Admired phytoconstituents gifted by Mother Nature for diabetes mellitus: pioneer remedies for modern era

Dr Surender verma,
Assistant Professor, Department of Pharmaceutical Sciences, KUK, Kurukshetra, Haryana, India
Gmail- svpharma.kuk@gmail.com
Mob. No. 919416235050

Charan singh
Research Scholar, Department of Pharmaceutical Sciences, KUK, Kurukshetra, Haryana, India
Gmail- s.charan6695@gmail.com
Mob. No. 919813560782

Abstract- Herbal medicine, Botanical medicine, phytomedicine all are synonyms, have used for medical purposes. Herbal medicine have used in the treatment and prevention of disease including diabetes has a long background as compared to conventional medicine. Mother Nature has medicinal and botanical plants to mankind; there is technical data which justify wide range in Ayurveda. There are lots of plants, herbs, fruits, roots, rhizomes, bark which posses pharmacology alterations on human being , plants like stevia rebaudiana, Momordica charentia, Syzygium cumini, Azadirachta indica, Allium cepa, allium sativum, Psidium guajava, Tinospora cordifolia, Lawsonia inermis, Panax ginseng, aloe barbadensis, Zingiber officinale, Ocimum sanctum, Plantago ispaghula, Mangifera indica, etc which are most popular remedy shows antidiabetic activity. People apparently faith on them due to lesser side effect, imposes no synergistic and antagonistic action.

Keywords - God gifted phytochemicals, benefits over synthetic drugs, technicalities behind hypoglycemic effect, all aspects like- mechanism of action, dose, formulations

INTRODUCTION

Diabetes mellitus compose a group of etiologically and clinically heterogeneous disorderliness with a common set of symptoms: uncontrolled thirst and hunger, muscular weakness and weight loss, excessive urination, and move up blood glucose level which, when it exceeds the renal threshold, results in the excretion of glucose in the urine [1]. India is savage to be the diabetic capital of the world, with 50.8 million diabetics. Diabetes mellitus (DM) is one of the most common constantly recurring metabolic diseases that characterized by a deficiency in insulin production and its action. It interfere most metabolic processes inside the human body which leads to many impediment, such as ulceration, cardiovascular diseases, nephropathy, neuropathy, and retinopathy [2].Rebaudioside A is a steviol glycoside derived from the herb Stevia Rebaudiana (bertoni) [3]. Rebaudioside A is a major constituent (20% w/w) of natural stevioside powder and possess strong insulinotropic (anti-diabetic) activity which result in lower down blood glycemic index with an extra glucose molecule than stevioside. The temporary acceptable daily intake (ADI) for steviol glycosides set by JECFA is 0-2 mg/kg bw/day. There is no confusion that herbal medicines provided the first basis for therapeutics before the development or occurrence of orthodox medicine [4]. There is fatten interest in herbal remedies due to the adverse effects associated with the oral hypoglycemic agents (therapeutic agent) for the treatment of diabetes mellitus, so the traditional herbal medicines are mainly used which are picked up from plant [5].

However, the selection of herbs might based on several factors, which include the stage of progression of diabetes, types of comorbidities that the patients are having, availability, affordability as well as the safety profile of the herbs. This review focuses on the herbal and natural remedies that play the role in the treatment or prevention of this morbid disorder – diabetes, including their underlying mechanisms for the blood glucose-lowering property and the herbal products already been marketed for the remedial action of diabetes[6].

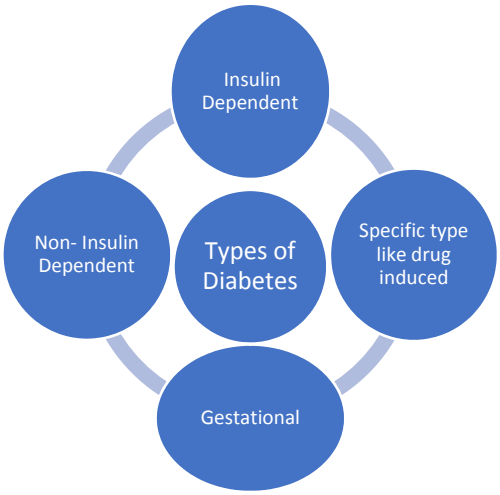
1. CLINICAL OVERVIEW ON DIABETES MELLITUS

Diabetes Mellitus (DM) is a metabolic, endocrine disorder. It is a chronic non-communicable disease which generally starts insidiously (over a period of long time), and even in the absence of symptoms (hence called as a silent killer) [7]. Diabetes is the condition in which the body does not properly process food for use as energy. Most of the food we eat is turned into glucose, or sugar, for our bodies to use for energy. The pancreas, an organ that lies near the stomach, makes a hormone called insulin to help glucose get into the cells of our bodies. When you have diabetes, your body either doesn't make enough insulin or can't use its own insulin as well as it should. This causes sugars to build up in your blood. This is why many people refer to diabetes as “sugar.” Diabetes can

cause serious health complications including heart disease, blindness, kidney failure, and lower-extremity amputations. Diabetes is the seventh leading cause of death in the United States [8]. Micro vascular complications include retinopathy, nephropathy, and diabetic neuropathies. These produce significant morbidity in patients, leading to loss of vision, loss of kidney function, impaired mobility, difficulties with cognition, and inability to work, increasing not only the quality of life costs to the patient but financial costs to society as a whole [9].

Sub-categories of diabetes

There are four sub-categories of diabetes: Diagrammatic representation



1. Type1 diabetes (due to autoimmune b-cell destruction, usually leading to absolute insulin deficiency) 2. Type2 diabetes (due to a progressive loss of b-cell insulin secretion frequently on the background of insulin resistance) 3. Gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation) 4. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation) [10].

TREATMENT OF DIABETES WITH HELP OF HERBALS

Complementary or alternative treatments using herbal medications draw the attention of many diabetic patients. Numerous common herbs are claimed to reduce blood glucose level, therefore the possibility of having better glycemic control or being less dependent on insulin injections by taking herbal medicines is unquestionably appealing. However the selection of herbs might depends on several factors, which include the stage of progression of diabetes, types of comorbidities that the patients are having, availability, affordability as well as the safety profile of the herbs [6].

