

The Role of Ethnomedicinal Plants for Treatment and Management of Diabetes Mellitus: An Updated Review

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Abstract

Diabetes mellitus is one of the prominent metabolic disorders nowadays worldwide and it is characterized by an increase in blood glucose, disturbances in the metabolism, and alteration in insulin secretion. Nowadays, phytopharmaceuticals has become a significant treatment mode for the diabetes, and bioactive compounds have expanded an increasing amount of consideration to this end for they have multiple biological potential, including the sustained secretion of insulin and revival of pancreatic islets cells. In this review article, we explained the role of bioactive compounds in treatment and management diabetes, and their mechanisms in the prevention.

Keywords: Diabetes mellitus, bioactive compounds, insulin, blood glucose.

1. INTRODUCTION:

One of the oldest and fastest growing chronic metabolic disorders is Diabetes. A disorder which is identified by raised levels of glucose commonly known as hyperglycemia which may due to inadequacy in secretion of insulin which may further lead to chronic hyperglycemia [1-2]. Insulin is required as an energy source for consumption or utilization of glucose and is generally synthesized as a hormone in the pancreatic beta cells. This inadequacy results in various abnormalities leading to complications in macro and micro level with increased cardiovascular disorders [3].

Diabetes has been now seen a global epidemic disorder due to more advancement in industrialization and increasing obesity in individuals. According to recent surveys it is predicted that diabetes will be increased from 4% in 1995 to 6.4% in 2025[4]. By the year 2025 the most affected countries are predicted to be China, USA and India. No. of individuals suffering will be increased from 194 million to 380 million [5].

Due to change in lifestyle and increased exposure to various chemical products as well as changing eating habits have increased the no. of individuals suffering from diabetes, affecting mainly the urban areas. Diabetes additionally produce short and long term affects which affect largely the individuals leading to increase in premature death rates [6]. Consequences of diabetes may lead to ulceration[7,8], neuropathy[9,10], CVS complications [11,12] and retinopathy [13,14], nephropathy [15,16]. Historically, Diabetes was about reported 3000 years ago in the manuscript of Egypt [17]. Diabetes has been classified into Type- I and Type- II. A clear Distinction b/w Type –I Diabetes and Type- II were made in the year 1936[18]. Based on the clinical and etiology Diabetes may largely classified into four classes

1. Type I Diabetes
2. Type 2 Diabetes
3. Gestational Diabetes
4. Other Specific class

Type-I is considered as Major class in most of the individuals, thought it also affect the younger age which should be considered worryful. The impact of this has been on rich as well as poor countries of the world [19]. Diabetes have now become the most serious topic globally and various measures are taken to treat this. This has been found that it may be caused due to various factors such as changed lifestyles, behavior patterns, urbanization and dietary changes and many more [20]. In almost every part of the population there is case of diabetes found as well as glucose intolerance [21]. Diabetes may further cause cerebrovascular diseases, cardiovascular as well as peripheral diseases. The next type of diabetes –Type –II diabetes cause irregular secretion of insulin and insulin peripheral resistance^[22]. Historically in the 6th century BC diabetes was classified as Medhumeha by Sushruta. He also described the treatment by exercise and good lifestyle [23]. Characteristic loss of weight, excessive passage of urine (polyuria), and vision impairment is some of the

symptoms of Diabetes. Chronic conditions may lead to ketoacidosis further leading to stupor and death, if not treated [24]. Various drugs are available for the treatment, the main aim to treat the disease or prevent long term complication by reducing the risk factors [25].

2. DIABETES CLASSIFICATION

According to revised classification of diabetes, clinical as well as etiological categories are covered. Etiological category includes better understanding of cause of diabetes. Clinical category involves various clinical stages of diabetes in its history. They are categorized on the basis of the stage of developing diabetes, as by the clinical characteristics [26]. Following are the types of diabetes:

1. Type-I diabetes mellitus:

In this type diabetes there is absence of insulin due to ruination of pancreatic Beta cells. Individuals genetically adequately form autoimmune response that destroy beta cells are more affected. There exist two types of diabetes type –I. Firstly autoimmune markers such as antibodies such as insulin and auto antibodies, islet cell antibodies causing immune –mediated disease. Mainly 85-90 percent are affected by this type. Secondly, Idiopathic type –I diabetes; whose cause is not known. Only few people people are affected by this [27]. Thirstiness, excessive urination, hyperglycemia, ketoacidosis are the various symptoms of this category [28].

2. Type-II diabetes mellitus:

One of the most common type of diabetes and is increasing. Due to low level of insulin secretion, leading to unwieldy absorption of glucose for energy into the cell. There are 90% of registered cases of diabetes affecting population above age of 65 [29]. They more reported in adults as compared to children. This form is mainly characterized by skin darkening and insulin resistance [30]. Normally patients suffering remain unrecognized and are asymptomatic. Insulin resistance is developed characterized by upper body obesity. Therefore, insulin secretion is increased for the compensation by Beta cells. Insulin dependency is caused due to loss of Beta cell [27].

3. Gestational diabetes:

Due to rapid hormonal changes during pregnancy there develops gestational diabetes. It mainly results due to body change for the consumption of insulin which leads to intolerance of carbohydrates. Though this type disappears after the child birth and infant born may or may not have diabetes [31]. The patient may develop IGT, type 2 diabetes or type 1 in the later life. Proper assessments should be done along with glucose testing marking the characteristics of risks during pregnancy [32].

4. Maturity Onset Diabetes

MODY (Maturity onset of diabetes of young), a type of monogenic diabetes includes minority of patients. It leads to mutation of genes such as glucokinase gene (MODY-2), HNF – I alpha, NEUROD 1 etc. HNF-1 alpha gene is the commonest [33].

