Table 1 (continued)

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105	<i>Tapinanthus bangwensis</i> (Engl. and K. Krause) Danser, Syn <i>Loranthus bangwensis</i> Engl. and K.Krause, often misnamed <i>Loranthus micranthus</i> Hook.f.	Loranthaceae	African mistletoe		SW, SE	An infusion of the leaves parasitic on <i>citrus limon</i> and <i>Psidium guajava</i> at a dose of 1.32mg/kg decreased blood glucose levels in normal and STZ-induced diabetic rats, but not that parasitic on <i>Jatropha curcas</i> (Obatomi et al., 1994) The blood glucose lowering effects of the methanol extract of the leaves was observed in alloxan-induced diabetic rats; an effect dependent on host plant and time of collection (Osadebe et al., 2004, 2010) <i>In vitro</i> antioxidant effects (Ogechukwu et al., 2012)	Anti-hypertensive, Anti-microbial, Immuno-modulatory, Anti-cancer	Leaves	Infusion, Decoction		Lupanone (Imam et al., 2007) Catechin-3-O-rhamnoside, Catechin-7-O-rhamnoside, 4-methoxy-catechin-7-O-rhamnoside (Ogechukwu et al., 2012); 7β, 15α-dihydroxyl-lup-20(29)-ene-3β-palmitate, 7β, 15α-dihydroxyl-lup-20(29)-ene-3β-stearate, 7β, 15α-dihydroxyl-lup-20(29)-ene-3β-deca decanoate (Ogechukwu et al., 2011); Stigmast-7,20(21)diene-3β-hydroxy-6-one, 3β-hydroxy-stigmast-23-ene, 7β, 15α-dihydroxyl-lup-20(29)-ene-3β eicosanoate (Omeje et al., 2011); Linamarin gallate, Walsuraside, Catechin, Rutin, Epicatechin, Gallate derivatives of epicatechin, Quercetin-3-O-β-D-glucopyranoside, Peltatoside (Agbo et al., 2013)	
106	<i>Telfairia occidentalis</i> Hook.f.	Cucurbitaceae	Fluted pumpkin	Ugwu/Ugu (I), Iroko or Apiroko (Y), Ubong (Ef), Umee (Urhobo), Umeke (Bi)		250 mg/kg ethanol extract of the leaves decreased blood glucose levels in normal and alloxan-induced diabetic rats; while 100 mg/kg ethanol extract of the seed decreased glucose levels in alloxan-induced but not in normal or glucose-loaded rats (Eseyin et al., 2005, 2007a) Alpha glucosidase and α-amylase inhibitory effects of the hydro-ethanolic extract of the leaves as well as Antioxidant effects (Obboh et al., 2012b) 50 mg/kg globulin proteins extracted from the seeds decreased blood glucose levels when pre-administered to normal high glucose fed rats (Teugwa et al., 2013a) <sup>§</sup>	Convulsion, GIT disorders, Anemia, Hypertension, Anti-tumour, Immune modulating, Anti-parasitic, Analgesia, Inflammation, High cholesterol, Anxiety	Leaves, Fruit, Seeds			Globulins, Carotenoids, γ-amino butyric acid, 13-hydroxy-9Z, 11E-octadecatrienoic acid, α- and β-moschins, Pectin, MAP 2, MAP 4, MAP 11, MAP 28 (Caili et al., 2006)	Co-administration of the leaves prior to or alongside chloroquine tablets altered its pharmacokinetics (Eseyin et al., 2007b)
107	<i>Terminalia catappa</i> L.	Combretaceae	Tropical almond, Umbrella tree	Belebo or Igifuruntu (Y), Ibulu (I)	SE, SS, SW	Methanol extract of the leaves decreased blood glucose levels in alloxan-induced diabetic mice by 59% (Ezeigbo and Asuzu, 2010)	Aphrodisiac, Hepato-protective, Analgesic, Inflammation, Anti-microbial, Insomnia, Anti-cancer, Anti-viral	Leaves, Stem bark, Fruit, Seeds	Maceration		Terminolic acid, β-sitosterol, β-sitosteryl palmitate (Idemudia, 1970); Terflavin A and B, Tercatain, Tergallagin,	Potential hepatic toxicity with high doses due to Punicalagin and punicalin (Lin et al., 2001)



Table 1 (continued)

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108	<i>Tetrapleura tetraptera</i> (Schum. and Thonn.) Taub.	Leguminosae		Aridan (Y), Kpokrikpo or Mkpuruma oshosho (I)	SW, SE, SS, NC	Varying doses (40–78 mg/kg) of the aqueous, methanol and petroleum ether extracts of the fruits administered for 3 weeks also produced a hypoglycaemic effect in alloxan induced diabetic rats as well as regenerated the pancreas (Nagappa et al., 2003) <sup>§</sup>	Hemorrhoids, Insect repellent, Convulsions, Asthma, Cough, Insomnia, Poison antidote, Gonorrhoea, Rheumatism, Infertility, Bilharzia, Sickle cell, Lactation	Pod, Bark	Decoction, Infusion		Punicalagin, Punicalin, Chebulagic acid, Geranin, Granatin B, Corilagin, 1-desgalloyl eugenin (Tanaka et al., 1986); Isovitexin, Rutin, Vitexin, Isoorientin, Apigenin galloyl glucopyranosides (Lin et al., 2000a); Cyanidin-3-glucoside, Gallic acid, Ellagic acid, Brevifolin carboxylic acid, Eugenic acid (Nagappa et al., 2003); Ursolic acid, Asiatic acid (Gao et al., 2004)	Ethanol extract of the leaves given to rabbits for 10 days (50–150 mg/kg) increased serum ALT levels (Odesanmi et al., 2009)
109	<i>Treculia africana</i> Decne, ex Trécu	Moraceae	Breadfruit	Ukwa (I), Afon (Y)	SW	800 mg/kg aqueous extract of the fruit produced a hypoglycaemic effect in normal and STZ-induced diabetic rats (Ojewole and Adewunmi, 2004) Aqueous extract of the fruit showed good antioxidant effects, moderate lipase inhibitory effects and little or no $\alpha$ -amylase inhibitory effects (Etoundi et al., 2010) <sup>§</sup>	Anti-microbial, Anti-helminth, Laxative, Skin diseases, Dental allergies, Depression				Olean-12-ene-28-oic acid, Echinocystic acid-3-O-sodium sulphate (Ngassapa et al., 1993); Butanoic acid derivatives, Myrcene, p-Cymene, 1,8-Cineol, Limonene, 2,4-dihydro-3,4-dimethylfuran, $\gamma$ -Terpinene, $\alpha$ -Terpinolene (Ngassoum et al., 2001) $\alpha$ - and $\beta$ -Pinene, Camphene, Myrcene, Phellandrene, $\alpha$ - and $\gamma$ -Terpinene, p-Cymene, Limonene, Linalool oxide, Thujanol, Geranylacetone, $\beta$ -Caryophyllene, Terpineol (Aboaba et al., 2007) ; Phyllocoumarin, 6,9-dihydroxy megastigmane-3-one, Catechin (Kueete et al., 2008); 3-Prenyl-2',4,4'-trihydroxy chalcone, 4-hydroxy benzoic acid, Bergapten, Morin, Epiphylloucoumarin, $\beta$ -carotene, Riboflavin (Mueno et al., 2008)	
110	<i>Urena lobata</i> L.	Malvaceae	Caesar's weed	Ilasa-omode or Ilasa- agborin (Y), Odoazezo (I), Rama rama (H)	SW	Fractions of the hydro acetone extract of the bark decreased blood glucose levels at a dose of 10 mg/kg in alloxan-induced diabetic rats but not normal rats (Oyelola et al., 2007) Hypoglycemic effect of 500 mg/kg aqueous extract of the leaves in normal fasted glucose-loaded and STZ-induced diabetic rats (Ogbonnia et al., 2008c)	Anti-microbial, Colic, Skin diseases, Dysentery, Expectorant, Emollient, Malaria, Rheumatism, Wound healing, Analgesic, Inflammation	Root, Flower			Tiliroside, Dihydro kaempferol 4'-O- $\beta$ -glucopyranoside, Kaempferol and Quercetin 3-O- $\beta$ -glucoside and 3-O- $\beta$ -rutinoside, Luteolin-4'-O- $\beta$ -gluco pyranoside, Kaempferol-7-O-glucoside, Kaempferol, Quercetin (Matlawska and Sikorska, 1999); $\beta$ -Sitosterol, stigmaterol,	