Traditional herbal mineral plays an important part in the treatment of diabetes. If we able to even identify some 5-6 herbal drugs that can reduce dose of insulin by increasing resistance sensitivity, reducing insulin resistance, then we would have positively contributed in the treatment of diabetes [11].

In Ayurveda, plant parts of different species have been used against various diseases since time immemorial. The ancient man used herbs as therapeutic agents and medicaments, which they were able to procure easily. The nature has provided abundant plant wealth for all living creatures, which possess medicinal virtues. Many traditional plant treatments for diabetes are used throughout the world. Plant drugs and herbal formulation are frequently considered to be less toxic and free from side effects than synthetic one. Based on the WHO recommendations hypoglycemic agents of plant origin used in conventional medication are important.

PATENTS

Summary of Invention	Patent Number	Inventor/Assignee
Anti-diabetic and cholesterol lowering preparation from fenugreek seeds	US7815946	Murthy, P.S., Moorthy, R., Prabhu, K.M., Puri, D.
Synergistic composition for the treatment of diabetes mellitus	US7641925	Bhaskaran, S., Mohan, V
Pharmaceutically active extracts of vitex leucoxylon, a process of extracting the same and a method of treating diabetes and inflammatory diseases therewith	US7780997	Raju, G.G., *et al*
Synergistic composition for the treatment of diabetes mellitus	US7736676	Bhaskaran, S., Mohan, V.
Methods of using pomegranate extracts for treating diabetes related atherosclerotic complications in humans	US7727563	Aviram, M.
Synergistic composition for the treatment of diabetes mellitus	US7674486	Bhaskaran, S., Mohan, V
Method of treating non-insulin dependent diabetes mellitus and related complications	US20100292178	Young, J.
Novel anti-diabetic herbal composition, method for preparing the same and use thereof"	US20090238900	Mitra, S.K., Saxena, E., Babu, U.V.
Methods for the treatment or prevention of Diabetes Mellitus and other metabolic imbalances"	US20090252817	Hayes, K.C., Sundram, K., Sambanthamurthi, R., Tan, Y.A.
Anti- diabetes extract isolated from Rauvolfia vomitoria and Citrus aurantium, and methods of using same	US20090041873	Campbell-tofte, J.
Natural herb composition for the treatment of diabetesand manufacturing method	US7482030	Mansilla, A.
Berry preparations for treatment of diabetes and metabolic syndrome	US20090176718	Ribnicky, D., Raskin, I.
Anti-diabetics extract isolated from Rauvolfia vomitoria and Citrus aurantium, and methods of using same	US7579025	Campbell-tofte, J.
Extracts, compounds and pharmaceutical compositions having anti-diabetic activity and their use	US7416744	Rubin, I.D., Bindra, J.S., Cawthorne, M.A.
Natural herb composition for the treatment of diabetes and manufacturing method	US20080299236	Mansilla, A.
Herbal product to be administered to diabetic people and process	US20080206372	Agreda, N.J., Martin, P.F., Belo, M.E.W.
Anti-diabetics extract isolated from Rauvolfia vomitoria and Citrus aurantium, and method of using same	US7429395	Campbell-tofte, J.
Pharmaceutically active extracts of Vitex leucoxylon, a process of extracting the same and a method of treatingdiabetes and inflammatory diseases	US20080199543	Gokaraju, G.R., Gokaraju, R.R., Gottumukkala, V.S., Somepalli, V.
Herbal extract and compound lupinoside and its analogues as anti-diabetic type-2drugs from plant Pueraria tuberose	US7276258	Dey, D., *et al*

In the present review we discussed about Herbal medicinal plants for the treatment of Diabetes mellitus. Herbs are used to manage Type 1 and Type II diabetes and their complications. For this, therapies developed along the principles of western medicine (allopathic) are often limited in efficacy, carry the risk of adverse effects, and are often too costly, especially for the developing world. This study may be useful to the health professionals, scientists and scholars working in the field of pharmacology and therapeutics to develop antidiabetic drugs [12]. Treatment of Diabetes mellitus without any adverse effects is still the biggest question to medical practioners. According to world ethanobotanical 800 medicinal plants are used for the pre- vention of diabetes mellitus. Clinically proven that only 450 medicinal plants possess anti diabetic properties from which 109 medicinal plants have complete mode of action. In ancient time doctor and lay person used traditional medicinal plants with their active constituents and properties for the treatment of various diseases such as heart diseases, cancer and diabetes. There is a long history of traditional plants used for the control of diabetes in India and China. There are various books available such as Charaka Samhita and Susruta Samhita which explains phytopharmacology features of diabetes and its adverse effect. Synthetic drugs which are used for treatment of diabetes are associated with various adverse effect such as sickness, vomiting, dysentery, alcohol flush, migraine, swelling, malignant anemia and faintness. Herbal drugs are proved to be a better choice over synthetic drugs because of less side effects and adverse effects. Herbal formulations are easily available without prescription. These herbal drugs are used for life threatening disease. These drugs are also used when chemical drugs are ineffective in treatment of disease [13].

Antidiabetic plants

[1] Stevia (Sweet leafs)

Stevia it is obtained from Stevia rebaudiana belonging to family bertoni. Stevia rebaudiana Bertoni is a perennial shrub of the Asteraceae family that is native to Paraguay. It is commonly known as the “sweet leaf” because it mainly accumulates secondary metabolites called steviosides (stevioside, rebaudioside A, B, C, D, and F, dulcoside, steviolbioside, and steviol) in its leaves. These metabolites are natural non-caloric sweeteners that do not contain metal residues in the form of a sweet extract and are not carcinogenic; thus, they di□er from artificial sweeteners. Further steviosides can be 300 times sweeter than sucrose. The beneficial e□ects of steviosides in terms of human health have led to increased consumption; thus, greater production is required. The quantity and quality of steviosides produced by a stevia plant can be altered by factors such as growing season, planting density, solar radiation, soil moisture, temperature, and plant nutrition [14].