3. ETIOLOGY

Etiology of Diabetes – Type- I

Due to destruction of pancreatic Beta- cells there is reduced formation of insulin. Usually the symptoms are seen only for a short time or not at time. Also, genes such as human leukocyte antigens commonly called HLA on WBC's Cause the risk of Type –I diabetes [34, 35]. Other factors include:

Environmental Factors: Factors such as toxins, food and viruses may cause type 1 diabetes.

Viruses and Infections: Though virus may not be cause for diabetes as such they include viruses which may be associated like rubella, mumps which may further produce type –I diabetes.

Destruction of Cells: T- cells in the lymphatic system may destroy Beta cells and cause type-1 diabetes [36].

Etiology of Type- II

1. Hyperthyroidism

2. Insulin gene mutations
3. Mature onset diabetes of the youth
4. Mutations in insulin receptor
5. mutations in mitochondria [37-40].

OTHER ETIOLOGICAL FACTORS:

1. Diseases related to endocrine system
2. Impairment of beta cells by drugs treating HIV
3. Syndrome such as – Klinefelter syndrome
 - Turner syndrome
 - Down Syndrome
 - Cushing syndrome
4. Chemical toxins [27]

4. PATHOPHYSIOLOGY: TYPE-I (IDDM)

Type –I occurs as result of destruction of Beta cells in the pancreas which is an autoimmune disease. The principal is hormone that help in the regular uptake of glucose from the blood to various cells. Hence deficiency of insulin results in diabetes. The function of pancreatic cells functions abnormally along with the deficiency of insulin. There is marked excess of glucagon. This excessive secretion of glucagon results in various metabolic effects caused by deficiency of insulin. IDDM individuals generally develop Ketoacidosis which is serious diabetes complication producing excess blood acids. Various biochemical reaction is reported for insulin effect on the impairment of tissue. Further the deficiency in insulin results in increased levels of fatty acids in plasma, lipolysis and a reduced glucose metabolism which results in deficiency of insulin for target tissues such as GLUT 4 class in adipose tissue, glucokinase in the liver. Hence these metabolic derangements result in diabetes [41].

TYPE-II DIABETES:

Type-II diabetes (NIDDM) is divided into following groups:

- (i) DM with fasting hyperglycemia

- (ii) DM with minimal fasting hyperglycemia
- (iii) Glucose tolerance (normal)
- (iv) Impaired glucose tolerance

Individuals having with impaired glucose tolerance are insulin resistant. The levels of insulin decrease in NIDDM individuals. Resistance of insulin and deficiency are common in NIDDM individuals [42]. Transformation occurs in the Beta cells to increase insulin and compacting exceeds demand. Therefore, insulin secretion concentration is increased. MODY is an autosomal trait due to mutations in gene of glucokinase gene. Which is responsible for glucose metabolism mainly in liver and beta cells.

Various classes of drugs were developed to elevated the insulin such as thiazolidines. The bound and altered the PPAR γ receptor which is a transcription factor .IT when activated activates another receptor or transcription factor call RXR – retinoid x receptor. Which is key regulator for differentiation of adipocyte cells.it also help in synthesis of biological active compounds from endothelial cells as described in figure 1 [43].

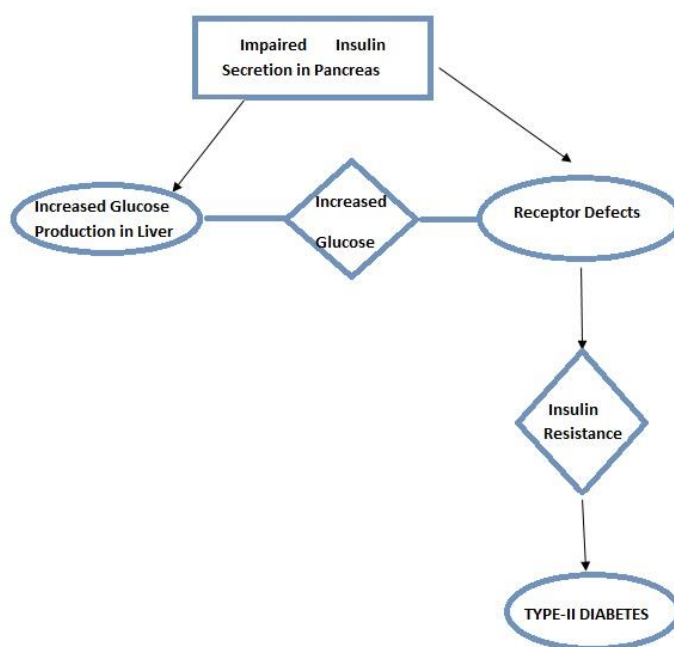


Figure 1: Pathophysiology of Type-II [43]

5. TREATMENT

There is various treatment for diabetes available:

5.1 DRUG TREATMENT:

Diabetes – mellitus is treated by reducing the blood glucose levels. Oral hypoglycemic agents such as Pramlinitide, Exenatide are given orally. These drugs increase the level of insulin in beta cells as well as increase the sensitivity of organs for the glucose [44]. Some agents decrease the rate for the absorption of glucose in the gastro intestinal tract. Various formulations include:

(I) MEGLITINIDES

These are often referred as short – acting secretagogues which aid pancreas to secrete more of insulin. they act by channel regulation. They generally close the K^+ channels in the Beta cells, while opening Ca^{+} elevating the secretion of insulin.

Examples: Nateglinide

(II) INSULIN

Usually insulin is given intravenously or by insulin pump. It is mainly used to treat type –I diabetes

(III) BIGUANIDES

They include drugs like Phenformin which reduce hepatic output of glucose and elevate the glucose uptake by the peripherals including muscles like skeletal muscle.

Other Examples : Buformin, Metformin

(IV) THIAZOLIDINES:

Commonly called as Glitazones are type of regulatory proteins. They bind to PPAR γ and are involved in genes which regulate glucose mainly the transcription genes. They elevate the insulin secretion by enhancing the production of mRNA's of enzymes that are insulin dependent. Example: Troglitazone, Rosiglitazone.

