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Role of Herbal Plants in Treatment of Type 2 Diabetes

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Abstract
Plants have shown to be beneficial for human health as they possess various activities that help to either prevent or treat various diseases. Herbal remedies are emerging to be more affordable, more effective in clinical practice and have less side effects than modern medicine. The literature indicates that attention to the use of phytochemical properties of medicinal plants in the pharmaceutical industry has increased dramatically. Secondary metabolites found in the plant are small molecules or macromolecules made from plants that include steroids, alkaloids, phenolic, lignans, carbohydrates and glycosides, etc. have a variety of biological benefits, such as anti-allergic, anticancer, antimicrobial, anti-inflammatory, antidiabetic and antioxidant activities. Diabetes mellitus is a chronic disease caused by metabolic disorders in the pancreas β cells with hyperglycaemia. Hyperglycaemia can be caused by a deficiency of insulin production by pancreatic cells (Type 1 diabetes mellitus) or insufficient insulin production (Type 2 diabetes mellitus). Current diabetes medications focus on controlling and lowering blood sugar levels to normal levels. However, many modern drugs have many side effects causing serious health problems during treatment. Therefore, traditional medicine has been used for a long time and plays an important role as other medicines. In addition, over the past few years, some of the new bioactive drugs isolated from plants have shown antidiabetic activity that is far more effective than oral hypoglycaemic agents used in clinical therapy. Traditional medicine has developed a good clinical practice and indicates a bright future in the treatment of diabetes. This paper briefly reviews the active ingredients, as well as the medicinal effects of certain popular herbs that have been widely used in the treatment of diabetes.

Keywords
Diabetes Mellitus; Medicinal plants; Herb; Bioactive compounds

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1. INTRODUCTION
Diabetes mellitus (DM) is a metabolic disorder caused by multiple reasons characterized by chronic hyperglycaemia associated with disruption of carbohydrate, fat and protein metabolism caused by impairments in insulin production, insulin function, or both. The effects of diabetes include long-term damage, dysfunction, and various organ failure.[1] Diabetes Mellitus is divided into three main types.[2] Type 1 diabetes (insulin-dependent diabetes mellitus) is an autoimmune disease that develops when the insulin-producing cells in the pancreas are damaged, and the pancreas produces less or no insulin at all. A person with type 1 DM has to take insulin daily to stay healthy. It often develops in children and adults. Type 2 diabetes is also known as "insulin-independent diabetes mellitus" which accounts for more than 90% of cases of DM in adults. It is a diagnosis when the pancreas produces enough insulin, but the body cannot use insulin effectively, a condition called insulin resistance. Gestational Diabetes mellitus (GDM) is characterized by elevated levels of glucose levels during pregnancy which first appears in the second or third trimester of gestation

period. GDM is caused by a pregnancy hormone or insulin deficiency. It is one of the most common metabolic disorders during pregnancy.

Hyperglycaemia damages organs such as the eyes, kidneys, nerves, heart and blood vessels [3]. According to International Diabetes Federation (IDF), In 2021, the number of diabetic adults in the 20-79 age group stands at 537 million with diabetes, which is set to increase to 643 million by 2030 and to reach 784 million by 2045 (Fig 1) [4]. There are around 541 million adults, which constitutes 10.6% of world's population, have impaired glucose tolerance which makes them highly susceptible to type 2 diabetes. There is one patient who dies of diabetes every 5 seconds. The prevalence of diabetes in men aged 20-79 is slightly higher than in women (10.8% vs 10.2%). The prevalence of diabetes is expected to increase for both men and women from 2021 to 2030 and 2045. Worldwide, there are 10 top countries with diabetes rates, including China, India, Pakistan, USA, Indonesia, Brazil, Mexico, Bangladesh Japan, and Egypt [4]. The dangers of GDM in pregnant women have been clearly identified, but there is uncertainty that treatment reduces and regulates women's blood sugar levels during pregnancy, but can it reduce those risks or not. In addition, GDM can increase the risk of developing type 2 DM after childbirth. Today, diabetes is on the rise along with rapid cultural and social changes, such as aging, population, minimal physical activity, diet, and so on. The expenditure on Diabetes is also increasing.