Fig. 1, Stevia rebaudiana [121]

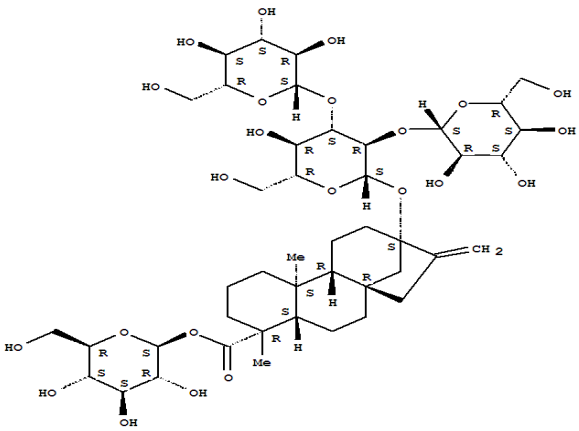


Fig. 22, Rebaudioside A [144]

[2] Momordica charentia (Karela, Bitter gourd)

It consists of fresh green fruits Momordica charentia belonging to family Cucurbitaceae. Chemical Constituents are- Chiratin (steroidal saponin) and mimordicin. Momordica charantia is not only a nutritious vegetable, but is also used in traditional medical practices to treat type 2 diabetes mellitus. In Southern India it is used in the dishes pachadi (which is considered a medicinal food for diabetics). Used in the treatment of diabetes. Other uses are stomachic, carminative, tonics, treatment of rheumatism, gout, disorder of spleen and liver[15].Owing to these functional components, bitter melon posses wide range of pharmacological activities for instance, antioxidant, antifungal, anti-diabetic, anti-obesity, stomachic, anticancer, hypotensive, and blood cholesterol lowering effects. The diabetes mellitus and associated complications are true example of life style related disorders [16].

Fig. 2, Momordica charentia [122]

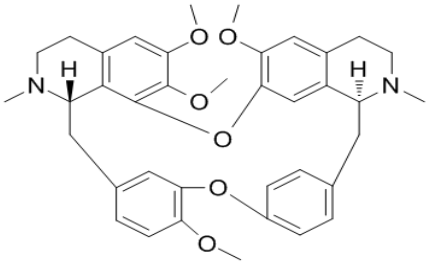


Fig. 23, Charantin [145]

[3] Syzygium cumini (Jamun, Jambul)

It consists of mature fruits and dried seeds of Syzygium cumini belonging to family myretaceae. Chemical Constituents are anthocyanin, delphinidine-3-gentiobioside, malvidin 3-laminaribiosidea and ferulic acid. Many research studies have shown that jamun is one of the best medicines for treatment of diabetes. It is an Antidiabetic drug. Diabetics are advised to consume 1 tsp of this jamun seed powder in empty stomach early morning [15]. Traditionally the jambul fruits, leaves, seeds, and bark are all used in ayurvedic medicine. The bark contains tannins and carbohydrates, accounting for its long-term use as an astringent to combat ailments like dysentery [17].

Fig.3,Syzygiumcumini[123]

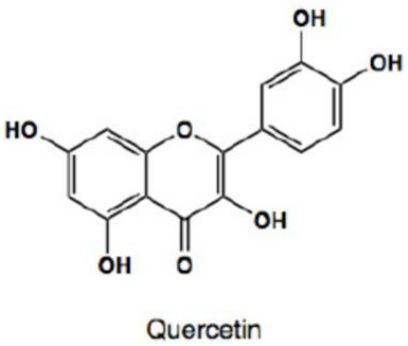


fig. 24, Quercetin [146]

[4] Azadirachta indica (Neem)

Azadirachta indica, commonly known as Neem, belongs to Family Meliaceae, is one of the most versatile medicinal plants that has gained worldwide importance due to medicinal and insecticide properties. There are several studies showing the effects of Azadirachta indica in experimental and clinical models [18]. A study was undertaken to evaluate the70% alcoholic neem root bark extract (NRE) in diabetes and results showed that neem root bark extract showed statistically significant results in 800mg/kg dose. Another experiment was performed to examine the pharmacological hypoglycemic action of Azadirachta indica in diabetic rats and results showed that in a glucotolerance test with neem extract 250mg/kg demonstrated glucose levels were significantly less as compared to the control group and Azadirachta indica significantly reduce glucose levels at 15th day in diabetic rats [19].

Fig. 4, Azadirachta indica [124]

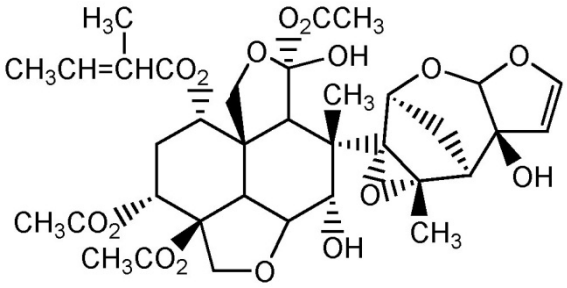


fig. 25, Azadirachtin [147]

[5] Allium cepa (Onion)

Many onion bulbs ether fractions showed significant hypoglycemic effects by decreasing the glucose peak in subcutaneous glucose tolerance tests. Among them, A. cepa increases the fasting serum high-density lipoprotein values, exhibiting alleviation of hyperglycemia in streptozotocin (STZ) diabetic rats. The hypoglycemic and hypolipidemic effects of onion were usually associated with a relevant antioxidant activity, as indicated by the increase in superoxide dismutase activity. No effects were observed on both lipid hydroperoxide and lipoperoxide levels [20].

Fig. 5, Allium cepa [125]

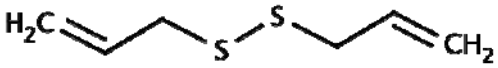
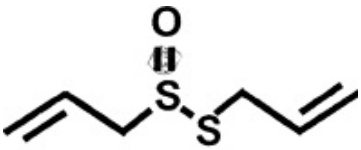


fig. 26, Allyl propyl disulfide [148]

[6] Allium cepa (Garlic)

Garlic (Allium sativum L., family: Alliaceae) has played important dietary and medicinal roles throughout the ages. It has been evaluated for a number of purposes, including treatment of hypercholesterolemia, hypertension, diabetes, rheumatoid arthritis, cold or the prevention of atherosclerosis and the development of tumors. Many available publications have indicated the possible antioxidant, antibacterial, antihypertensive and anti-thrombotic properties of various garlic varieties [21]. The health beneficial effects of A. sativum are due to reduction of risk factors for cardiovascular diseases and cancer, stimulation of immune function, enhanced detoxification of foreign compound, Hepatoprotection, anti-microbial effect and antioxidant effect [22].