PEPTIDE ANALOGS

(i) GLUCAGON – LIKE PEPTIDE (GLP)

GLP agonists tend to bind with GLP receptor. Insulin secretion is increased by the Beta cells. Example: Exenatide

(ii) INCRETIN MIMETICS: These are insulin secretagogues.

GASTRIC INHIBITORY PEPTIDE ANALOGS

- (i) AMYLIN ANALOGUES: These suppress glucagon and slow the rate of gastric emptying. They administer by subcutaneously.

(II) DDP-4 INHIBITORS

By inhibiting the dipeptidyl peptidase-4 incretin conc. In the blood [27].

5.2 Reported bioactives for treatment of Diabetes:

The various medicinal plants have been used as a dietary supplement from a long time and in the treatment of various diseases without the proper prescription of a qualified doctor. Although herbal therapy continues to be used in globally in many countries, rare medicinal plants have gotten scientific and medical scrutiny. Moreover, a large number of medicinal plants retain some extent of toxicity. It is also proclaimed that one-third of medicinal plants used in the remedy of diabetic complications is examined to be toxic [6,17]. Since a long time, several plants are examined to be an alternative source of potent antidiabetic drugs and these herbal drugs getting more popularity among the peoples because they are examined to be lacking any side effects. It has been prophesied that more than 400 plants species and their secondary metabolites such as alkaloids, glycosides, terpenoids, flavonoids, carotenoids, tannins, and polyphenolic derivatives or derived products are being used for the treatment of diabetes mellitus and their complications [45, 46].

Following bioactive compounds and Herbs used for Treatment of Diabetes mellitus

Gymnema sylvestre, Family: *Asclepiadaceae*

Various evidences demonstrated that the leaves of *G.sylvestre* also known as Meshashringi, Kavali, Dhuleti, Gurmar can act as hypoglycemic agent for the treatment of diabetes. There were various studies conducted by different scientists which showed its action by decreasing the levels of FBG, PPBG & HbA1c in type 2 diabetes when 400 mg of the extract was taken per day for 1.5 years. The increase in the action of insulin was also observed [47-49].

Aegle marmelos, Family- *Rutaceae*

It is also known as bael. According to a study conducted by Ismail(2009a), a significant reduction in PPBG was seen when patients were given 206 ± 6 mg/dl were given decoction of 5g *A. marmelos* leaf powder per day [50].

Momordica charantia Family- *Cucurbitaceae*

According to the studies, the dried powder consumption of *M. charantia* fruit led to decrease in the FBG in different diabetic patients. The aqueous & alcoholic extracts of *M.charantia* also produced similar effect [51].

Nigella sativa Family- *Ranunculaceae*

Nigella sativa was appeared to altogether improve lab boundaries of hyperglycemia & diabetes control after treatment with a huge fall in fasting blood glucose, blood glucose level 2 h postprandial, glycated haemoglobin, obstruction of insulin & an ascent in serum insulin [52].

Panax quinquefolius, Family- *Araliaceae*

These are the most preferable ginseng is found in America. According to different researches it has been found that this species led to the reduction in PPBG level when given to type 2 diabetic patients. The reduction in area under curve by 20% was observed when the patients were given 3g of ginseng [53-54].

Silybum marianum, Family- *Asteraceae*

The seeds of *Silybum marianum* are found to be of great importance & is highly beneficial in the disorders of the liver. The flavonolignans of *S. marianum* lead to the reduction in the level of the glucose & are therefore useful in the diabetic patients [55]. According to the clinical study, it has been observed that this species led to the reduction in HbA1c, FBG, TG, LDL, SGOT & SGPT when given to the type 2 diabetes patients in the dose 200mg three times in a day [56].

Salacia reticulate, Family- *Celastraceae*

It has been observed that *Salacia reticulate* in the form of an aqueous extract was used in diabetes treatment. 240mg of the drug was given every day for 6 weeks & it led to the reduction of Hb1c

& FBG levels in type 2 diabetes patients [57]. The same observations were reported when the patients were given Salacia reticulate tea for the period of 3 months [58].

***Trigonella foenum-graecum*, Family - Fabaceae**

The seeds of *Trigonella foenum-graecum* popularly known as fenugreek seeds have been proved as effective hypoglycemic agent. There have been more than thirty studies done in animal models, cell cultures & humans which show antidiabetic effect [59]. 100g of these seeds given regularly for 10 days to a diabetic patient may cause a significant decrease in TG, total cholesterol, FBG & glucosourea. In another study, the same amount of seeds were soaked in hot water or were mixed in yoghurt. The results showed the reduction in VLDL, TG & FBG when the soaked seeds were given to the patients with type 2 diabetes for 8 weeks [60].

***Allium cepa*, Family- Amaryllidaceae**

It is popularly known as onion. It was reported by Mathew and Augusti in 1975 that when it is consumed orally may lead to improvement in the glycemic control. There effective antidiabetic property was studied when the patients with type 1 & type 2 diabetes were given 100 g of *A. cepa* & also led to significant reduction in levels of FBG. The improvement in the glucose tolerance test (GTT) was also observed [61].

***Purslane portulaca oleracea*, Family-Portulacaceae**

The extract of *Purslane Portulaca oleraceae* lowers blood glucose and the level of fasting glucose in diabetic patient. The studies were carried out in rats for observing the antidiabetic activity. It was seen that when the rats were given the extract doses of 50, 100 & 200mg/kg by the intraperitoneal route, there was a reduction in the serum glucose levels [62].

***Acacia arabica or nilotica*, Family -Mimosaceae**

The powdered seeds of *Acacia arabica* mainly act by increasing insulin secretion in Beta cells of pancreas. This tree, discovered everywhere on the subcontinent yields a bountiful stock of gum. The decoction of its bark is utilized in loose bowels, diarrhea & swishes for light gums [63].