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111	<i>Vernonia amygdalina</i> Delile	Compositae	Bitter leaf	Ewuro (Y), Shuwaka (H), Olugbu (I), Etidot (Ib)	NW, NC, SE, SS, SW	80 mg/kg aqueous extract of the leaves produced a dose dependent decrease in blood glucose levels in normal and alloxan-induced diabetic rabbits (Akah and Okafor, 1992); Antioxidant effects (Igile et al., 1994; Fasakin et al., 2011); Chronic intake of 400 mg/kg ethanolic extract of the fresh leaves significantly decreased fasting blood glucose levels, increased serum and pancreatic insulin levels, increased the activity of liver antioxidant enzymes as well as increased the expression and distribution of Glut 4 receptors in STZ-induced diabetic rats (Ong et al., 2011) <sup>§</sup> ; 150 ml of a (1:1:1) decoction mix of the leaves of <i>Vernonia amygdalina</i> , <i>Ocimum gratissimum</i> and <i>Gongronema latifolium</i> decreased baseline blood glucose levels in normal subjects when preadministered to normal subjects 45 min before an OGTT (Ejike et al., 2013)	Hemorrhoids, Measles, Ringworm, Analgesic, Malaria, Pneumonia, Anti-microbial, Anti- cancer, Anti-feedant	Leaves, Roots	Decoction, Juice extract		Imperatorin, Mangiferin, Quercetin, Palmitic and Linoleic acid triglycerides (Morelli et al., 2006); Syringic acid, Gluco- syringic acid, Salicylic acid, Protocatechuic acid and its methyl ester, Caffeic acid, Hexatriacontanoic acid, Pentadecanoic acid, Hexadecanoic acid, Maleic acid, Heptadecanoic acid, Diisobutyl phthalate (Lu et al., 2009); Ceplignan-4-O- β-D-glucoside, Urenoside A (Jia et al., 2010) Vernodalol, Vernolide, Vernomygdin, Vernolepin (Kupchan et al., 1969); Vernodalol, 11,13- dihydrovernodalin (Ganjian et al., 1983); Vernonioside A1, A2, A3, A4 and its aglycone, B1, B2 and B3 (Jisaka et al., 1993); Luteolin, Luteolin 7-O- glucoside and 7-O- glucuronide (Igile et al., 1994); Vernonioside D and E (Igile et al., 1995); Luteolin 7-O- and 4'-O- rutinoside, Caffeoyl quinic acid, Chlorogenic acid, Rutin, 1,5-Dicaffeoyl quinic acid, Apigenin glucuronide, Luteolin (Ola et al., 2009)	Aqueous extract of the leaves inhibited P-gp efflux activity in Caco-2 cells (Oga et al., 2012)
112	<i>Ximenia americana</i> L.	Olacaceae	Sour plum, Hog plum, Yellow plum, Sea lemon, False sandal wood	Tsaada (H), Igo (Y)	NW	Graded doses (200, 400 and 600 mg/kg) of the extract produced significant blood glucose reduction to control levels 6 h after administration in alloxan- induced hyperglycaemic rats (Siddaiah et al., 2011) <sup>§</sup>	Anti-parasitic, Anti- microbial, Inflammation, Pesticidal, Analgesic, Anti-pyretic, Anti- cancer, Hepato- protective, Ulcers, Skin infections, Purgative	Fruits, Stem, Stem-bark, Leaves	Decoction		Mandelonitrile lyase (Kuroki and Conn, 1989); Xymenynic acid, Tariric acid (Fatope et al., 2000); Ximoncaine, Stigmastane (de Araújo et al., (2009)); Benzaldehyde, Hydroxy benzyl cyanide, Geraniol, Isophorone, Linalool, Caryophyllene oxide,	Aqueous extract of the stem bark and the root increased levels of hepatic enzymes ALT, AST and ALK-P significantly (James et al., 2008; Wurochekke et al., 2008); Inhibited P-gp mediated Rh-123

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S/ no.	Plant name	Family	Common name	Local Nigerian name(s) <sup>+</sup>	Region of use for diabetes <sup>#</sup>	Experimental evidence for its use in diabetes management	Other medicinal uses	Plant part (s) used	Traditional preparation method	Identified active constituent(s)	Other relevant phytoconstituents identified in the plant	Interaction/toxicity studies
113	<i>Xylopia aethiopica</i> (Dunal) A.Rich.	Annonaceae	Ethiopian or Negro pepper, Long nose pepper	Erunje or Eeru (Y), Uda (I), Kimba (H)		Administration of 1 g/kg of a 1:1 mixture of a hydroethanolic extract of <i>Alstonia congensis</i> bark and <i>Xylopia aethiopica</i> fruits decreased blood glucose levels in normal mice (Ogbonnia et al., 2008a); 250 mg/kg of a herbal mixture Okudiabet <sup>®</sup> ) made up of bark of <i>Alstonia congensis</i> , aerial parts of <i>Stachytarpheta angustifolia</i> and fruits of <i>Xylopia aethiopica</i> administered for 30 days had a marked hypoglycaemic effect in alloxan-induced diabetic rats (Ogbonnia et al., 2010); Potent inhibitory effects against pancreatic lipase, $\alpha$ - amylase and $\alpha$ -glucosidase enzymes; Antioxidant effects (Etoundi et al., 2010; Adefegha and Oboh, 2012)	Purgative, Neuralgia, Amenorrhea, Anti- convulsant, Bronchitis, Stomach ache, Cough, Hemorrhoids, Asthma, Insect antifeedant, Anti- microbial, Diuretic	Fruit, Seeds			Methyl benzoate (Mevy et al., 2006); Hydrocyanic, Linolenic, Arachidonic, Erucic, Eicosatrienoic and Nervonic acids; Methyl-14,14-dimethyl-18-hydroxy hepta triacont-27,35-dienoate, Dimethyl-5-methyl-28,29-dihydroxy dotriacont-3,14,26-triendioate (Saeed and Bashier, 2010); Riproximin (Bayer et al., 2012); Sambunigrin, Gallic acid, Quercetin, $\beta$ -glucogalline, 1,6-digalloyl- $\beta$ -glucopyranose, Quercetin-3-O-(6-galloyl)- $\beta$ -glucopyranoside, Quercitrin, Avicularin, Quercetin-3-O- $\beta$ -xylo pyranoside, Kaempferol-3-O-(6'-galloyl)- $\beta$ -glucopyranoside (Le et al., 2012)	efflux in Caco-2 cells (Ezuruike et al., 2012)
											Xylopic acid (15 $\beta$ -acetoxy kaur-16-en-19-oic acid) (Ekong and Ogan, 1968); Kauran-16 $\alpha$ -ol, Kauran-16 $\alpha$ , 19-diol, Kaur-16-en-19-oic acid (Leboeuf et al., 1980); $\alpha$ - and $\beta$ -pinene, 1,8-cineole, Cuminic aldehyde, $\alpha$ -terpineol, $\beta$ -caryophyllene, Limonene, Linalool, Ocimene, $\alpha$ - and $\beta$ -Phellandrene, Sabinene, $\alpha$ -murolene (Lamaty et al., 1987); Kaur-15-en-17-al-19-oic acid, 15-oxo-trachyloban-19-oic acid, 15-hydroxy-(-)-trachyloban-19-oic acid, 15 $\beta$ -hydroxy-(-)-kaur-16-en-19-oic acid, 15-oxo-(-)-kaur-16-en-oic acid, Sitosterol glucoside (Harrigan et al., 1994a); Oxophoebine, Liriodenine, Oxoglucaine, O-methyl moschatoline, Lysicamine (Harrigan et al., 1994b); 7 $\beta$ -acetoxy (-)-kaur-16-en-19-oic acid, E-3-(4-hydroxy-3-	

Table 1 (continued)