Fig. 6, Allium cepa [126]



Allicin

fig. 27, Allicin [149]

[7] Psidium guajava (Amrud)

Guava leaf "Psidium guajava L." belonging to Myrtacea family has a long history of folk medicinal uses in Egypt and worldwide as a cough sedative, in the management of hyper tension, obesity and in the control of diabetes mellitus [23]. Guava is used not only as food but also as folk medicine in subtropical areas around the world because of its pharmacologic activities. In particular, the leaf extract of guava has traditionally been used for the treatment of diabetes in East Asia and other countries. It is generally used in the treatment of diarrhoea, jaundice dysentery, conjunctivitis, cough, Rheumatism. Whole fruit is found to possess good anti-oxidant activity [24].

Fig. 7, Psidium guajava [127]

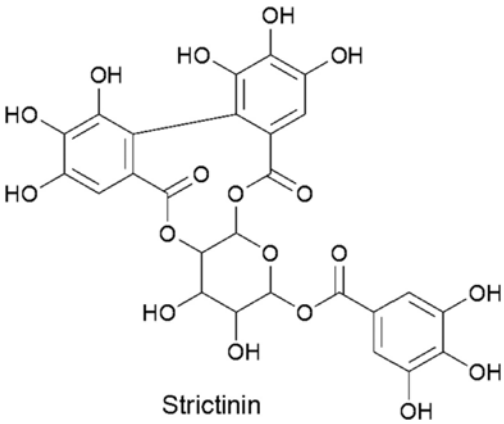
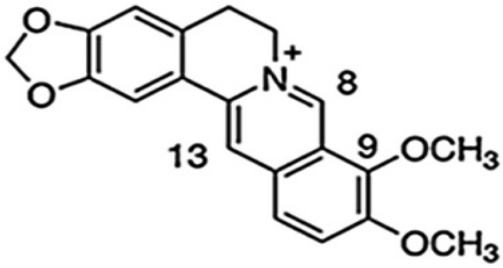


fig. 28, Strictinin [150]

[8] Tinospora cordifolia (Giloya)

The herb Tinospora cordifolia belongs to the Menispermaceae family and is commonly known as Gulancha or Tinospora in English and Giloya or Ambervel in Hindi. It has a long history of use in Ayurvedic medicine [25]. Medicinal plants are being looked up once again for the treatment of diabetes. Current study is performed to evaluate the antidiabetic potential of Tinospora cordifolia; Family: Menispermaceae. This family is a rich source of alkaloid and terpenes. All parts of this plant are documented to be useful in ethno botanical surveys [26]. It is a large, glabrous, deciduous climbing succulent shrub, commonly found in hedges. It has been known for long in the Ayurvedic literature (i.e. the system of traditional medicine native to India and practiced in other parts of the world as a form of alternative medicine) as a tonic and vitalizer and as a remedy for diabetes and other metabolic disorders [27]. Phytochemistry of T. cordifolia belongs to different classes such as alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds and polysaccharides [28].

Fig. 8, Tinospora cordifolia [128]



Berberine

fig. 29, Berberine [151]

[9] Fenugreek (Methi)

Fenugreek (Trigonella foenum graecum) is an annual herb, belonging to the Leguminosae family [29] Fenugreek leaves and yellow colored seeds were used as a spice as well as medicinal herb. In fact, fenugreek could be used for the treatment of metabolic disorders, respiratory and digestive problems [30]. The hypoglycemic property of fenugreek was observed in diabetic patients [31]. Reports also suggest that fresh fenugreek leaves contain ascorbic acid (220.97 mg/100 g) and β-carotene (19 mg/100 g) and are a rich source of calcium, iron and zinc content [32].

Fig. 9, Fenugreek [129]

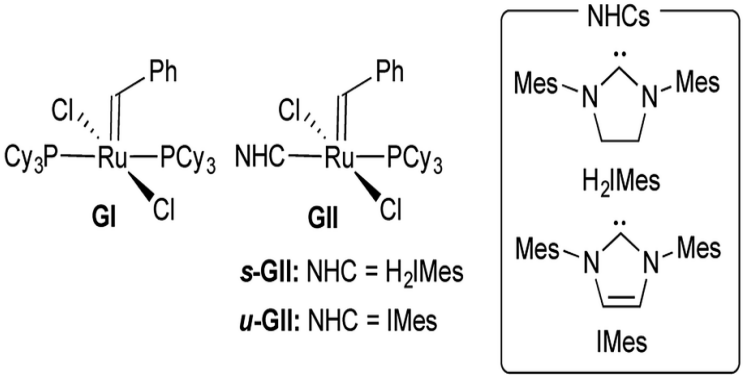


fig. 30, GII [152]

[10] Lawsonia inermis (Henna)

Lawsonia inermis commonly called as Henna and the synonym is Lawsonia Alba Linn. belongs to family Lythraceae [33] Phytochemistry: Almost 70 phenolic compounds have been isolated from various parts of the plant. Naphthaquinones, which include the dyeing principle lawsone, have been linked to many of the pharmacological activities. The terpene, β-ionone is largely responsible for the pungent odour of the essential oil isolated from the flowers. In addition to other volatile terpenes, some non-volatile terpenoids, a single sterol, two alkaloids and two dioxin derivatives have also been isolated from the plant A wide range of biological activities have been attributed to henna, including antifungal, antibacterial, virucidal, antiparasitic, anti-inflammatory, analgesic and anticancer properties, as well as hepatoprotective, immunomodulatory, anthelminthic, antitrypanosomal and anti-oxidant activities [34]. Total phenolic compound was 2.56 and 1.45 mg tannicper mg of Henna dry matter as extracted with methanol and water respectively. In effect of different concentrations of methanolic extract of henna in comparison with synthetic antioxidant [35].