***Abelmoschus moschatus*, Family- Malvaceae**

Aerial part generally lead to the enhancement in GLUT 4 and P13 Kinase insulin sensitivity is increased. According to the studies conducted in rats was found that the bolus IV injection of this species led to the decrease in the concentration of glucose in the plasma [64]. The area under curve of insulin & glucose reduced the insulin tolerance during the glucose tolerance test by intraperitoneal route [65].

Aloe barbadensis, Family- *Asphodelaceae*

Leaves act by stimulating secretion of insulin from the beta cells. The oral administration of 500 mg/kg & administration of bitter principle interperitonally 5 mg/kg resulted in the hypoglycemic response of single oral dose. It was even administered 2 times & bitter principle was administered one time for 4 days in the chronic studies [66].

Artemisia alba, Family-*Asteraceae*

Aerial part generally containing sesquiterpene lactones cause significant decrease in blood sugar levels. It was reported by Al-Waili that the extract of this species which led to an important role in lowering the raised circulatory strain & glucose levels in the blood, & it additionally had antiarrhythmic & anxiolytic properties. Later on Ibrahim also led to the similar outcomes [67].

***Canavalia ensiformis* DC**, Family- *Leguminosae*

Concentration of cholesterol, triacyl glycerol in plasma indicated antihyperlipidemic effect. When the aqueous extract of seeds of this species was administered orally for one week, it led to the significant reduction in hyperketonemia & hyperlipidaemia in the rats with diabetes [68].

Psidium guajava, Family- *Myrtaceae*

Activity of hepatic hexokinase was increased and it was decreased by aqueous extract. An oral glucose tolerance test was carried out in long term feeding rats showed a significant reduction in the blood sugar level in diabetic rats fed with either the aqueous or ethanol extract of guava leaves [69].

The numbers of herbal plants have been used in the formulations to treat diabetes as shown in table 1 and the mechanism of action of medicinal plants explained in figure 2. Their chemical structures

shown in figure 3, 4 and 5. they contain ingredients which are describes as an alternative to allopathic medicines as well as does not produce any side effects on the body.