S/ no.	Plant name	Family	Common name	Local Nigerian name(s) <sup>*</sup>	Region of use for diabetes <sup>#</sup>	Experimental evidence for its use in diabetes management	Other medicinal uses	Plant part (s) used	Traditional preparation method	Identified active constituent(s)	Other relevant phytoconstituents identified in the plant	Interaction/toxicity studies
114	<i>Zea mays</i> L.	Poaceae	Corn Maize	Agbado (Y), Oka (I), Masara (H)	SW	0.2 g/d aqueous extract of corn silk improved kidney parameters in STZ-induced diabetic rats but no significant hypoglycaemic effect (Suzuki et al., 2005); 100 mg/L ethanol extract of the corn silk showed PPAR $\alpha$ and $\gamma$ agonist activities (Rau et al., 2006) <sup>§</sup> ; Inhibitory effects of the aqueous and ethanol extract of the maize kernels on $\alpha$ -glucosidase enzymes and antioxidant effects (Lee et al., 2010) <sup>§</sup>	Hypertension, Analgesic, Inflammation, Contraceptive, Nose bleeds	Seed silk	Decoction		Chrysoeriol 6-C- $\beta$ -boivino pyranosyl-7-O- $\beta$ -gluco pyranoside, Alternanthin (Suzuki et al., 2003)	methoxy phenyl)-N-2-[4-hydroxy phenylethyl]-2-propenamide, E-3-(3,4-dihydroxyphenyl)-N-2-[4-hydroxyphenylethyl]-2-propenamide, Grossamide, Demethylgrossamide, Cannabisin B and D (Lajide et al., 1995); 7 $\alpha$ -hydroxy trachyloban-19 $\beta$ -oic acid (Ngouela et al., 1998)  Glucose yield and glycaemic index of maize starch has been shown to be high, which may pose a problem for diabetic patients (Izuagie et al., 2007; Omoregie and Osagie, 2008)
115	<i>Zingiber officinale</i> Roscoe	Zingiberaceae	Ginger	Atale (Y), Jinga (I), Chita (H)	SW	Ethanol extracts of the rhizome reduced blood glucose levels dose dependently (50–800 mg/kg) in normal and STZ-induced diabetic rats (Ojewole, 2006); Alpha amylase and Alpha glucosidase inhibitory effects and <i>In vitro</i> antioxidant effects (Oboh et al., 2010); <i>in vivo</i> antioxidant effects (Morakinyo et al., 2011)	Typhoid, Nausea, Cold symptoms, Asthma, Stimulant, Rheumatism, Hemorrhoids, Liver disorders, Obesity, Git disorders	Rhizome	Maceration	6-, 8- and 10-Gingerols increased glucose uptake in L6 muscle cells primarily by an increased GLUT4 expression (Li et al., 2012); Aldose reductase inhibitory effects of methoxy phenyl derivatives (Kato et al., 2006)	2-(4-Hydroxy-3-methoxy phenyl) ethanol, 2-(4-hydroxy-3-methoxy phenyl) ethanoic acid, 2-(3,4-dimethoxyphenyl) ethanoic acid, 4-(4-hydroxy-3-methoxy phenyl)-2-butanone, (4-hydroxy-3-methoxy phenyl) methanol (Kato et al., 2006); Zingerone, Geraniol (Chen et al., 2007); Gingerols and its derivatives, Gingesulfonic acids, Shogasulfonic acids, Gingerdiols, Zingerone, Shogaols, Paradols and its derivatives, Zingiberene, Curcumene, $\beta$ -bisabolene, Citral, Camphene, Neral, $\beta$ - and Sesqui-phellandrene, Diarylheptanoids, Cineole, Gingerdiones, Geraniol, Terpeneol (Ali et al., 2008; Kubra and Rao, 2011)	Insufficient evidence for a possible interaction with warfarin or CYPs (Vaes and Chyka, 2000); 6-gingerol increased the accumulation of daunorubicin and rhodamine and decreased efflux of daunorubicine indicating possible P-gp modulatory effect (Nabekura et al., 2005)

\* Bi-Bini, Ef-Efik, Es-Esan, F-Fulani, H-Hausa, I-Ibo, Ib-Ibibio, Id-Idoma, Ig-Igala, Ige-Igede, Ij-Ijaw, Nu-Nupe, Ti-Tiv, and Y-Yoruba.

<sup>#</sup> NC=North central, NE=North east, NW=North west, SE=South east, SS=South south, and SW=South west.

<sup>§</sup> Experimental evidence involving plant samples not collected from within Nigeria.

other *in vivo* models used include spontaneous diabetic animal models obtained as a result of one or more genetic mutations such as obese Zucker fatty rats, db/db mice and KK-A<sup>y</sup> mice; as well as the use of high glucose or fructose-fed animals. This latter group simulate the development of diabetes from insulin resistance better as is more commonly found in patients with type-2 diabetes (Srinivasan and Ramarao, 2007).

Although most plants were only evaluated experimentally in a type-1 diabetes model, some of these have been shown to be effective hypoglycemic agents in type-2 diabetes patients, such as extracts of *Bridelia ferruginea* Benth. Daily administration of 15 mg of the leaves as an infusion to type-2 diabetic patients previously on insulin injections for eight weeks resulted in a significant decrease in their blood sugar levels (Iwu, 1983).

Only two out of the 96 plant species were ineffective in the *in vivo* experimental model of study, namely *Zea mays* L. (Suzuki et al., 2005) and *Cucumeropsis mannii* Naudin (Teugwa et al.). Despite its identified *in vitro* PPAR $\alpha$  and  $\gamma$  agonist activities and  $\alpha$ -glucosidase inhibitory effects (Lee et al., 2010), extracts of *Zea mays* failed to produce a significant hypoglycemic effect *in vivo* (Rau et al., 2006). This could possibly be as a result of the absence of the bioactive constituent(s) responsible for the hypoglycemic effect in the sample used for the *in vivo* study. The absence of an *in-vivo* hypoglycemic effect would however not 'eliminate' its use in the clinical management of diabetes, which also takes into account co-morbid conditions. In this regard, *Zea mays* could also provide protection against diabetic nephropathy, as it has been shown to improve kidney parameters *in vivo* (Suzuki et al., 2005).

In the case of *Cucumeropsis mannii*, its traditional use involves the ingestion of its ashes or its juice (Gbade, 2009). This may indicate that its use is based on its oligo-elements and/or vitamins. In fact the supplementation of elements such as chromium, magnesium and vanadium is actively explored in the treatment of diabetes (Anderson et al., 1997; Halberstam et al., 1996; Rodríguez-Morán and Guerrero-Romero, 2003); some of which have been identified in the seeds of *Cucumeropsis mannii* (Badifu and Ogunsua, 1991).

### 3.2. *In vitro* pharmacological evidence

It is recommended that *in vitro* experiments are carried out to ascertain the mechanism of action for the plant. Certain plants produce their hypoglycemic effects as a side effect of their *in vivo* toxicity (Marles and Farnsworth, 1995). There is also the risk that the hypoglycemic effect is being mediated – at least in part – through an unwanted physical mechanism, rather than a physiological one, such as was observed with *Gymnema sylvestre* (Retz.) R. Br. Ex Sm (Persaud et al., 1999). This immediately eliminates the potential use of such a plant as a therapeutic hypoglycemic agent. In addition, due to the ethical considerations surrounding animal use (Festing and Wilkinson, 2007), it is advised that validation experiments are 'replaced' with non-animal models where possible.

Over one-third of the plants in our review have been studied for *in vitro* in models that could possibly explain some or all of their mechanism of action. Twenty-nine plants have inhibitory effects against either  $\alpha$ -amylase or  $\alpha$ -glucosidase enzymes; five plants have agonist activity on the PPAR $\gamma$  receptor, whose activation enhances glucose metabolism; four plants increase insulin release from pancreatic cells; five plants increase glucose uptake in muscles or liver; while two plants increased the expression of the glucose transporter GLUT4, which in turn increases glucose uptake into muscles and adipose tissues. Two plants were identified as potential DPP-IV inhibitors, while six plants were identified as aldose reductase inhibitors (Fig. 1).

*In vitro* experiments are often designed to 'reflect' the mechanism of existing drugs used in diabetes management. Plants that possess alpha amylase or alpha glucosidase inhibitory effects reflect the action of acarbose, PPAR $\gamma$  agonist activity reflect the thiazolidinediones, while aldose reductase inhibitors are potential agents for preventing diabetic complications like the drug epalrestat. Thus with this identified mechanisms, researchers and healthcare professional alike can immediately identify the potential therapeutic benefit of the plant. This information could contribute to a more rational therapeutic regimen for diabetes patients, possibly benefitting from a synergistic effect with herbal remedies.

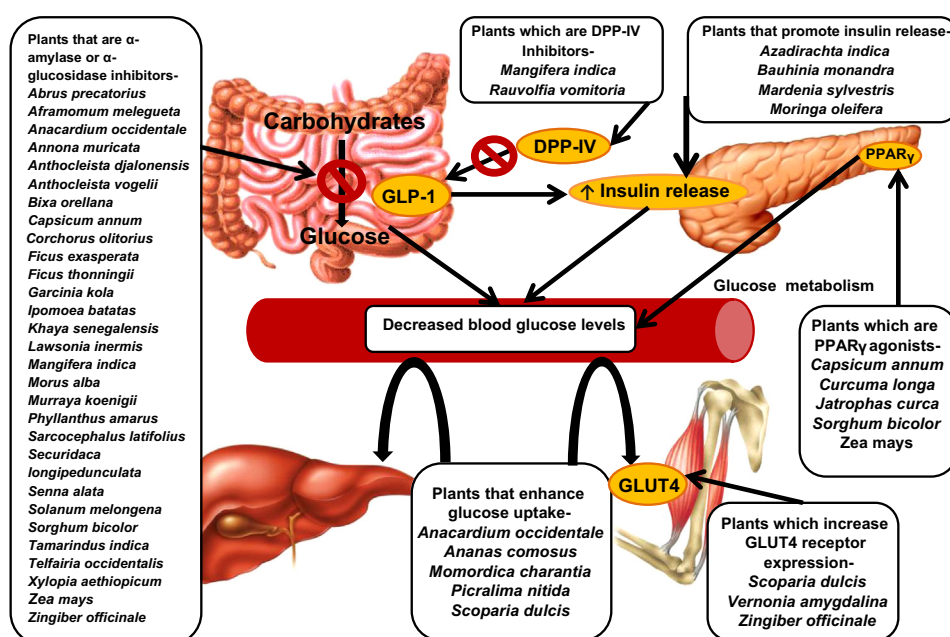


Fig. 1. Proposed molecular mechanisms of hypoglycemic effects for species studied so far.