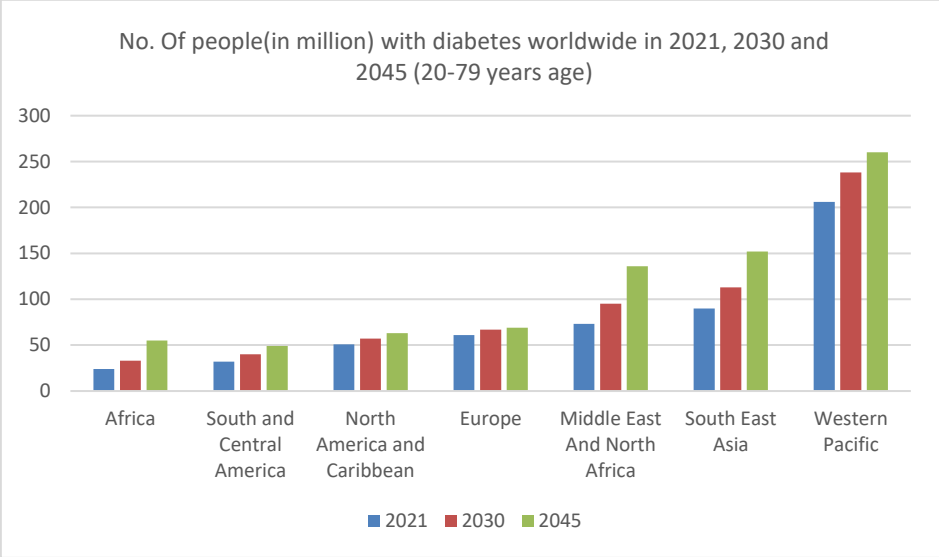


Fig 1

2. Management of Diabetes Mellitus

The treatment of diabetes is dependent on the understanding of pathogenesis of disease. The American Diabetes Association has recommended that the goal of glycemic control include a pre-prandial blood sugar level of 80 to 120 mg / dL (4.4 to 6.7 mmol / L), bedtime blood sugar levels are 100 to 140 mg / dL (5.6 to 7.8 mmol / L), and HbA1c levels - less than 7% [2]. Healthy food, physical activity, and weight management is the basis of any treatment program for patients with DM. [5] This lifestyle change not only helps lowers blood glucose levels, but also, reduces the risk of heart disease, and helps in weight loss as well. However, many patients do not have a healthy lifestyle [6] , so patients should rely on medication for treatment. Current DM treatment is focused on controlling and lowering blood sugar levels to normal levels. The mechanisms by which both modern medicine and traditional medicine reduce blood glucose levels are:

a) Stimulate β cells in the pancreatic islet to release more insulin.

b) Inhibit the action of hormones that increase blood glucose uptake.

c) Increase local insulin receptor sensitivity.

d) Inhibit hydrolysis of glycogen in the liver.

e) To improve glucose uptake into tissues and organs. [7].

There are 6 main categories of modern medicine and 2 categories of injections used worldwide to control blood sugar levels. The pills are called Biguanides (metformin), Sulfonylureas, thiazolidinediones (glitazones), meglitinides (glinides), alpha-glucosidase inhibitors and DPP-4 inhibitors. The categories of drugs given by injection are incretin mimetics and insulin . [8] However, many modern

medicines have many side effects, causing some serious medical problems during drug processing. Metformin is a drug of biguanides category that can inhibit the production of glucose molecules in the human liver and increase insulin sensitivity. However, metformin also causes other side effects such as dyspepsia, nausea, and diarrhoea. Metformin must be avoided for those with severe kidney function, untreated heart failure, severe liver disease and other serious medical problems. Thiazolidinediones in the treatment of diabetes improve insulin sensitivity, reduce insulin resistance, and reduce cardiovascular risk. However, the most common side effects of thiazolidinediones are weight gain and fluid retention, which leads to peripheral edema and heart failure. The drugs were avoided for use in patients in similar circumstances, including heart failure and severe liver problems. Rosiglitazone can cause heart attacks and increase the risk of heart attack. Pioglitazone is not available in some countries due to concerns about an increased risk of bladder cancer.

The data in IDF atlas 2021, states that there has been considerable increase in health expenditure due to diabetes from USD 232 million in 2007 to USD 996 million in 2021 for adults aged 20-79 years. IDF estimates that total diabetes-related health expenditure will increase to USD 1.03 trillion by 2030 and USD 1.05 trillion by 2045. [4] Hence the expenditure on medicines has become another problem for diabetic patients in many countries around the globe.

Apart from modern medicine, traditional medicine has been used for a long time and plays an important role as other medicines. According to the WHO, a traditional plant-based treatment program is still the primary basis for about 75-80% of the world's population, especially in development countries with plant diversity. Traditional medicine is often the first choice in primary health care for patients in developing countries like India because of better cultural acceptance and less side effects than modern medicine. Recently, some medicinal plants have been reported to be beneficial for sugar worldwide and have been used extensively as an antidiabetic and antihyperlipidemic remedy. More than 400 species of hypoglycaemic plants have been found in the literature [9], however, investigating new antidiabetic drugs from natural plants remains interesting because they contain phytoconstituents that show unique and safe effects in the treatment of diabetes. Many plants contain bioactive compounds, such as phenolic, glycosides, alkaloids, terpenoids, flavonoids, carotenoids, etc., which are enhanced as they have antidiabetic activities [10].