MECHANISM OF ACTION OF ANTIDIABETIC PLANT

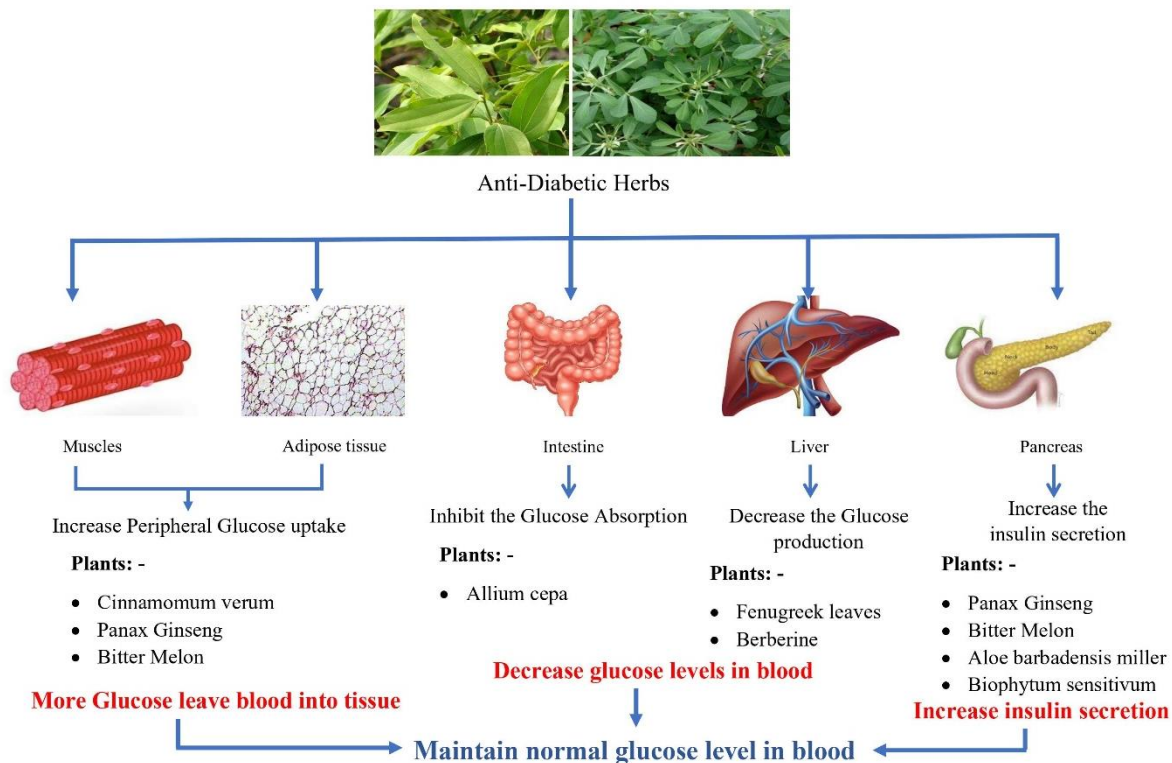


Figure 2: Mechanism of action of antidiabetic medicinal plants

Table 1: Reported bioactive Compounds for treatment of diabetes

S.NO	Common Name	Botanical Name	Plant Part used	Major Phytoconstituents	Mechanism of Action	Reference
1.	Indian gum Arabic Tree/Babul/Kikar	<i>Acacia arabica</i> or <i>nilotica</i> Mimosaceae	Powdered seeds	Contains arabin, a mixture of salts of Arabic acids of calcium, magnesium and potassium.	Mainly act by increasing insulin secretion in Beta cells of pancreas.	[45]
2	Aloe	<i>Aloe barbadensis</i> , Asphodelaceae	Leaf, powder	glucomannans [beta-(1,4)-acetylated mannan	Also act by stimulating secretion of insulin from the beta cells.	[46]
3.	Vegetable Insulin/Bitter melon	<i>Momocardia charantia</i> , <i>Cucurbitaceae</i>	Seed powder	Charantine, Foetidin, Cucurbitane	Increase insulin sensitivity and signaling in hfd induced resistance	[47,48]
4.	Okra, Abelmosk,	<i>Abelmoschus moschatus</i> , Malvaceae	Aerial part	Mycricelin	By enhancement in GLUT 4 and P13 Kinase insulin sensitivity is increased.	[49,50]
5	Bael	<i>Aegle marmelose</i> (Rutaceae)	Fruit	Skimmianine, aegelin, lupeol, cineole.	Lowers blood glucose level as well as hemoglobin glycosylated and increase release of insulin	[51,52]
6	Cucumber tree/sorrel	<i>Averrhoa bilimbi</i>	Leaves	cyanidin-3-O-h-D-glucoside, phenolics, potassium ion, sugars	Increase in insulin secretion	[52, 69]

		(Oxalidaceae)				
7	Wormwood	<i>Artemisia herba alba</i> (Asteraceae)	Aerial part	Sesquiterpene lactones	Cause significant decrease in blood sugar levels.	[70]
8	Chinese snake gourd	<i>Trichosanthes kirilowii</i>	Root	Trichosanthin	Stimulate the D-glucose into lipids	[71]
9	Purslane	<i>Portulaca oleracea extract</i>	Seeds	kaempferol, luteolin,	Lowers blood glucose and the level of fasting glucose in diabetic patient	[72,73]
10	Tree Spinach/Chaya	<i>Cnidoscolus aconitifolius</i>	Leaves	n-Hexadecenoic acid; 9-Octadecenoic acid	Considerable decrease in blood glucose and cholesterol levels	[74,75]
11.	Neem	<i>Azadirachta indica</i> (Meliaceae)	Leaves, seeds & bark	tetranortriterpenoids, pentanortriterpenoids, hexanortriterpenoids	Reduced level of glucose not significantly known	[76]
12.	Maachi Patram	<i>Artemisia pallens</i> , <i>Atemisia</i>	Aerial part	Germacranolide	Glucose utilization in peripheral part is increased and decreased reabsorption of glucose in the PCT of the renal tubules.	[77]

13.	Betel Palm/Areca Nut	<i>Areca catechu</i> (Arecaceae)	Powered leaves	Arecaidine, arecoline	Reduced hypoglycemic effect	[78,79]
14.	Punarnava	<i>Boerhaavia diffusa</i> Linn. (Nyctaginaceae):	Whole plant, root, and leaf	Punarnavine, β -Sitosterol	Control of glycosylated hemoglobin	[80,81]
15	Little Tree Plant,	<i>Biophytum sensitivum</i> (Oxalidaceae)	Whole plant	Amentoflavone, Isoorientin	Due to release of beta cells in langerhans which stimulate insulin	[82,83]
16	Orchid tree	<i>Bauhinia candicans</i> (Leguminosae)	Leaves	Alpha-pinene, occidental	Peripheral metabolism of glucose is increased.	[84]
17	Achiote, Anatto	<i>Bixa orellana</i> (Bixaceae)	seeds	Bixin	Reduces postprandial increase in blood glucose.	[85]
18	Black mustard	<i>Brassica nigra</i> L (Brassicaceae)	Seed	Glycerides of stearic and oleic acid	Insulinotropic effect	[86]
19	Wild Hop	<i>Bryonia alba</i> (Cucurbitaceae)	Roots	<i>Bryonin, hydrobryotin</i>	Lower the effect of alpha amylase	[87]
20		<i>Bridelia ndellensis</i> Beille. (Euphorbiaceae)	Stem bark	ethyl acetate and dichloromethane	Only decreased glucose level in the blood	[88]
21	Great Bougainvillea	<i>Bougainvillea spectabilis</i> Linn. (Nyctaginaceae)	Stem Bark	Alpha ionone, alpha copaene	Antiglycemic	[89]

22	Ivy Gourd	<i>Coccinia indica</i> Wight & Arn. (Cucurbitaceae)	Fruits and leaves	Glucose, gum, carbonic acid	Insulin like activity	[90]
23	Madagascar periwinkle	<i>Catharanthus roseus</i> Linn. (Apocynaceae)	Leaf powder	linolenic acid ethyl ester	Plasma levels in C+CR group showed antihyperglycemic activity	[91]
24	Jack bean	<i>Canavalia ensiformis</i> DC. (Leguminosae)	seeds	Proteins, phospholipids	Concentration of cholesterol, triacylglycerol in plasma indicated antihyperlipidemic effect	[92]
25	Coffee senna	<i>Cassia kleinii</i> Wight & Arn. (Caesalpiniaceae)	leaves,	Chrysophanol, emodin	Decreased glycogen level, body weight	[93]
26	Myrobalan, hard	<i>Terminalia chebula</i> Retz. (Combretaceae)	fruits	Coumarin	Decrease in glycosylated B and increase in total haemoglobin in diabetic rats	[94]
27	Asian ginseng	<i>Panax ginseng</i> , Araliaceae	Roots and rhizomes	Ginsenoside	Serum insulin is reduced	[95]