The disadvantage of the molecular approach for experimental validation of plant activity is that the biological assays only explore known targets and do not take into account extracts that might be acting on unknown targets, possibly through innovative mechanisms. In addition, herbal medicines are often complex mixtures of various phytochemicals which work synergistically to achieve a desired therapeutic outcome (Campbell-Tofte et al., 2012). In such cases, a single end-point *in vitro* biological assay will not be sufficient in evaluating the clinical effect of the plant. For instance, the methanol extract of the root and stem of *Gongronema latifolium* Benth. produced a greater anti-hyperglycemic effect in glucose loaded rats than each of its fractions, indicating a synergistic effect of its constituents possibly acting through different molecular mechanisms (Adebajo et al., 2013).

There is also a holistic approach in the herbal management of diabetes such that plants which are not hypoglycemic themselves may be included in multi-component preparations because of their benefits in co-morbid conditions. Thus, *in vitro* studies might not immediately indicate the beneficial effect of the plant. A good example is the use of the aphrodisiac plant *Mondia whiteii* (Hook. f.) Skeels (Quasie et al., 2010). Despite not showing *in vitro* hypoglycemic effect (Etoundi et al., 2010), it is commonly included in multi-component preparations for diabetes management in men since erectile dysfunction is a common complication of the illness (personal communication during field work). This however does not preclude any *in vivo* activity which is yet to be evaluated.

### 3.3. Bioactive compounds

Over forty compounds from twenty three of the reviewed plants have been identified, either through an activity guided

fractionation or *in silico* studies as the bioactive constituents responsible for some or all of the plants' beneficial effects in diabetes. Some of these constituents are species-specific such as the alkaloid mahanimbine from *Murraya koenigii* (L.) Spreng (Dineshkumar et al., 2010), while others are known to be present in many plants like the alkaloid trigonelline, which is responsible for the hypoglycemic effect of *Abrus precatorius* L. (Monago and Nwodo, 2010) and *Trigonella foenum-graecum* L. (fenugreek), a plant whose use in diabetes management is popular across India and Europe (Bailey and Day, 1989). We hereby classify these compounds according to similar chemical features (which may not necessarily refer to similar biosynthetic pathways) as follows: compounds containing nitrogen (1–9) (Fig. 2), terpenes (10–16) (Fig. 3), phenolic compounds (17–33) (Figs. 4 and 5), and compounds containing hydroxyl groups including sugars (34–40) (Fig. 6).

#### 3.3.1. Nitrogen containing compounds

A number of alkaloidal and non-alkaloidal active principles from plants used in diabetes management have been reported. Some of these were isolated from samples not collected from Nigeria such as hypoglycin A (1) and B (2) – from the fruit of *Blighia sapida* K.D.Koenig. (Chen et al., 1957). *Murraya koenigii* leaves are also used traditionally in Indian Ayurvedic system to treat diabetes. Mahanimbine (5) isolated from the Indian plant samples decreased blood glucose levels in STZ-induced diabetic rats and also produced a dose-dependent  $\alpha$ -amylase and  $\alpha$ -glucosidase inhibitory effect (Dineshkumar et al., 2010). Its cellular mechanism of action is also thought to be mediated by an increase in glucose utilization (Dinesh Kumar et al., 2013). Paradoxically, this and other related carbazole alkaloids isolated

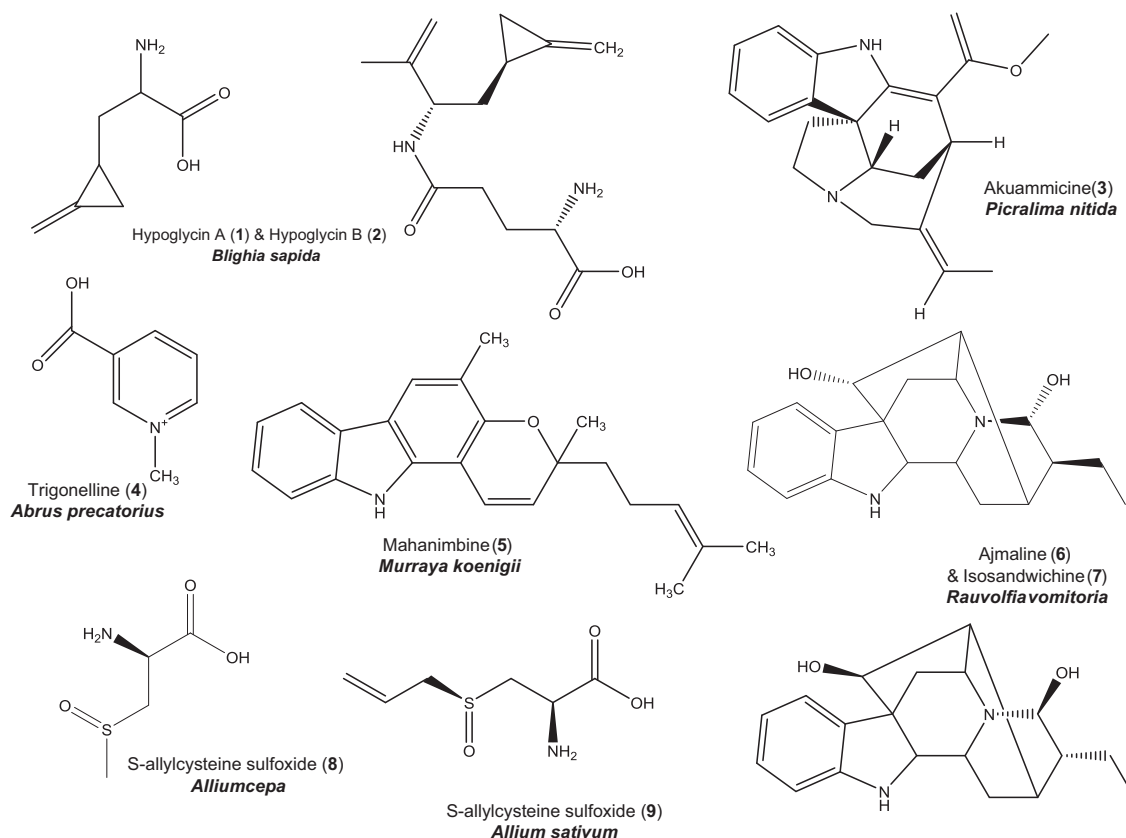


Fig. 2. Nitrogen containing compounds with beneficial effects in diabetes.



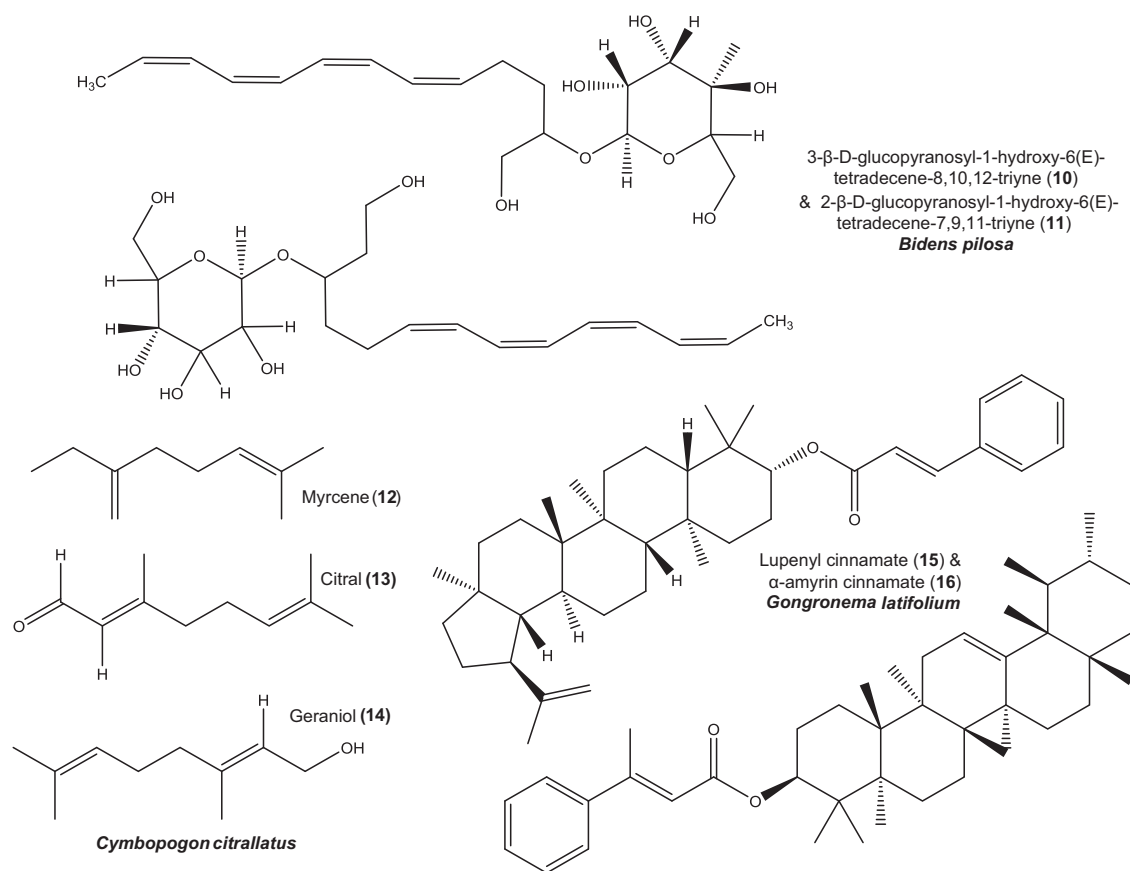


Fig. 3. Terpenes with beneficial effects in diabetes.