Fig. 10, Lawsonia inermis [130],

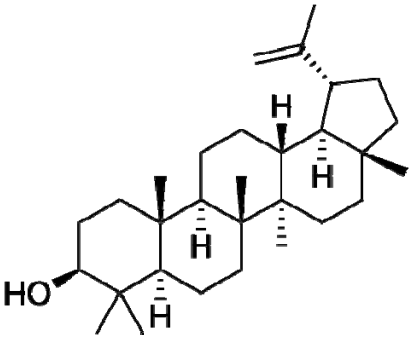


fig.31, Lupeol [153]

[11] Panax ginseng

Ginseng, often described as the "king herb," holds an important position in traditional Oriental medicine in many countries. The highly valued plant is currently cultivated in China, Korea, Japan, Russia, and in the United States and Canada as well [36]. Ginseng is an herb derived from several species of the plant family Araliaceae and genus Panax indigenous to Asia and North America, and has been valued for centuries by local cultures as a tonic and remedy for many ailments [37]. Human and animal studies showed that ginseng extracts can also have hypoglycemic effects especially modulating effects on insulin sensitization and/or insulin secretion and regulating actions on digestion and intestinal absorption [38]. Extracts and bioactive compounds isolated from ginseng are studied for their various health promoting activities such as antioxidant, antitumor, antihyperglycemic, skin protecting, anti-osteoporotic anticancer, anti-infective and respiratory problems [39]. It shows antihyperglycemic activity by increasing plasma insulin levels, the number of insulin receptors and insulin sensitivity [40].

Fig. 11, Panax ginseng [131]

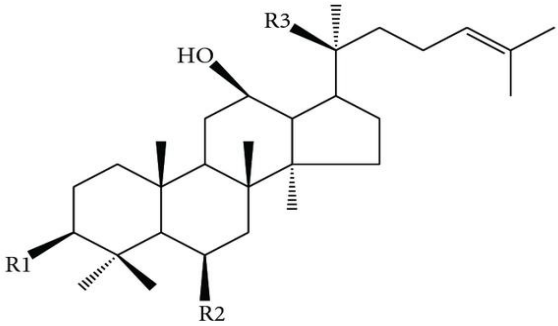


fig. 32, Panax ginseng [154]

[12] Aloe vera

Plants extracts have been used for a long time as a traditional remedy for diabetes in many parts of the world. For instance, Aloe vera (Aloe barbadensis Miller), a perennial succulent xerophyte, with elongated pointed fleshy leaves consisting of two parts, an outer skin (green rind) and an inner pulp [41]. The chemistry of the plant has revealed the presence of more than 200 different biologically active substances, which include antimicrobial, antibacterial, antifungal, antiviral, activities of the non-volatile constituents of the leaf [42]. The plant leaves contains numerous vitamins, minerals, enzymes, amino acids, natural sugars and other bioactive compounds [43]. Use of antioxidants such as the flavonoids found in aloe vera is an important step in decreasing the prevalence of diabetes mellitus [44].

Fig. 12, Aloe Vera [132]

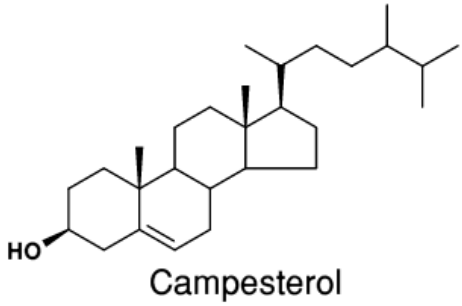


fig. 33, Campesterol [155]

[13] Zingiber officinale (Zinger)

Ginger, the rhizome of Zingiber officinale Roscoe (Zingiberaceae), a perennial herbaceous plant is native to Southern Asia [45]. A few isolated studies about the hypoglycaemic properties of ginger in animals have reported variable results [46]. Ginger is a commonly used spice in the African Kitchen and has been used as spice for over 2000 years. It is a perennial plant with narrow, bright green, grass-like leaves and yellowish green flowers with purple markings [47]. It was reported that ginger juice has significant blood glucose lowering effect. Furthermore, a decreased blood glucose and urea were also observed by other investigators. Ginger also decreased LDL-cholesterol, VLDL-cholesterol and triglycerides levels in apolipoprotein-E deficient mice [48].

Fig. 13, Zingiber officinale [133]

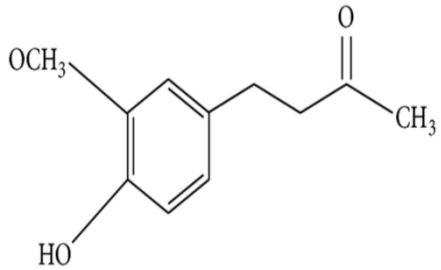


fig. 34, Zingerone [156]

[14] Ocimum sanctum (Tulsi)

Ocimum Sanctum is commonly known as Holy Basil or Tulsi (in Hindi). It is also known as “Queen of herbs” due to its medicinal properties [49]. The active constituents of herb include volatile oil eugenal and B-caryophyllene, flavonoids and a number of other components present in fixed oil [50]. Also it produced significant antihyperlipidaemic effect and thus proves to be effective in preventing and managing complications of diabetes [51]. O. sanctum has been reported to possess very good anti diabetic properties. The anti-diabetic activity of hydroalcoholic extract of O. tenuiflorum against streptozotocin and nicotimanide induced diabetes in rats was found to be significant at the dose levels of 250 and 500 mg/kg body weight and this effect was comparable with glibenclamide [52].