28	Aloe	<i>Aloe vera</i> (Asphodelaceae)	leaves	Aloin	Levels of fasting glucose is reduced	[96]
29	Sugar apple	<i>Annona squamosa</i> Linn. (Annonaceae)	seeds	Squamocenin	Improves plasma insulin	[97]
30	Milkvetch	<i>Astragalus membranaceus</i> (Fisch.) (Fabaceae)	root	Astragaloside	Protection of pancreatic cells from cell death and decrease onset of diabetes.	[98]
31	Grey Nicker	<i>Caesalpinia bonducella</i> (Fabaceae):	seeds	Caesalpinin, Bonducellin	Potent activity of hypoglycemia	[99,100]
32	Karira	<i>Capparis deciduas</i> , Capparaceae	Aerial parts	Isocodonocarpine, Capparisinine	Inhibition of alpha amylase	[101]
34	Broom creeper	<i>Cocculus hirsutus</i> , Menispermaceae	Leaves	Coclaurine, Triobine	Serum level of glucose is lowered.	[102]
35	Bitter yam	<i>Dioscorea dumetorum</i> Pax.	Tuber	Tryptophan, threonine	Decreased blood conc. of	[103]

		(Dioscoreaceae)			glucose, body weight and conc. of insulin	
36	Pitanga	<i>Eugenia uniflora</i> , Myrtaceae	Leaves	Atractylone, curzerene	Inhibit level of triglycerides	[104]
37	Elephant Foot	<i>Elephantopus scaber</i> , Asteraceae	Leaves and roots	hexadecanoic acid, isopropyl dimethyl tetrahydronaphthalenol	Positive control on diabetic activity	[105]
38	Indian banyan	<i>Ficus bengalensis</i>	Aerial roots	beta-sitosterol-alpha-D-glucose	Fall in BGL	[106]
39	Bitter kola	<i>Garcinia kola</i> (Clusiaceae)	Seeds	Kolaviron	Reduced level of glucose	[107]
40	Chinese Foxglove	<i>Rehmanniae Radix</i> , Orobanchaceae	Root	Catapol, vit A, B, C, D.	Inhibit diabetic nephropathy	[108]
41	Chinese cassia	<i>Cinnamomum cassia</i> , Lauraceae	bark	Cinnamaldehyde	inhibit fibronectin	[109]
42	Malabar kino	<i>Pterocarpus marsupium</i> , Fabaceae	Wood	Liquiritigenin, isoliquiritigenin	Regenerate Beta cells of pancreas	[110]

43	Fenugreek	<i>Trigonella foenum-graecum</i> , Fabaceae	Seed Extract	kaempferol 3-O- β -d-glucopyranoside.	Decreased absorption of glucose	[111]
44	Korean angelica-tree	<i>Aralia elata</i> , Araliaceae	Seeds	Silphioside A, araloside A,C,D	Inhibitory of intestinal alpha-glucosidase.	[112]
45	Guar	<i>Cyamopsis tetragonoloba</i>	Leaves, seeds	P-hydroxycinamyl, astragalin.	Lowering of lipid and blood sugar	[113]
46	Chinese goldthread	<i>Coptis chinensis</i> , Ranunculaceae	Roots	Berberine, Palmatine	CCPW-1 inhibited the blood glucose level	[114]
47	Alfalfa	<i>Medicago sativa</i> , Fabaceae	Seeds	Stachydrine, betaine	Beta cells are regenerated and increased sensitivity	[115]
48	Henna	<i>Lawsonia inermis</i> , Lythraceae	Whole Plant	hennotannic acid	Ethanollic extract reduced diabetes and had antidiabetic effect	[116]

49	Common guava	<i>Psidium guajava</i> , Myrtaceae	Leaves	guajanoic acid, uvao	Activity of hepatic hexokinase was increased and it was decreased by aqueous extract	[117]
50	Heart-leaved moonseed	<i>Tinospora cordifolia</i> , Menispermaceae	Stem Bark	Columbin, tinosporaside	Prevent Hyperalgesia in diabetic neuropathy	[118]
51	Ginger	<i>Zingiber officinale</i> , Zingiberaceae	Rhizomes	Zingerone, gingerols	Improved PON-1 And TAC activity in diabetes patients	[119]
52	Java grass	<i>Cyperus rotundus</i> , Cyperaceae	Rhizomes	Iridoids	Serum triglycerides were reduced	[120]
53	Quince	<i>Cydonia oblonga</i> , Rosaceae	Seeds	Cyprene, Mustakone	Lowered lipid levels	[121]
54	Butterfly pea	<i>Clitoria ternatea</i> , Fabaceae	Leaves and Flowers	Cliotides, steroids	Decreased glycosylated levels	[122]

55	Star flower	<i>Hypoxis hemerocallid ea,</i> Hypoxidacea e	Rhizom es	pentenyne glycoside	Hypoglyce mic activity	[123]
56	Common Agrimony	<i>Agrimony eupatoria,</i> Rosaceae	Aerial part	Volatile oils	Insulin like activity	[124]
57	Pigeon pea	<i>Cajanus cajan</i> (Fabaceae)	Leaves	Cajanin	β -cells of Islets of Langerhan were developed	[125]
58	Teripod	<i>Caesalpinia digyna ,</i> Fabaceae	root	Tannins, bonducin	Glycogen storage increased	[126]
59	Avacado	<i>Persea Americana,</i> Lauraceae	Fruit	Vitamin, Minerals	Glucose uptake in liver is regulated	[126]
60	Bilberry	<i>Vaccinium myrtillus,</i> Ericaceae	Leaf, Fruit	Anthocyanoside	Prevention of HDL- C, LDL,VLDL	[127]