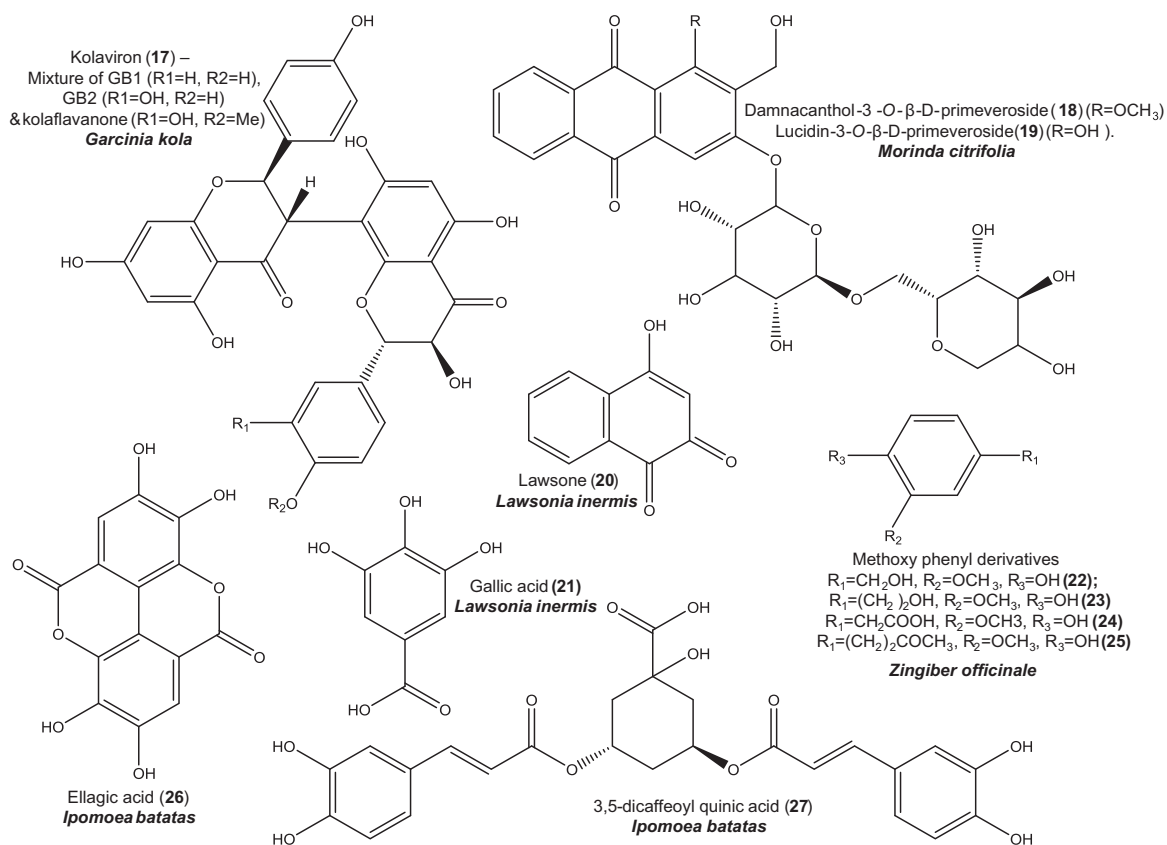


Fig. 4. Phenolic compounds with beneficial effects in diabetes.



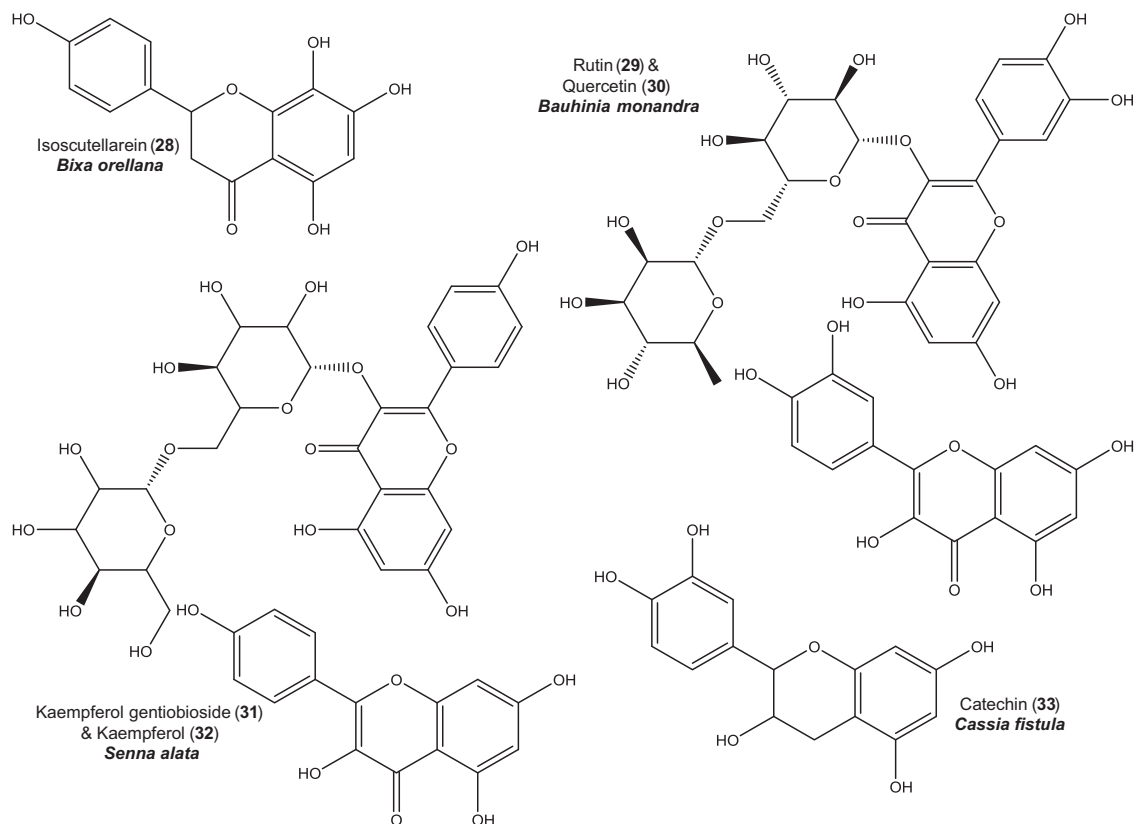


Fig. 5. Phenolic compounds (flavonoids) with beneficial effects in diabetes.

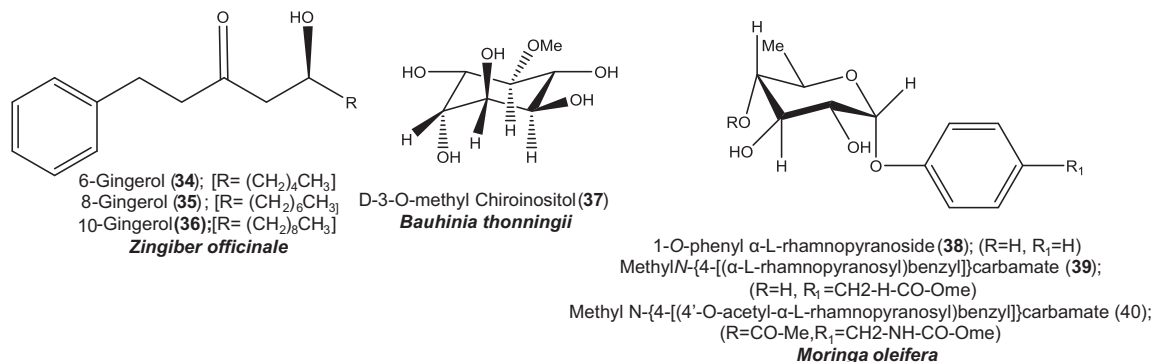


Fig. 6. Other hydroxylated compounds with beneficial effects in diabetes.

from plant samples from Nigeria decreased the glucose-mediated insulin release from INS-1 cells when compared to control, even though the amount of glucose released was dose dependent. This effect may however be explained by their known *in vitro* cytotoxicity (Adebajo et al., 2005).