Fig. 14, Ocimum sanctum [134]

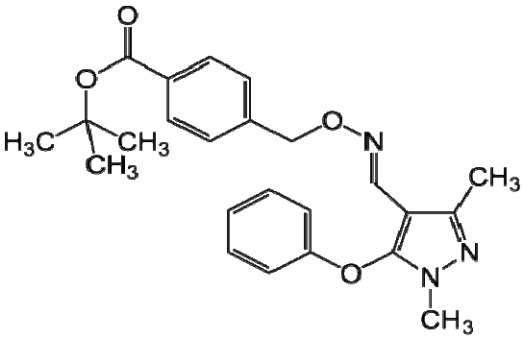


fig. 35, Circimaritin [157]

[15] Psyllium (Plantago ispaghula)

Psyllium seed is obtained from a plant of the Plantaginaceae family and called “Ghatuna” and “Espaghool” in Iranian traditional medicine. It is said to be cold and humid in nature Existence in large amount of bran and fiber in the seeds delays the intestinal absorption of glucose and controls the blood glucose level [53]. It could be concluded that the intake of chicory leaves or psyllium seeds may be useful for controlling blood glucose level and combating the metabolic disorders and complications that accompanied with diabetes [54]. Scientific evidence of the efficacy of ispaghula for the treatment of several human diseases, such as constipation, diarrhea, inflammatory bowel diseases (IBDs), diabetes, hypercholesterolemia, has been demonstrated by many studies in recent years [55]. It has been suggested that psyllium may enhance insulin action or insulin-independent effects [56].

Fig. 15, Ocimum sanctum [135]

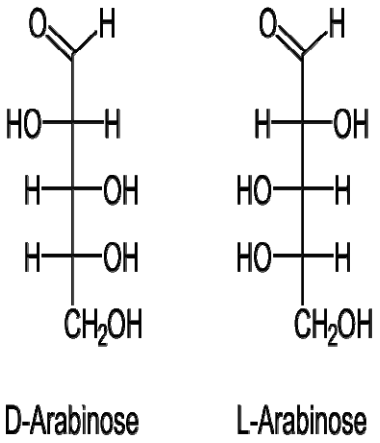


fig. 36, Arabinose [158]

[16] Mangifera indica

Mangos belong to the genus Mangifera of the family Anacardiaceae [57]. The tree is found throughout India and traditionally its seeds and fruits are used for treatment of various ailments. The extract showed antidiabetic activity this action could be due to reduction in intestinal absorption of glucose [58]. Phytochemical research from different parts of M. indica has demonstrated the presence of phenolic constituents, triterpenes, flavonoids, phytosterol, and polyphenols [59]. The reported pharmacological activities of mangiferin include antioxidant, radio protective, antitumor, immunomodulatory, anti-allergic, anti-inflammatory, antidiabetic, lipolytic, antiboneresorption, monoamine oxidase inhibiting, antiviral, antifungal antibacterial and antiparasitic properties, which may support the numerous traditional uses of the plant [60]. The ethanolic extracts of Mangifera indica showed significant antidiabetic activity as compare to standard glibenclamide [61]. Antidiabetic action may be due to an intestinal reduction of the absorption of glucose. The leaves of MI used for antidiabetic properties using normoglycaemic, glucose-induced hyperglycaemia and streptozotocin (STZ) induced diabetic mice [62]. Half-ripe fruit eaten with salt and honey is used for a treatment of gastro-intestinal disorders, bilious disorders, blood disorders, and scurvy. Ripe mangos are a rich source of vitamin A, and are used to treat vitamin A deficiencies such as night blindness [57].

Fig. 16, Mangifera indica [136]

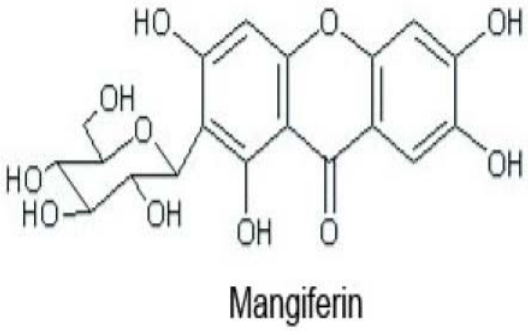


fig. 37, Mangiferin [159]

[17] Pomegranate (Anar)

Pomegranate fruit is obtained from punica granatum linn belonging to family punicaceae [63]. Punica granatum flowers (PGF) is prescribed in Unani and Ayurvedic medicines in the treatment of diabetes for centuries although pomegranate flower has been reported in many studies for its anti-diabetic activities [64]. Phytochemical found in Pomegranate (Punicagranatum, Punicaceae) includes ellagitannins, gallotannins and anthocyanins. Role of pomegranate in diabetes have been reported due to its flavonoids [65]. Administration of crude powder of Punica granatum husk decreased the concentration of glucose, triglycerides, cholesterol, LDL cholesterol and raised the level of HDL cholesterol and hemoglobin content in the blood of normal group and alloxan diabetic group treated rats [66].

Fig. 17, Pomegranate [137]

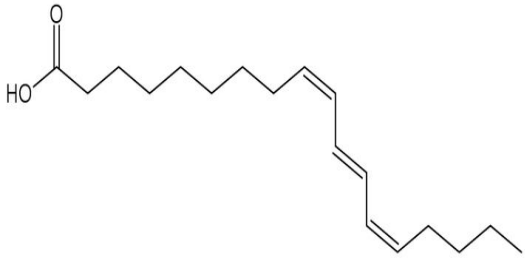


fig. 38, Punicic acid [160]

[18] Acacia arabica (Babhul)

It is a bark of tree belongs to family Leguminosae and is known as Babul or Babur in Hindi, Kikar in Punjabi1. Ancient Greeks were well known to this tree in 300 BC [67]. It may also be used for medicinal purposes, as a demulcent or for conditions such as gonorrhoea, leucorrhoea, diarrhea, dysentery or diabetes [68]. Acacia arabica seeds contained a substance(s) which depressed the blood glucose level in normoglycemic but not in alloxan-diabetic rabbits. The hypoglycaemic effect of the legumes was due to its direct or indirect stimulation of β–cells of islets of langerhans to secrete more insulin [69]. The plant extract acts as an antidiabetic agent by acting as secretagouge to release insulin. It induces hypoglycemia in control rats but not in alloxanized animals. Powdered seeds of Acacia arabica when administered (2, 3 and 4 g/kg body weight) to normal rabbits induced hypoglycemic effect by initiating release of insulin from pancreatic beta cells [70].