3. Plants having antidiabetic Property:

3.1 Tinospora cordiflora

Tinospora cordiflora is commonly known as Guduchi or Amrita in Sanskrit. It is also often referred to as Giloy. It belongs to the Menispermaceae family. It is an herbaceous plant which is native to India and other tropical areas viz Myanmar and Sri Lanka. The plant leaves are large and heart shaped around 6-12cm long. The plant has 2-3 flowers which are yellow in color. Male flower is longer than the female flower. The stems of this plant are fleshy with blunt tubercles. [11] In India, it is used as traditional ayurvedic medicine for various therapeutic purposes such as jaundice, urinary disorder, Diabetes, Inflammation, skin diseases etc. These activities are because of the presence of chemical constituents in different parts of plant body like root, stem and whole plant [12].

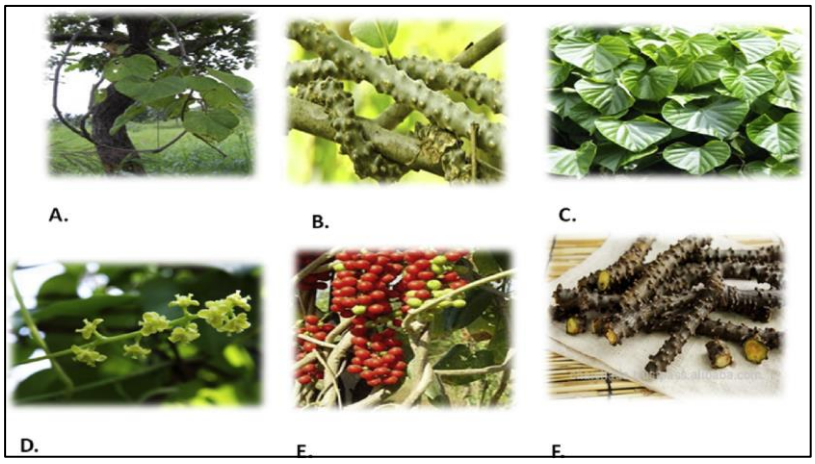
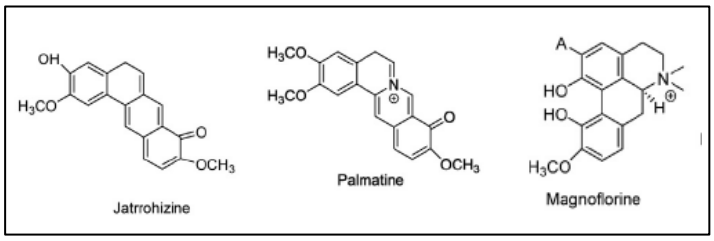


Fig: Morphology of *Tinospora cordifolia* A.) Stem, B.) Root, C.) Leaves, D.) Flowers, E.) Fruits, F.) Seeds

Phytoconstituents

Tinospora cordiflora contains several secondary metabolites. Studies reveal the presence of 65 active compounds have been isolated and identified such as alkaloids, terpenoids, essential oils, glycosides, phenolic compounds, steroids etc. These

constituents exhibit various biological activities such as antiseptic, anti-inflammatory, anti-cancer, antimicrobial, antidiabetic and immunomodulatory. Currently, 3 flavones and 3 flavone glycosides (namely diosmetin, genkwanin, genkwanin 7-glucosideetc.), a number of diterpenoids and triterpenoids (namely tinocrispol A, borapetols B, cycloeucalenol etc.), alkaloids (namely *N*-formylnornuciferine, tyramine, jatrorrhizine, palmatine etc.) and other phytoconstituents have been isolated and identified from the stem of TC. [11] The structure of alkaloids playing an important role in diabetes are as follows:



Antidiabetic Activity

T. cordiflora (TC) is vastly studied for its antidiabetic property by various researchers. Chougale AD et al., 2009 studied the inhibition of enzyme alpha glucosidase on albino rats using TC stem extract. The study demonstrated that the stem extract gives dual results of inhibiting the alpha glucosidase and also reducing the blood glucose level. [13] In another study, Sangeetha MK et al., 2011 proved that hyperglycemic rats when administered with TC stem extract (200mg/kg dosage) showed elevated insulin secretion when compared to control hyperglycaemic group. [14] Furthermore, Patel MB et al., 2011, studied *in vitro* and *in vivo* hypoglycaemic activity of alkaloidal fraction of TC stem extract. The study revealed that the alkaloids isolated from TC stem extract are potent antidiabetic agent as it shows insulin secretion, insulin sensitizing and gluconeogenesis inhibitory activities [15]. In another study, Patel MB et al., 2012 reported the inhibition of alpha glucosidase enzyme and antiglycemic activity of alkaloids namely jatrorrhizine, palmatine and Magnoflorine in TC extract. Magnoflorine showed complete inhibition of sucrase and maltase. Palmatine and jatrorrhizine also showed potential inhibition of maltase and sucrose. The alkaloidal fraction also showed a significant decrease in blood glucose levels in the *in vivo* studies [16]. Sharma P et al., 2019 reviewed that the root extract showed an antihyperglycemic effect in the alloxan-induced diabetic rat model. The study demonstrated decrease in excess glucose level in urine as well as in normal group [12]. In another study, Sharma R et al., 2013 reported that Guduchi satva has no anti hyperglycaemic activity against glucose overload but shows slight hypoglycaemic activity [17].

3.2 *Ocimum sanctum*

Ocimum sanctum (OS) commonly known as 'Tulsi' has been used as traditional medicine in India. It is also known as holy Basil. The plant is a member of the Lamiaceae family.

Ocimum sanctum is a tall, branched shrub which is around 30-60cm tall. The leaves are euther green or purple in colour that are strongly scented and are around 5cm long. The stems of this plant have trichomes present on them. The leaves, flowers, stem, root, seeds etc. are known to possess therapeutic potentials such as expectorant, analgesic, anticancer, antiasthmatic, antiemetic, diaphoretic, antifertility, hepatoprotective, hypotensive, hypolipidemic and antistress agents. Fever, Bronchitis arthritis, convulsions are some of diseases that can be treated by using this plant**.** [18] Recently there have been evidences suggesting its use as a remedy against diabetes mellitus**.** [19]

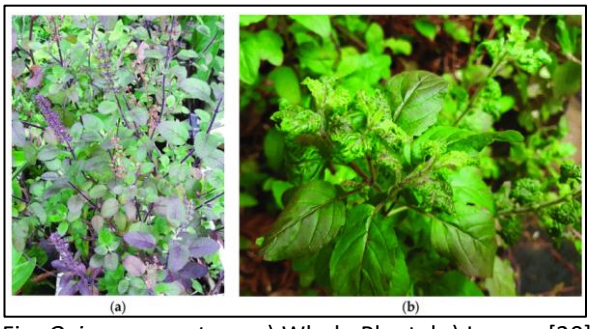
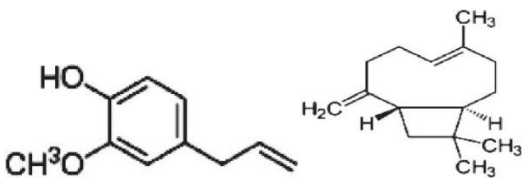


Fig: *Ocimum sanctum* a.) Whole Plant, b.) Leaves [20]

Phytoconstituents

The active compounds playing a role in treatment of certain diseases are found throughout the plant. The nutritional and medicinal properties of the plant in its natural state, as it has long been used, are due to the synergistic interaction of many active phytochemicals. In the leaf *of O. sanctum*, a flexible oil extracted and identified by chemical composition, contains many important components such as eugenol, methyleugenol, and p-caryophylen. The essential oils of this plant contain various bioactive compounds, such as terpenoids, esters, aliphatic aldehydes and phenolic acids. The plant also contains a variety of secondary metabolites, including phenolic, flavonoids, terpenoids, lignans, steroids, fatty acids and their derivatives [19]



Eugenol p-Caryophylen
(Structures taken from Rahman et al., 2011)

Antidiabetic Activity

Vats V et al., 2003 studied the anti-hyperglycemic and hypoglycemic effect of *Oscimum sanctum*, Trigonella *foenum-graecum*, *Pterocarpus marsupium* extracts in normal and diabetes induced rats. The study revealed that in normal rats the OS plant extract showed maximum hypoglycemic effect amongst the 3 extracts. It was also seen that there was dose dependent reduction in blood glucose level after 60 mins and 120 mins of administration of OS extract. Similar results in reduction of blood glucose levels were observed when the extracts were administered to alloxan induced diabetic rats. [21] In another study Vats V et al., 2004 demonstrated that the administration of OS leaves ethanolic extract to streptozotocin induced diabetic rats lowered plasma glucose level by 9.06% and 26.4 % on 15th and 30th day of experiment. Also it was concluded that the OS extract has no effect on glycogen content of any tissue. [22] Furthermore, Hannan JMA et al., 2006 prepared 4 fractions of OS using ethanol, aqueous butanol, ethyl acetate. The study proved that these fractions stimulated insulin secretion. The study also demonstrated that ethanol extract can lower blood glucose levels and also it can increase insulin secretion. [23] In other in vivo study done revealed that the OS extract was able to lower oral glucose tolerance. It was also able to lower serum glucose level and increase glycogen synthesis in liver. In their research Patil R et al., 2011 found that triterpenoid(16-hydroxy-4,4,10,13-tetramethyl-17-(4methyl-pentyl)-hexadecahydro-cyclopentaphenanthrene-3-one) which was isolated from OS possessed antidiabetic and hypoglycaemic activities in in vivo studies. This compound was found to increase the increase insulin secretion from β cells and also it enhanced the glucose utilisation. This study revelation led to discussion on using this triterpenoid as a medicine [24]. Somasundaram et al., 2012, found out that when OS administered along with Glibenclamide helped in achieving glycaemic control efficiently in Type 2 Diabetic Patients. [25]