The alkaloid trigonelline (4) isolated from the seeds of *Abrus precatorius* (L.) collected from the eastern part of Nigeria decreased blood glucose levels in alloxan-induced diabetic rats as well as reduced the activity of glucose-6-phosphatase and glycogen phosphorylase, two enzymes important for glucose production (Monago and Nwodo, 2010). Akuammicine (3) isolated from the chloroform extract of the seeds of *Picalima nitida* (Stapf) T.Durand and H.Durand stimulated glucose uptake in 3T3-L1 adipocytes (Shittu et al., 2010). It is also present in plants of the genus *Alstonia* such as *Alstonia boonei* De Wild. and *Alstonia Congensis* Engl. and

would most likely be contributing to their blood glucose lowering activity. Ajmaline (6) and isosandwichine (7) from *Rauvolfia vomitoria* Afzel. were identified as DPP-IV inhibitors using an *in silico* approach (Guasch et al., 2012).

Garlic and onions are commonly used as part of the diet in many Nigerian households and the hypoglycemic effect of plant samples collected from Nigeria has also been studied (Eyo et al., 2011). This hypoglycemic effect is possibly due to the presence of S-methylcysteine sulfoxide (8) (SMCS) in onions and S-allylcysteine sulfoxide (9) (SACS) in garlic, which have been isolated from Indian plant samples and have been shown to improve glucose tolerance in alloxan-induced diabetic rats (Sheela et al., 1995). Clinical studies in humans have shown that the supplementation of garlic to diabetic patients in combination with hypoglycemic drugs improves glycemic control in addition to

the reduction of cardiovascular risk (Sobenin et al., 2008). Although they both contain nitrogen, SMCS and SACS are primarily classed as sulfur containing compounds.

### 3.3.2. Terpenes

A number of terpenes have been isolated as bioactive constituents in plants used for diabetes management (Fig. 3). The leaves of *Gongronema latifolium*, otherwise known as 'utazi' or 'madumaro' in Ibo and Yoruba respectively is commonly used as a food vegetable and is widely recognized for its traditional use in diabetes management. Lupenyl cinnamate (15), lupenyl acetate and  $\alpha$ - and  $\beta$ -amyryl cinnamates (16) isolated from the combined root and stems of locally obtained samples have recently been identified as the bioactive compounds, possessing both anti-hyperglycemic effects in glucose-fasted rats as well as insulin stimulating effects in INS-1 cells (Adebajo et al., 2013).

Foetidin from the whole plant and the unripe fruits of *Momordica foetida* collected in Nigeria also decreased blood glucose levels of normal fasted, but not alloxan-induced rats at only 1 mg/kg (Marquis et al., 1977). Acetylenic glucosides (10) and (11) from *Bidens pilosa* decreased blood glucose in the murine type 2 diabetes model C57BL/Ks-db/db mice (Ubillas et al., 2000), and inhibited the spontaneous development of diabetes in non-obese diabetic (NOD) mice by modulating the differentiation of T-helper cells (Chang et al., 2004).

The monoterpenes myrcene (12), citral (13) and geraniol (14) found in *Cymbopogon citratus* were identified as aldose reductase inhibitors using *in-silico* docking methods (Vyshali et al., 2011). They are also components of the essential oil of many medicinal plants used in Nigeria as shown in Table 1. This preliminary information warrants further *in vitro* and *in vivo* studies involving plant samples from Nigeria previously shown to contain these compounds, given that the beneficial effect of the essential oil of *Cymbopogon citratus* containing high amounts of these monoterpenes has now been validated *in vivo* in experimentally induced type-2 diabetic rats (Bharti et al., 2013).

### 3.3.3. Phenolic compounds

A wide range of phenolic compounds have been identified as active principle(s) in some of the plants here reviewed. Anthraquinone glycosides from *Morinda citrifolia* L, namely damacanthol-3-O- $\beta$ -D-primeveroside (18) and lucidin 3-O- $\beta$ -D-primeveroside (19), decreased blood glucose levels in STZ-induced diabetic mice at 100 mg/kg (Kamiya et al., 2008). Incidentally, this plant is not native to Nigeria and is not known to grow in Nigeria. However, the use of a registered herbal product of the juice extract, Tahitian noni juice® (TNJ) is quite popular in Nigeria for various ailments including diabetes. Administration of 1 ml/150 mg body weight of the rats twice daily for four weeks prior to and after the induction of diabetes with alloxan resulted in significant decrease in blood sugar levels, indicating a prophylactic effect of the extract against alloxan-induced diabetes (Horsfal et al., 2008). The presence of these phenolic compounds in the marketed product has however not been confirmed.

Kolaviron (17) is a mixture of flavanones isolated from the acetone extract of the edible nuts of *Garcinia kola* Heckel (bitter kola), which is valued in most parts of West Africa. It decreased blood sugar levels in normal and alloxan induced diabetic mice at a dose of 100 mg/kg, as well as inhibited rat lens aldose reductase (RLAR) activity (Iwu et al., 1990a).

Other phenolic compounds have been identified as bioactive constituents but not from plant samples collected in Nigeria. A diacylated anthocyanin peonidin 3-O-[2-O-(6-O-E-feruloyl)- $\beta$ -D-glucopyranosyl]-6-O-E-caffeoyl- $\beta$ -D-glucopyranoside]-5-O- $\beta$ -D-glucopyranoside isolated from the root of *Ipomoea batatas* (L.) Poir.

showed potent maltase inhibitory effects *in vivo* (Matsui et al., 2002), while ellagic acid (26) and 3,5-dicaffeoylquinic acid (27) isolated from the hot water extract of the leaves showed potent aldose reductase inhibitory effects (Terashima et al., 1991). Lawsone (20) (a naphthoquinone) and gallic acid (21) isolated from the ethanol extract of the aerial parts of *Lawsonia inermis* L. inhibited the formation of advanced glycated end products *in vitro* (Sultana et al., 2009). Some methoxy phenyl derivatives (22–25) isolated from the rhizomes of *Zingiber officinale* Roscoe have been identified as aldose reductase inhibitors both *in vitro* and *in vivo*, suppressing sorbitol accumulation in human erythrocytes as well as lens galactitol accumulation in 30% galactose-fed rats (Kato et al., 2006).

Several isolated flavonoids have also been identified as bioactive constituents. Isoscutellarein (8-hydroxy apigenin) (28) is a flavonoid isolated from the hot water extract of the leaves of *Bixa orellana* L., which was identified as an aldose reductase inhibitor (Terashima et al., 1991). Rutin (29) and quercetin (30) were isolated from the leaves of *Bauhinia monandra* Kurz as the anti-hyperglycemic constituents in alloxan-induced diabetic rats (Alade et al., 2011, 2012). A bioassay guided fractionation of the stem bark of *Cassia fistula* L. led to the identification of catechin (33) as the bioactive agent. It decreased plasma glucose levels in STZ-induced diabetic rats, with direct effects on glucose metabolizing enzymes and expression of the glucose transporter GLUT4 (Daisy et al., 2010). Fractionation of the methanol extract of the leaves of *Senna alata* (L.) Roxb. (syn- *Cassia alata*), which showed potent  $\alpha$ -glucosidase inhibitory effects, identified kaempferol gentiobioside (31) and kaempferol (32) as the bioactive compounds (Varghese et al., 2013). Increased translocation of GLUT4 receptors to the plasma membrane of L6 myotubes was also observed with a flavonoid-rich fraction of *Scoparia dulcis* L. (Beh et al., 2010), although the bioactive constituent(s) was not identified.

The presence of aromatic hydroxyl groups in the benzo- $\gamma$ -pyran structure of flavonoids is associated with its antioxidant properties, particularly its free radical scavenging effects. These properties have been shown to protect pancreatic islet cells from oxidative stress as well as help in the regeneration of  $\beta$ -cells as shown with epicatechin found in green tea (Sabu et al., 2002) and quercetin (Coskun et al., 2005). More importantly, they can prevent the formation of advanced glycated end products (AGEs) and other diabetic complications associated with high oxidative stress conditions such as arteriosclerosis, nephropathy, neuropathy, retinopathy and erectile dysfunction (Rahimi et al., 2005). Thus, the presence of quercetin and epicatechin as well as other potent antioxidant flavonoids in a wide range of plants such as *Irvingia gabonensis*, *Khaya senegalensis*, *Mangifera indica*, *Securidaca longipedunculata* and *Ocimum gratissimum*, will contribute to – and in some cases may be the basis for – their use in the holistic management of diabetes which includes the prevention of diabetic complications.