Fig. 18, Acacia arabica [138]

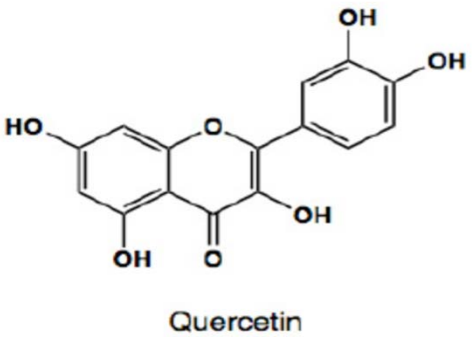


fig. 39, Quercetin [161]

[19] Ficus religiosa (peepal)

Ficus religiosa, commonly known as peepal in India, belongs to family Moraceae. Ficus religiosa has been reported to be used in the traditional system of Ayurveda for the treatment of diabetes [71]. Its leaves roots have been used for the treatment of diabetes mellitus and to treat infertility in women. It shows significant increase in serum insulin by initiating the release of insulin by beta cells of pancreas and having an extra pancreatic effect to possibly increase the number of insulin receptors [72]. There occur selective decreases in the hyperglycemic state after the administration of extracts of different parts of the species of Ficus, which may be mediated through a number of bioactive compounds present in the extract and these drugs gaining popularity both in developing and developed countries because of their natural origin, lesser side effects and low cost [73]. Phytochemical investigation of plant barks, showed the presence tannins, saponins, flavonoids, steroids, terpenoids and cardiac glycosides [74]. B- Sitosterol-D-glycoside was isolated from the root bark of F. glomerata and F. religiosa, which has a peroral hypoglycemic activity [75]. The anti-diabetic activity is highly effective in the aqueous extract of

F. religiosa bark [76]. This nature of effect was related with the hypoglycaemic drug glybenclamide. It has been also proved that F. religiosa significantly increases serum insulin, body weight and glycogen content in liver. Bark of F. religiosa shows similar effects and exhibits maximum fall of the blood sugar level [77].

Fig. 19, Ficus religiosa [139]

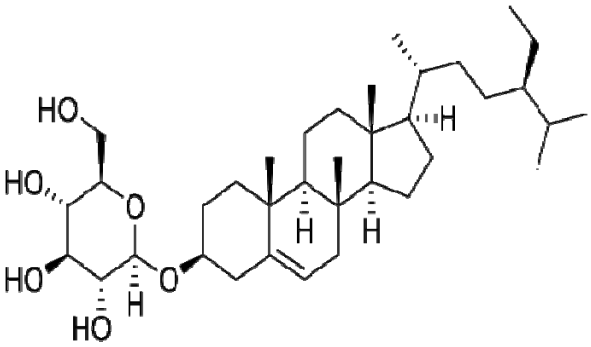


fig. 40, Sitosterol-d-glucoside [162]

[20] Curcuma longa (Haldi)

It is obtained from Curcuma longa L. belonging to family Zingiberaceae [78]. Commonly known as Haldi in Hindi has been used as spice and coloring agent [79]. It is also recommended for treating diabetes, high cholesterol, abdominal pains, menstrual disorder, wounds, eczema, jaundice, inflammations and cancerous symptoms and as a blood purifying activity [80]. The most active component of turmeric, curcumin, has caught scientific attention as a potential therapeutic agent in experimental diabetes and for the treatment of the complications of diabetes patients primarily because it is effective in reducing glycemia and hyperlipidemia in rodent models and is relatively in expensive and safe [81]. The compounds of C. longa, curcumin and bisdemethoxycurcumin have caught scientific attention as a potential therapeutic agent in the treatment of diabetes Curcumin is a competitive inhibitor of α-amylase and it reduce the level of blood glucose in diabetic and normal rats [82].

Fig. 20, Curcuma longa [140]

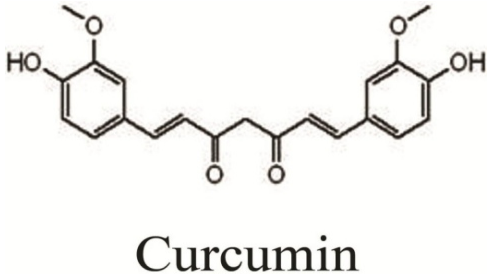


fig. 41, curcumin [163]

[21] Ipomoea batatas (sweet potato)

Ipomoea Sweet potatoes are a good food choice for diabetics as they are high in fiber and have a low glycemic index. Foods with a low glycemic index have less of an immediate impact on blood glucose levels, and therefore can diabetics control their blood sugar. Sweet potato (Ipomoea batatas) is one of the major food-producing tubers for human consumption belonging to the convolvulaceae family [83]. It is also a valuable medicinal plant having anti-cancer, antidiabetic, and anti-inflammatory activities. Sweet potato is now considered a valuable source of unique natural products, including some that can be used in the development of medicines against various diseases and in making industrial products [84]. Sweet potatoes are a good food choice for diabetics as they are high in fiber and have a low glycemic index. Foods with a low glycemic index have less of an immediate impact on blood glucose levels, and therefore can help diabetics control their blood sugar [85]. Ipomoea batatas continues to be highly valued in the local management of diabetes because of its effectiveness in the control of blood glucose and its low cost [86]. The effect of the extracts on glucose uptake and GLUT 4 translocation in an insulin resistant model is important to establish the therapeutic benefit in type 2 diabetes [87]. I. batatas leaves are rich in soluble dietary fiber. They have high mineral content, particularly iron, as well as high vitamin content, such as carotene, vitamin B2, vitamin C, and vitamin E [88]. It decrease in blood glucose level it also decreased protein glycation level total cholesterol, triglycerides, and LDL-cholesterol. Increase in HDL-cholesterol was also observed after treating the rats with aqueous extract of Ipomoea batatas [89].