3.3 Momordica charantia

Momordica charantia (MC) is popularly known as bitter melon or bitter gourd. It is most common vegetable consumed in the tropical region, particularly in Vietnam, India, China, East Africa, South–North Asia, and Central and South America.It belongs to Cucurbitaceae family. The plant is climber which usually grows up to 5m. It bears bitter elongated fruits whose surface is not smooth. This plant has many medicinal properties because of which it is extensively cultivated and consumed. The fruits are rich source of antioxidants and vitamins. This plant contains phytoconstituents which help in the treatment of Diabetes [26]

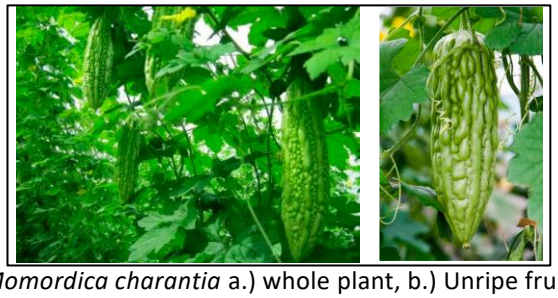


Fig*: Momordica charantia* a.) whole plant, b.) Unripe fruit [20]

Phytoconstiuents

MC conatins a lot of active compounds responsible for antidibetic activities. These compounds are triterpene, proteoid, steroids, alkaloids, phenolic acids etc.[27] .The important bioactive compounds and their role is depicted below in the table below:

Bioactive Compound	Role
Polypeptide -p	Acts as insulin like protein
Momordicosides	Enhances uptake of glucose
Saponin	Increases insulin secretion
Momordin	PPAR δ activation
Conjugated Linoleic Acid	Release intestinal GLP1

Table 1: Bioactive compounds and its role [20]

Antidiabetic Activity

In a study Akhtar N et al., 2011 suggested that Charantin, a vicine and polypeptide-p are active compounds derived from MC whole green fruit act as an insulin-like protein.It not only lowers blood sugar, but also stimulates insulin production. This compound may be responsible for enhanced glucose absorption, and also posiibly stimulates glycogen synthesis in liver, in rabbits with alloxan-induced diabetes at 200 mg / kg b.w dose. [28] Ma C et al., 2017 reported that the treatment of MC extracts on Type 2 diabetes induced rats showed reduced blood glucose levels and increased insulin levels. Hence it was concluded that MC ethanol extracts can improve insulin resistance in rats. [29] In other study Ma et al., 2017 reported that that Momordicoside U compound could enhance uptake of glucose in in vitro insluin secretion assay. Keller AC et al., 2011 reported that the saponin rich fraction of MC ethonal extract stimulated insulin secretion in concentration dependant manner. [30] Dans AML et al., 2007 studied the effect of MC capsule on glycemic control in patients having type 2 diabetes. The results showed that there was lowering Of HbA1c seen but there was no significant difference observed in fasting blood sugar [31]. Jiang B et al., 2016 reported that the compound K16, acurcubitane type triterpenoid treatment to the alloxin induced diabetic mice results in enhanced glucose tolerence and lowering blood glucose levels to some extent. It was also reported that the compound upregulates the expression of glucometabolic associated genes [32]. Mahmoud MF et al., 2017 studied the antidiabetic activities of MC fruit juice in diabetic mice induced by streptozotocin. It was observed that this plant has the potential to improve the production of insulin for pancreatic cells, increasing serum insulin rate, improve cell function, reduce insulin resistance, increase glucose utilization at a dose of 10 mL / kg / day for 14 days [33]. Virdi J et al.,2003 reported that the 3 extracts of MC at low dosage (20mg/kg) can reverse the hyperglycemia in alloxin induced rats with no effects on liver and kidney. It was concluded that te higher dose will not be effective and also will be toxic to other organs [34]. Singh N et al., 2007, studies revealed that acetone extract of fruit has the ability to regenerate beta cells in the Langerhans of the pancreas was confirmed when used in alloxin induced albino mice were administered 25 mg, 50 mg and 75 mg doses 8 to 30 days teatment [35]. In addition, the aqueous ethanolic extract of MC seeds revealed protection of pancreatic cells in vitro testing. Poovitha S et al., 2016 investigated the inhibition of diabetic-related enzymes, such as alpha-glucosidase and alpha-amylase from MC release.[36]