Other flavonoids have also been shown to directly affect specific therapeutic targets in diabetes. For instance, supplementation of mice diet with naringin or hesperidin modulated the activity of glucose metabolizing enzymes, with an increase in hepatic glucokinase activity and decrease in hepatic glucose-6-phosphatase activity in diabetic db/db mice (Jung et al., 2004) and GK type-2 diabetic rats (Akiyama et al., 2009). These two flavonoids are constituents of all citrus fruits and have also been identified in *Senna alata* (Hennebelle et al., 2009) and *Rauvolfia vomitoria* (Campbell-Tofte et al., 2011) and as such may account for some of their effects. Myricetin is another flavonoid that has shown direct beneficial effects in diabetes through enhanced glycogen metabolism (Ong and Khoo, 2000) and improved insulin sensitivity (Liu et al., 2007). It has been identified in some of the plants either in its aglycone form or as a glycoside. These are the

*Allium* species, *Aloe vera*, *Azadirachta indica*, *Citrus* species, *Carica papaya*, *Bryophyllum pinnatum*, *Cassia sieberiana*, *Chrysophyllum albidum*, *Ipomoea batatas* and *Bridelia ferruginea*.

### 3.3.4. Hydroxylated compounds including sugars

Some other non-phenolic hydroxylated cyclic compounds have been isolated and identified as bioactive agents. These include the gingerols (**34–36**) from *Zingiber officinale*, which were shown to enhance glucose uptake into muscles as a result of a direct increase in the expression of the GLUT4 receptor (Li et al., 2012). An inositol derivative, D-3-O-methyl chiroinositol (**37**) isolated from the methanol extract of the stem bark of *Bauhinia thonningii* Schum. produced a dose-dependent decrease in blood glucose levels in alloxan-induced diabetic rats (Asuzu and Nwaehujor, 2013).

Finally, a number of benzyl derivatives including carbamates and thiocarbamates have been isolated from fractions of the methanol extract of the fruits of *Moringa oleifera* Lam. These compounds have been shown to possess insulin secretory effects, stimulating  $\geq 15$  ng insulin/mg protein in pancreatic INS-1 cells at 100 ppm. Some of these compounds were identified as 1-O-phenyl  $\alpha$ -L-rhamnopyranoside (**38**), methyl N-{4-[( $\alpha$ -L-rhamnopyranosyl)benzyl]}carbamate (**39**), and methyl N-{4-[(4'-O-acetyl- $\alpha$ -L-rhamnopyranosyl)benzyl]}carbamate (**40**).

Many plant secondary metabolites have been associated with specific beneficial effects in diabetes, which might account for the therapeutic effect of the herbal drug (Qi et al., 2010; Singh et al., 2013). Thus, apart from a bioguided fractionation, the biologically active agent of a plant can also be inferred by evaluating the phytochemical constituents that have previously been isolated. These can thereafter be confirmed in specific pharmacologic experiments.

### 3.4. Clinical studies

The validation of biologically active plants in randomized, placebo-controlled clinical trials involving human subjects is a necessary step towards the possible integration of traditional herbal products into health systems. For these purposes, isolation of the active constituent may not be necessary. The European Directive of Traditional Herbal Medicinal Products is an example of how reports of traditional use and a sound safety profile are enough to regulate herbal medicines (Cox and Roche, 2004). However, knowing the identity of the active principle would be ideal in order to ensure a better quality control and perhaps a more defined dosage.

Fourteen of the plants reviewed in this paper have been clinically evaluated in human subjects, either singly or in combination. These are *Bridelia ferruginea*, *Citrus aurantium*, *Gongronema latifolium*, *Ocimum gratissimum*, *Rauvolfia vomitoria*, *Vernonia amygdalina*, *Carica papaya*, *Curcuma longa*, *Ipomoea batatas*, *Irvingia gabonensis*, *Gymnema sylvestre*, *Phyllanthus amarus* and *Solanum aethiopicum* (Table 1), of which the first six involved plant samples collected from Nigeria. Only *Phyllanthus amarus* did not produce the desired clinical effect (Moshi et al., 2001).

Most of the clinical studies were not randomized, controlled trials but preliminary studies evaluating the therapeutic effect of the plant in human subjects. Exceptions to these were those carried out on *Rauvolfia vomitoria* and *Citrus aurantium* (Campbell-Tofte et al., 2011), *Irvingia gabonensis* (Ngondi et al., 2009) and *Ipomoea batatas* (Ludvik et al., 2004). Similarly, a meta-analysis by Leung et al. (2009) of all clinical studies carried out on *Momordica charantia* identified flaws in their study design, despite the extract consistently producing a hypoglycemic effect. As a result,

appropriate conclusions that will act as guidelines for their clinical use cannot be drawn.

A good knowledge of the traditional use of these plants based on ethnobotanical studies is very important in the design of a good clinical study. This is especially important for plants which are used as mixtures, as the individual components may be working synergistically to produce the overall desired effect. An example is the synergistic effect produced by a decoction mix of the leaves of *Gongronema latifolium*, *Ocimum gratissimum* and *Vernonia amygdalina* in modulating baseline blood glucose levels, which was not observed with the individual plants (Ejike et al., 2013). Given that many of these herbal remedies are currently being taken by diabetic patients alongside their prescription medicines, a concerted effort between clinicians and researchers would be an ideal way to recruit patients to such studies.

To ensure the reliability of conclusions drawn from any clinical study, they should always involve proper planning with appropriate controls and ought to be conducted within a reasonable time frame, in line with the guidelines of the Declaration of Helsinki. In addition, the recommendations for reporting randomized clinical trials, as defined in the 'Consolidated Standards of Reporting Randomized Clinical Trials (CONSORT) statement' (Schulz et al., 2010) should also be followed. Nonetheless, this relatively high 'success' rate amongst the various studies conducted highlights the potential of harnessing ethnobotanical information in enhancing patient therapy.

## 4. Toxicological evidence and considerations

The administration of whole plant extracts or fractions consisting of a myriad of compounds, can elicit different biological effects in the body, some of which may be harmful toxic effects. Sometimes, these toxic effects are only associated with certain parts of the plant. For example, the leaves of *Senna occidentalis* have hepatoprotective effects and are used traditionally for the treatment of liver disorders (Jafri et al., 1999). However, ingestion of toxins found in the seeds (beans) is thought to be the probable cause of acute hepato-myoecephalopathy (HMP) in children (Vashishtha et al., 2009). This risk of toxicity associated with the use of herbal products is one of the main reasons for the hesitance amongst healthcare practitioners towards promoting their integration into healthcare systems.

Adequate knowledge about the traditional use of such plants is very necessary as this often helps to forestall the ingestion of such toxic plants or plant parts. Sometimes the toxic component may have been identified such as abrin, a toxic protein found in the seeds of *Abrus precatorius*, with an estimated human fatal dose of 0.1–1  $\mu$ g/kg (Kirsten et al., 2003). In rare cases, the hypoglycemic agent in the plant could also be the toxic agent, such as with hypoglycin from *Blighia sapida* (Sherratt, 1986). Thus, the therapeutic use of such a plants as whole extracts is therefore not recommended.

Various plants in Table 1 have been associated with specific organ toxicity. Examples include the nephrotoxic effects of *Alstonia congenensis*, *Aristolochia* spp., *Cassia sieberiana*, *Ficus exasperata*, *Securidaca longipedunculata* and the hepatotoxic effects of *Cassia sieberiana*, *Ficus exasperata*, *Morinda citrifolia*, *Picralima nitida* and *Senna occidentalis*. The hepatotoxic effects of some extracts such as *Ocimum gratissimum* and *Sphenocentrum jollyanum* are directly linked to their effect on the liver function enzymes. The cardiotoxic and neurotoxic effects of some other extracts have also been identified. Sometimes, these toxic effects are only seen at high doses, which would therefore not preclude their continued use as medicinal plants so long as there is appropriate information



about the safe dose ranges. The use of other more toxic plants would however need to be completely discontinued.

A thorough analysis of the plant's extracts as well as identified phytochemical constituents with respect to their safety/toxicity profile particularly in humans can ensure a critical assessment of its therapeutic potential. Previously, coumarins which are a component of a wide range of plants were identified as hepatotoxic based on various studies carried out in rodents. However, further studies have showed that certain animal species are resistant to coumarin-induced toxicity. The 7-hydroxylation metabolic pathway is the most favored in humans leading to the formation of non-toxic metabolites, whereas in rats the most favored pathway is a 3,4-epoxidation leading to the formation of toxic metabolites. Knowledge of this and a quantitative health risk assessment have now confirmed its safety in humans (Felter et al., 2006; Lake, 1999).