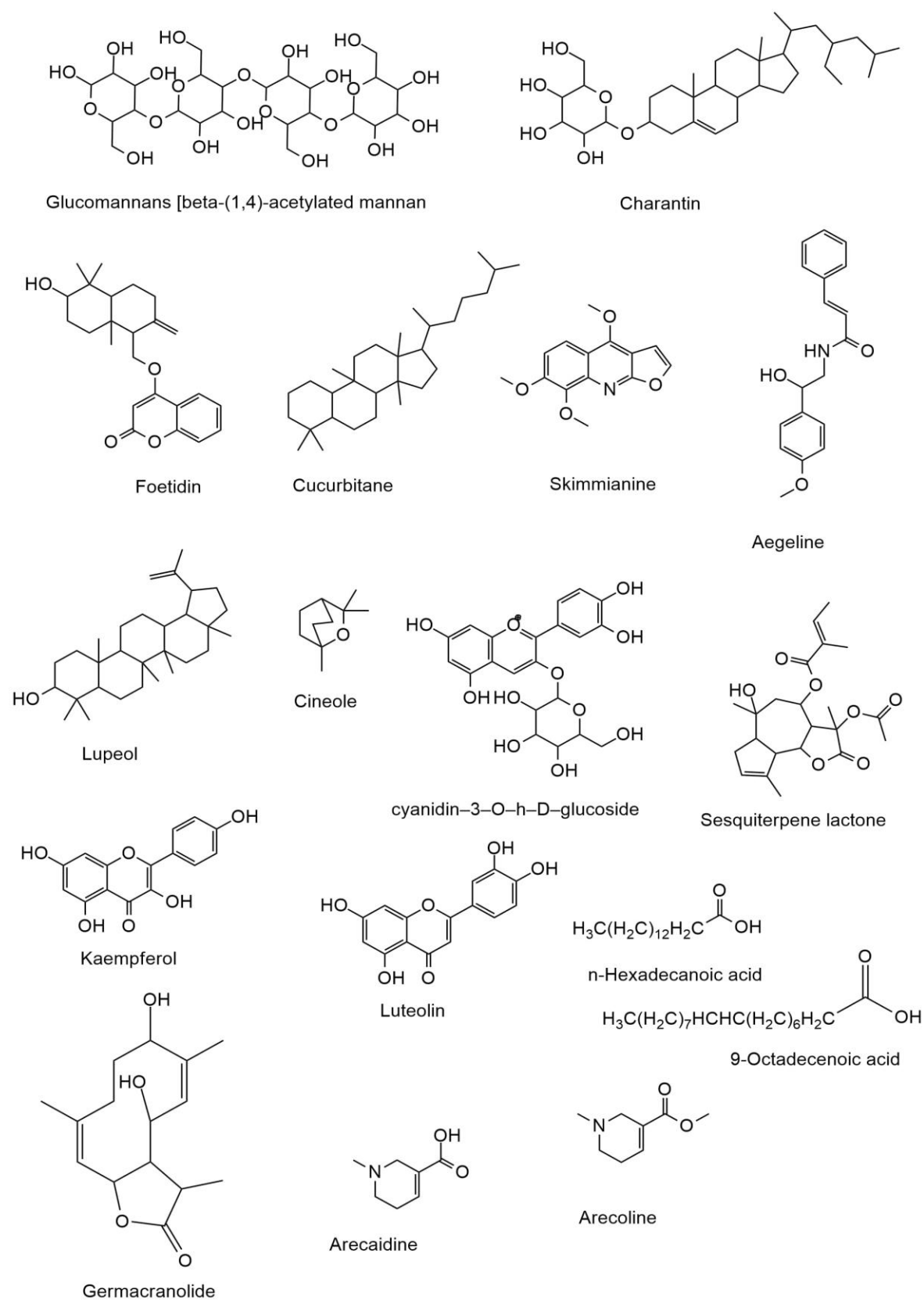


Figure 3: Chemical structures of bioactive compounds

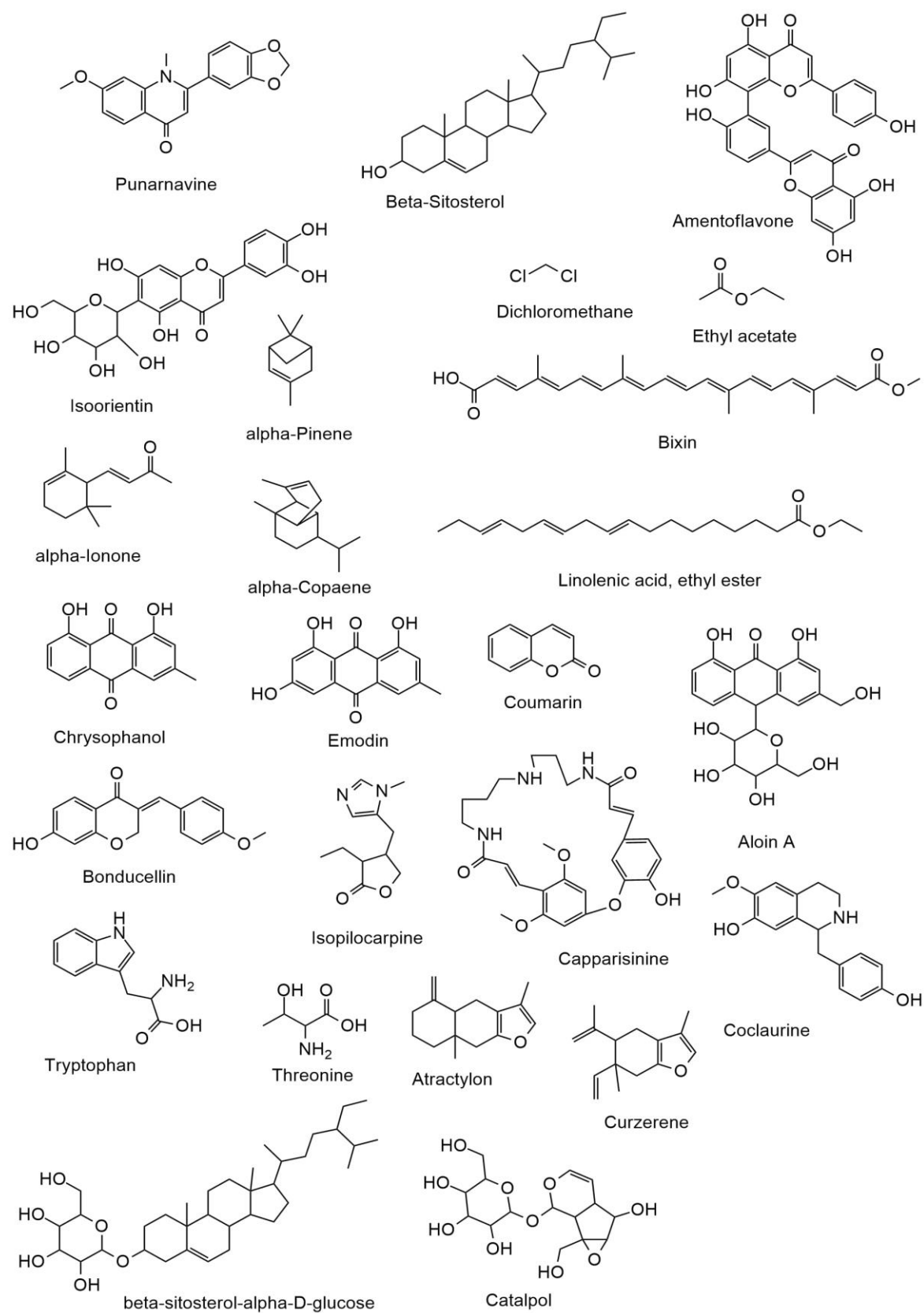


Figure 4: Chemical structures of bioactive compounds

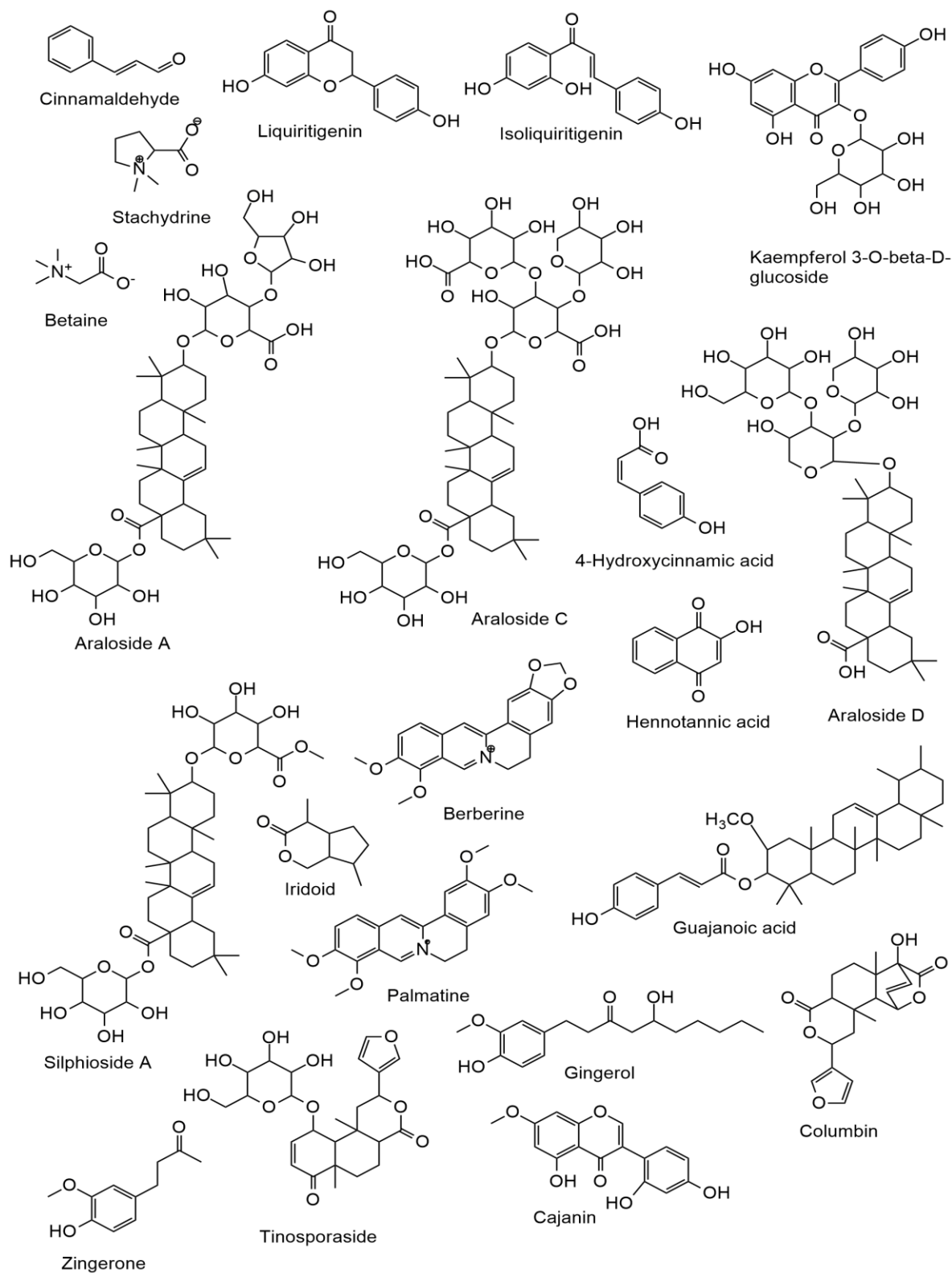


Figure 5: Chemical structures of bioactive compounds

CONCLUSION:

Diabetes has been reported as the fastest growing disorder in the recent years. It has been reported to be associated with co- morbidities and hyper lipidemia like hypertension. Herbal drugs are beneficial to diabetes management. They possess very minimum side effects with maximum potency. Theses herbal drugs help in reducing glucose levels in the blood. Various mechanism possesses the antidiabetic properties. The drugs are describing on the basis of common names, part used, chemical constituents and mechanism of actions. Therefore, herbal plants play a very important role in the traditional medicine system.

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None.

Conflict of interest

The authors declare no conflict of interest, financial or otherwise.

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