3.4 Allium sativum

Allium sativum (AS) is commonly known as garlic and belongs to the family Amaryllidaceae. This plant is often found in Asia, Africa and Europe. It is prevalently cultivated in Asia and is used as a condiment in Asian cuisine. It has medicinal properties which help in the treatment of wide range of diseases. [20] The research reveals that garlic possesses anti-tumour, antimicrobial, anti-hyperglycaemic, hepatic protective, immune modulatory, cardiovascular protective activities. [37].

Fig: a.) Green Garlic, b.) Dried garlic bulb

Phytoconstituents

Garlic contains many active compounds which include sulphur containing compounds like ajoene (E-ajoene, Z-ajoene), thiosulfinates (allicin), vinyl dithiins (2-vinyl-(4H) -1,3-dithiin, 3-vinyl-(4H)-1,2-dithiin), sulfides (diallyl disulfide (DADS), diallyl trisulfide. These compounds account for 82% of the overall garlic sulphur content. [37] It also contains alkaloids, flavonoids, terpenes, steroids, glycosides and resin etc.

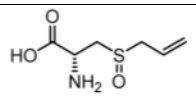
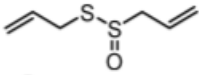
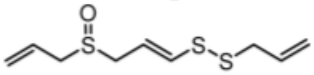
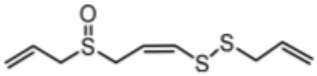
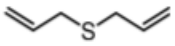
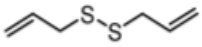
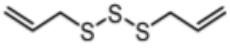
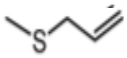
Compound	Molecular Formula	Structure
Alliin	$C_6H_{11}NO_3S$	
Allicin	$C_6H_{10}OS_2$	
E-Ajoene	$C_9H_{14}OS_3$	
Z-Ajoene	$C_9H_{14}OS_3$	
Diallyl sulfide (DAS)	$C_6H_{10}S$	
Diallyl disulfide (DADS)	$C_6H_{10}S_2$	
Diallyl trisulfide (DATS)	$C_6H_{10}S_3$	
Allyl methy sulfide(AMS)	C_4H_8S	

Table: Structure and Molecular formula of active compounds found in AS [37]

Antidiabetic activity

Liu CT et al., 2005 studied the effects of garlic oil and diallyl trisulfide on glycaemic control in rats with streptozotocin-induced diabetes. The rats were administered garlic oil (100 mg/kg body weight), diallyl trisulfide (40 mg/kg body weight), or corn oil by gavage for 3 weeks and controlled rats received only corn oil. It was reported that this led to gradual increase in insulin secretion, there was significant improvement in insulin resistance, oral glucose tolerance improved with the increase in insulin secretion. The soleus muscle's ability to form glycogen (but not lactate or carbon dioxide) from glucose in the presence of 10 or 100 AU/ml of insulin was significantly improved after treatment in rats with both garlic compounds as compare with controlled rats [38]. In another study**,** Eidi A et al., 2006 studied the effects of oral administration of garlic ethanolic extract (0.1, 0.25, and 0.5 g/kg body weight) on serum glucose, total cholesterol, triglycerides, urea, uric acid, creatinine, aspartate amino transferase (AST), and alanine amino transferase (ALT) in normal and streptozotocin-induced diabetic rats for 14 days. It was reported garlic extract lowered serum glucose, total cholesterol, triglycerides, urea, uric acid, creatinine, AST and ALT levels in diabetic rats, while increase in serum insulin levels in normal rats was observed. The action of garlic extract was compared to that of glibenclamide (600 mg/kg), a well-known anti-diabetic drug. The extract's anti-diabetic effect was more potent than that of glibenclamide [39]. Thomson M et al., 2007 studied hypoglycaemic, hypocholesterolaemia and hypotriglyceridaemic of garlic effects on STZ-induced diabetic rats. The raw garlic was administered to diabetic rats daily for 7 weeks and as a result it was observed that there were 50% decreased in the levels of glucose, cholesterol and triglyceride as compared to the non-diabetic rats. 50% lowering of urinary protein level was observed in garlic treated diabetic animals compared to non- diabetic animals. These findings suggest that raw garlic has the potential to reverse proteinuria and also lowering blood sugar, cholesterol, and triglycerides in diabetic rats [40]. El Demerdash FM et al., 2007 studied the effect of the garlic juice on alloxan induced diabetic rat and evaluated its effects on various parameters.It was concluded that garlic can help to normalise blood glucose levels. Furthermore, juices may help to improve renal function, prevent liver damage, and reduce the induced free radicals associated with alloxan diabetes [41]**.** Padiya R et al., 2007 attempted to examine effect of orally administered raw garlic homogenate on insulin sensitivity and associated metabolic syndrome in fructose-fed rats. It was reported that administration of raw garlic, orally showed beneficial effects after eight weeks. Lowering of blood glucose and improvement of insulin sensitivity in garlic treated rats was reported.