Evaluation of medicinal plants for potential herb–drug interactions is equally as important as its evaluation for efficacy and safety. Two types of herb–drug interactions exist: pharmacodynamic interactions and pharmacokinetic interactions. If a herbal plant alters the expected pharmacological effect of a drug as a result of its biochemical or physiological effect on the body, this is known as a 'pharmacodynamic interaction'. If the herb and the drug are both expected to produce the same pharmacological effect, there may be an increased therapeutic effect produced with their co-administration. This knowledge can be harnessed towards producing a synergistic effect between the two, which would possibly require a dose adjustment. Otherwise, the resulting effect could be detrimental if appropriate monitoring and evaluation is not done. A good example is the severe hypoglycemic that was observed in a female diabetic patient taking chlorpropamide and a meal containing *Momordica charantia* and *Allium sativum* (Izzo and Ernst, 2001).

A synergistic effect should however not be assumed. It is sometimes advisable for patients not to take drugs alongside their herbal products due to negative drug interactions that may occur. For instance, the water soluble fraction of okra fruits has been shown to decrease the absorption of metformin (Khatun et al., 2011). Although both would otherwise be beneficial in diabetes management, taken together would result in a decrease in the therapeutic concentration of metformin, which in turn may not bring about the desired hypoglycemic effect in the patient.

Constituents of medicinal plants also undergo the four main pharmacokinetic processes of absorption, distribution, metabolism and elimination (ADME). There is therefore the possibility of an interaction with one of the different ADME parameters by the herb, which could invariably affect the fate/bioavailability of a co-administered drug and possibly, the resulting therapeutic benefit (s). This is known as a 'pharmacokinetic interaction'.

Out of the one hundred and fifteen plants reviewed in this paper, over thirty of them have shown *in vitro* and/or *in vivo* modulation of the activity of one or more of these ADME parameters (Fig. 7). Some of these interactions were on absorption, either by modulating the effect of P-glycoprotein (P-gp), an intestinal efflux transporter, or by direct effects on the intestinal tight junctions. Other pharmacokinetic interactions were on metabolism, by interacting with one or more cytochrome P450 enzymes responsible for phase 1 metabolism or either of the phase 2 metabolic enzymes (Table 1).

The role of P-gp in the intestinal epithelium is the extrusion of certain xenobiotics from the blood to the intestinal lumen as well as to minimize the entry of drugs in the lumen into the bloodstream, ultimately resulting in decreased absorption and decreased oral bioavailability (Sharom, 2007). For drugs that are P-gp substrates such as glibenclamide, this effect of the efflux transporter is one of the determinant factors in the recommended

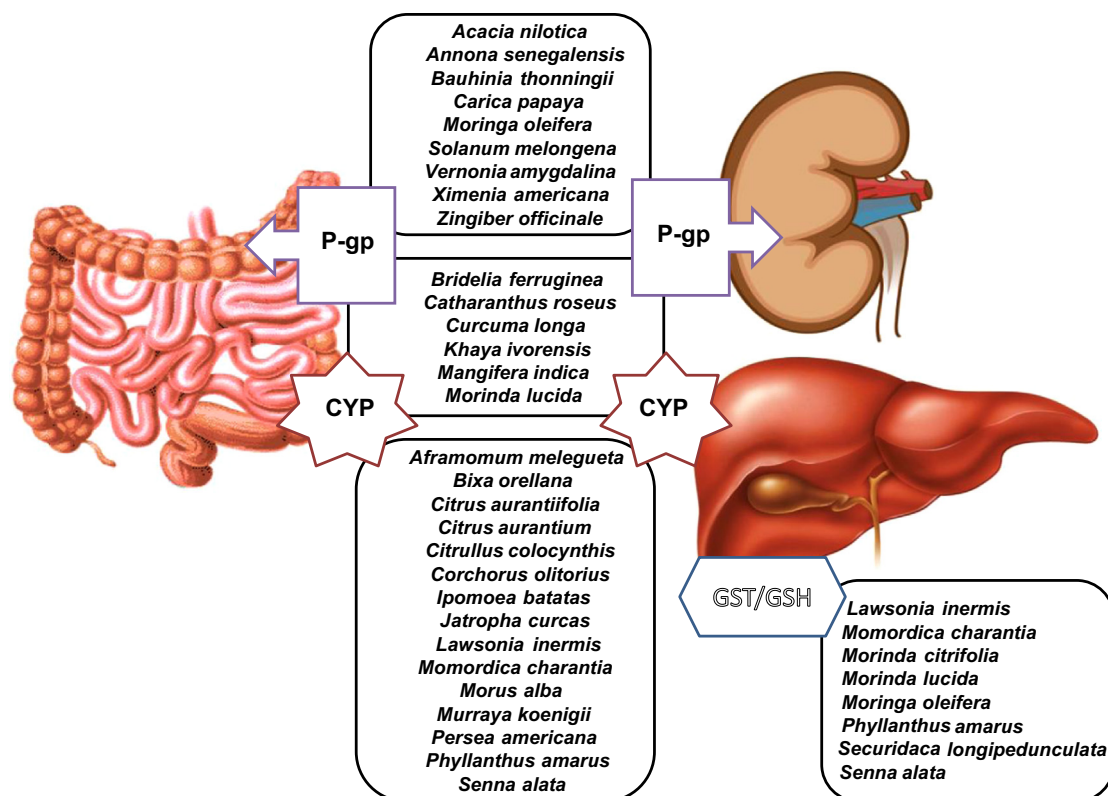


Fig. 7. *In vitro* pharmacokinetic herb–drug interactions identified based on the literature reviewed.

dose of the drug to ensure that an adequate therapeutic concentration is achieved in the bloodstream. Co-administration of the drug with a herb with inhibitory effects on P-gp such as *Acacia nilotica*, *Annona senegalensis*, *Bauhinia thonningii*, *Bridelia ferruginea*, *Carica papaya* and *Morinda lucida* might result in increased plasma concentration of the drug.

The cytochrome P450 (CYP) family of enzymes are responsible for phase 1 oxidative, peroxidative and reductive metabolic transformations of drugs, environmental chemicals and natural compounds into less toxic, more water-soluble products, in order to facilitate their excretion from the body. They are most abundant in the liver, which is the primary site for metabolism. The activity of CYP enzymes can be modified either by induction or inhibition as seen with the extracts of *Bixa orellana* and *Jatropha curcas* respectively. The biological activity of the xenobiotics metabolized by these enzymes can be greatly altered as a result (Rendic and Carlo, 1997). St John's wort (*Hypericum perforatum*) is a very good example of a herbal product that has produced clinically significant effects as a result of its interactions with P-gp and CYP enzymes (Henderson et al., 2002).

*In vitro* interactions have also been identified with the phase 2 metabolizing enzymes, particularly with the glutathione transferases (GSTs). As with P-gp and CYPs, such interactions can alter the plasma concentration and the resulting therapeutic effect of the co-administered substrate drug. In addition, GSTs directly control the levels of glutathione (GSH) within the cell. GSH also acts as an antioxidant within cells, and is particularly important in diabetic conditions characterized by oxidative stress. Unfortunately, plants such as *Securidaca longipedunculata* which decrease GSH levels might be counter-productive in diabetic patients.

For many of these plants in Fig. 7, the phytochemical constituents responsible for the pharmacokinetic interaction are still unknown. Polyphenols present in plants especially flavonoids have been the most implicated in herb–drug interactions, with direct effects seen with specific flavonoids on P-gp and drug metabolizing enzymes (Morris and Zhang, 2006) (Galati and O'Brien, 2004) (Hodek et al., 2002). It should however be taken into account that many of the *in vitro* pharmacokinetic interactions or alarming case studies published in primary literature fail to translate into significant clinical risks for the patients, as seen with many herbal remedies taken in Europe (Williamson et al., 2013). There is still an urgent need for effective pharmacovigilance of herbal medicines to ensure their safe and effective use in therapeutic management (Shaw et al., 2012).

## 5. Conclusions

Nigeria is endowed with a biodiversity of medicinal plants, many of which are currently used in the traditional management of diabetes. Our review shows that there is very good preclinical evidence for the efficacy of most of these plants, either as hypoglycemic agents or as useful agents in the management of diabetic complications. We have mapped their pharmacological mechanism of action as this can serve to promote a more rational use of these plants as herbal medicines based on the expected therapeutic outcome and their tabulated toxicological effects. Last but not least, we have also highlighted potential interactions with key parameters of the ADME process that can arise from the use of these plants in therapeutic management.

These available data can provide evidential support for the clinical development of a number of medicinal plants as adjuvant therapy. We believe that the criteria for selection should be based on social acceptance/frequency of use, efficacy and toxicity profile, and availability/sustainability of the supply chain, possibly tailored to each region. A set of quality parameters for the standardization

of these plants as herbal preparations (such as pharmacopoeial monographs) would be required to ensure the reproducibility of their therapeutic effects. Finally, as a means of giving credence to the pre-clinical experimental evidence, intervention or clinical studies with the standardised materials should be carried out in order to validate their usefulness in diabetes management. We hope that in this manner the therapeutic potential of these medicinal plants can be best harnessed, towards a possible integration into the healthcare system.

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## Appendix A. Supplementary information

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.jep.2014.05.055>.

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