Fig. 21, Ipomoea batatas [141]

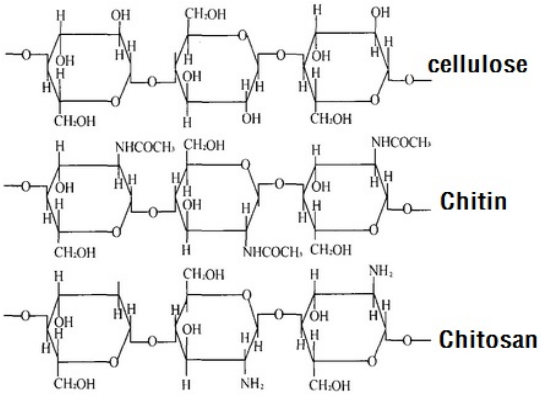


fig. 42, Dietary fibers [164]

Plant	Common name/ constituents	M.O.A.	Family/formulation	Dose/Reference
Stevia rebaudiana Bertoni	Stevia leaf/ stevioside, rebaudioside A	↑ Insulin secretion and sensitivity.	Asteraceae/ Sugar free	0-2 mg/kg/ 14
Momordica charentia	Karela/ Charantin	Regenerating β-cells of pancrease	Cucurbitaceae/ Karela (Himalaya)	10&25 µg/mL / 15,95
Syzygium cumini	Jamun/ quercetin	Restoration of β-cells, antioxidant action	Myrtaceae/ Madhunashini vati (Patanjali)	100 mg/kg /17, 96
Azadirachta indica	Neem/ Azadirachtin	Inhibits Gluconeogenesis	Meliaceae/ Madhunashini vati (Patanjali)	250 mg/kg /18, 97
Allium cepa	Onion/ Allyl propyl disulfide	Reduction in lipid profile	Liliaceae	300 mg/kg/ 20, 98
Allium sativum	Garlic, Lahsun/ Tellurium, Allicin	Decrease in hepatic cholesterogenesis	Alliaceae/ Lasuna (Himalaya)	300 mg/kg/ 21,99
Psidium guajava	Amrud/ Pedunculagin, Isostrictinin, Strictinin	Stimulating insulin release from pancreatic β-cells, Enhancing peripheral glucose metabolism	Myrtacea	250 mg/kg / 24, 100, 101
Tinospora cordifolia	Giloya/ Berberine	Regeneration of β-cells of islets of Langerhance	Menispermaceae/ Divya Madhunashini vati (Patanjali)	50, 100, 200 mg/kg /25, 102
Trigonella foenum	Methi / GII	Regeneration of the pancreas is an interesting improvement by GII	Leguminosae /Madhukalp vati (Patanjali)	50 mg/kg/ 29, 103
Lawsonia inermis	Henna/ Lupeol	Alpha-glucosidase inhibition	Lythraceae	1 gm/kg / 33, 104, 105
Panax ginseng	Ginseng/ Panax ginseng	Modulate insulin sensitization, secrertion, Intestinal glucose absorption	Araliaceae / Ginsomin (Mega)	10-50 mg/kg/ 37, 106, 107
Aloe barbadensis	Ghritkumari/ (Sitosterol,	Showed increase of pancreatic β-cells activity.	Liliaceae/ Glucocare (Himalaya)	0.5 ml / 100 g B.wt./ 42,108,109

	Campesterol and Lupeol			
Zingiber officinale	Adrak/ Zingerone	Enhances insulin synthesis, has high antioxidant activity	Zingiberaceae	500 mg/kg/ 45, 110,111
Ocimum sanctum	Tulsi/ Circimaritin	Promote insulin secretion by closure of K+ ATP (adenosine 5-monophosphate) channels	Lamiaceae/ Glucocare (Himalaya)	200mg/kg / 51, 112,113,114
Plantago ispaghula	Ispaghgul/ Arabinose	Reduce carbohydrate absorption	Plantaginaceae/ Natural psyllium fiber (Kirkland)	0.5g/Kg / 53, 115,119
Mangifera indica	Mango/ Mangiferin	Reduction in intestinal absorption of glucose	Anacardiaceae/ Glucodab	300mg/kg B.wt/ 58, 59, 60
Punica granatum	Anar/ Punicic acid	Reduce oxidative stress and lipid peroxidation	Punicaceae/ pomegranate (just vitamins)	100 mg/kg/ 63
Acacia arabica	Babhul/ Quercetin	Stimulate insulin secretion from pancreatic beta-cells	Leguminosae/ Diabecon DS (Himalaya)	20 mg/kg / 67, 68, 69, 116
Ficus religiosa	Peppal/ Sitosterol-d-glucoside	Stimulate insulin secretion	Moraceae/ madhuna-D (Ganga)	500mg/kg / 71
Curcuma longa	Haldi/ curcumin	Inhibits gluconeogenesis	Zingiberaceous/ Madhumehri vati (Baidyanath)	300 mg / Kg/ 79
Ipomoea batatas	Sweet potatos/ Dietary fibers	pancreatic insulin secretion from β cells of islets of Langerhans	Convolvulaceae	168 to 336 mg/ 83, 84, 85, 106
Beta vulgaris	Beet/ Caffeic acid	Reduce blood glucose level by regeneration of β cells	Amaranthaceae	0·5 g/kg/ 90, 117
Carica papaya	Papita/ Kaempferol	Decrease in the rate of intestinal glucose absorption	Caricaceae/ Zanduzyme forte (Zandu)	125 mg/kg / 91, 118
Eucalyptus globulus	Eucalyptus/ Eucalyptol	Protection or regeneration of pancreatic beta-cells as insulin producing cells of islets	Myrtaceae/ Organic Eucalyptus globulus (Plant therapy)	62.5 g/kg / 92, 120
Gymnema sylvestre	Gurmar / Gymnemic acid	Decrease the uptake of glucose from the small intestine, stimulating insulin release from the pancreatic islets of Langerhans	Ascelpidaceae/ Madhumehri (Baidyanath)	(250 mg/ kg/body weight/ 93, 121
Mentha spicata	Spicata/ Carvone, Limonene, Menthone, Menthol, Pulegone, Dihydrocarvone and s-carveol in spearmint oil	High antioxidant activity reduces blood glucose levels in diabetic rats	Labiateae/ stream-x Detox capsules (Streamline Pharma)	300 mg/kg / 94

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