Furthermore, other metabolic complications observed in diabetic rats, such as increased serum triglyceride, insulin, and uric acid levels, were also normalised after garlic administration [42]. Kalhotra P et al., 2020 studied anti-diabetic effects of ultrasonication-assisted garlic bulb extract using in-vitro assays such as DPP-4 inhibitory and antioxidant activities. It was reported that garlic bulb extract at 70.9 g/mL inhibited DPP-4 activity by 50%.

3.5 *Zingiber officinale*

Zingiber officinale is commonly known as Ginger. It belongs to the Zingiberaceae family. It is widely distributed in tropical Asia and is commonly used in India, China and other countries in South East Asia [20]. Ginger is a fragrant rhizome with warts and branches. It has straight stems and 2 small green leaves arranged on each stem. The stem is surrounded by smooth slopes of two standard leaves. The flower may be white or yellowish-green and is rarely seen. The fresh and dried rhizome is used medicinally and spice. It has a pungent odour and a slightly bitter taste [44]. Ginger possesses antidiabetic, anti-inflammatory, anti-microbial, hepatoprotective, anti-parasitic, antioxidant, gastroprotective and many other activities which help human health.

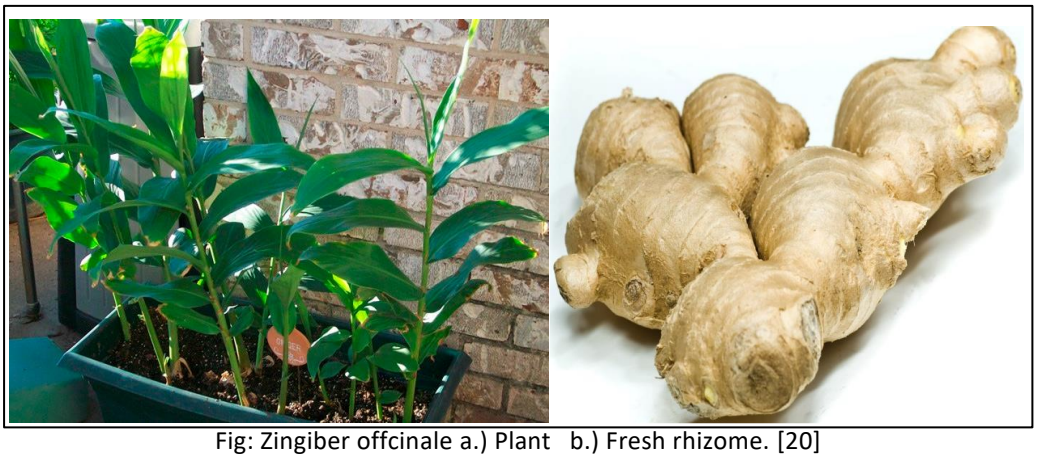


Fig: Zingiber offcinale a.) Plant b.) Fresh rhizome. [20]

Phytoconstituents

Ginger contains many active compounds such as Volatile oils, phenolic compounds and others. The Volatile oils, also called as ginger essential oil, is a mixture of terpenoid compounds, such as sesquiterpene hydrocarbons, monoterpene hydrocarbons, carbonyl compounds, alcohols and ester. In particular, phenolics in ginger are the most important components. The phenolic compounds can be divided into two groups: gingerol-, gingeron- and shogaol-related group and diarylheptanoids. Gingerol is a spicy component of this plant and contains a wide variety of bioactive substances. Furthermore, this plant is rich in various amino acids, including glutamate, aspartic acid, serine, glycine, threonine, alanine, etc. In addition, ginger contains polysaccharides and organic acids, such as oxalic acid, tartaric acid, etc.[45]

Antidiabetic Activity

Shidfar F et al**.,** 2015 studied the effect of ginger supplementation on glycaemic indices in Iranian patients with type 2 diabetes. They conducted clinical trials on patients with type 2 diabetes who did not receive insulin. Participants in the intervention and control groups were administered 3 g of powdered ginger or placebo (lactose) (in capsules) daily for 3 months. It was reported that after 3 months, improvement in glucose homeostasis and antioxidant capacity in T2DM patients was observed [46] . Rani MP et al., 2012 evaluated antioxidant and antidiabetic potential of ginger extract in L6 mouse myoblast and myotubes**.** The extract characterization revealed the presence of phenolic components gingerol and shaogal as major constituents. The ethyl acetate extract increased the glucose uptake. The extract also suppressed LDL oxidation, inhibited ACE, and inhibited adipocyte differentiation, indicating that ginger has anti-diabetic and cardioprotective properties [47]. Oboh et al., 2010 evaluated inhibitory effects of 2 types of ginger on the activities of α-amylase and α-glucosidase, key enzymes linked to type-2 diabetes using in vitro model. The results show that red ginger aqueous extracts had higher phenolic contents as well as higher antioxidant activities than white ginger aqueous extracts. White ginger inhibited α-amylase and α-glucosidase activities more efficiently than red ginger. Furthermore, both extracts inhibited α-amylase and α-glucosidase, indicating their potential use in dietary intervention in the management or control of postprandial hyperglycaemia associated with type 2 diabetes [48]. Akhani SP et al., 2010 investigated the effect of Z. officinale juice on streptozotocin (STZ)-induced type I diabetic rats, with a focus on the role of serotonin (5-hydroxytryptamine; 5-HT) receptors

in glycaemic control. *Z.officinale* juice reduced hyperglycaemia and hyperinsulinemia which was caused by 5-HT in normoglycemic rats. In diabetic rats, Z. officinale treatment resulted in a significant increase in insulin levels and a decrease in fasting glucose levels. The treatment also reduced serum cholesterol, triglyceride levels, and blood pressure [49]. Abdulrazzaq NB et al., 2012 studied the antihyperglycemic effect of ginger aqueous extract administered orally (daily) in three different doses (100, 300, 500 mg/kg body weight) for a period of 30 d to streptozotocin (STZ)-induced diabetic rats. The study revealed the lowering of plasma glucose level after a month when 500mg/kg dosage is administered. The study also revealed that ginger can control tissue glycogen content in diabetic rats by improving the peripheral utilization of glucose and repairing the impaired liver [50]. Al amin ZM et al., 2006 studies revealed that an aqueous extract of raw ginger has potential hypoglycaemic properties. This may be due to effects involving serotonin receptors, an increase in pancreatic secretion of insulin from β cells or release of bound insulin [51]**.** Mahluji S et al., 2013 reported that when diabetic patients were given ginger for 8 weeks there can be change in insulin levels and sensitivity be observed, with no significant changes in the concentrations of glucose and HbA1c.[52]

Other Plants having Antidiabteic Activity

- ***Euphorbia hirta***

RM Widharna et al., 2010 reported that the ethanolic and ethyl acetate extract of this plant inhibit α glucosidase activity. [53] Sheliya M et al., 2016 studied in vitro α-glucosidase and α-amylase inhibition by aqueous, hydroalcoholic, and alcoholic extract of E. hirta. It was observed that the methanolic extract of E. inhibited α-glucosidase and mildly inhibited α-amylase, two proteins involved in diabetes mellitus. [54]

- ***Aloe Vera L Burm***

Kim K et al., 2009 studied the effect of processed aloe vera gel on dibetes induced rats. The study reported that wen aloe vera gel administered orally for 8 weeks reduced blood glucose concentrations to a normal level. In addition, the administration of aloe vera gel significantly decreased plasma insulin. Processed aloe vera gel appeared to lower blood glucose levels by decreasing insulin resistance [55].

- ***Coriandrum sativum***

Naquvi et al., 2011 examined anti-diabetic activity of the aqueous extract of this plant in STZ-induced diabetic rats. The administration of extract in Doses of 500 and 250 mg/kg lowered blood glucose levels in the experimental group, compared to the control group. It was concluded that 500mg/kg dosage was most effective.[56]

CONCLUSION

Diabetes mellitus is considered to be a major disease that is affecting the health of people across the globe and also affecting economy of patients, their families and the community. In addition, uncontrolled diabetes can lead to serious chronic problems such as blindness, kidney failure, and heart failure. To alleviate this problem, research on new antidiabetic agents is the need of the hour. Because of the side effects of modern medicines, many traditional medicines have been recognized. In addition, herbal extracts today can be used in combination with conventional medicine. Each plant has its own active ingredients that can lower blood sugar levels and can help managing diabetes problems. To formulate an effective diet for diabetes, isolation and identification of these active compounds plays an important role. This review provides the information of some plants that can be used to manage diabetes.

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