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PHYTOCHEMICAL INTERVENTIONS IN DIABETES MELLITUS: A TRANSITION FROM CONVENTIONAL THERAPY TO INTEGRATIVE MANAGEMENT

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ABSTRACT: Diabetes mellitus is a long-term condition that affects how the body processes glucose, leading to constantly high blood sugar levels due to issues with insulin production and after effects. The widespread incident of diabetes is increasing, and it is associated with owing to sedentary lifestyles, obesity, unhealthy dietary habits, genetic predisposition, and environmental factors. Chronic hyperglycemia contributes to oxidative stress, inflammation, mitochondrial dysfunction, and dysregulation of signaling pathways such as NF- κ B, PI3K/Akt, AMPK, MAPK, leading to microvascular and macrovascular complications. Conventional diabetes treatment mainly manages sugar level that might lead to long term challenges such as low blood sugar, stomach problems, harm to organs, weight increase, resistance to drugs, and restricted capability to avoid diabetes-related complications. Plant-based treatments a supportive and targeted approach for managing diabetes. With strong abilities to lower blood sugar, reduce oxidative stress, fight inflammation, and protecting insulin-producing cells and signaling, expand sugar usage by cells, reducing harmful free radicals, and confining inflammation-related substances. Current development in nano-based formulations and technique for delivering plant chemicals have also improved the effectiveness and absorption of these natural compounds. This review outlines the underlying mechanisms, proven effects, and achievable advantage of plant-based treatments as a hopeful novel plan in the oversight of diabetes mellitus.

INTRODUCTION: Diabetes mellitus has become one of the most significant non communicable metabolic diseases around the world ¹. This influences the body to causing severe health challenge in the kidneys, eyes, nerves, heart, and liver. Over the past few decades, the number of people afflicted by diabetes has increased enormously, driven by demographic transitions, urbanization, lifestyle modifications, and increasing rates of obesity ².

Presenting to the International Diabetes Federation (IDF), around 537 million adults had diabetes in 2021, and this figure is expected to rise to nearly 783 million by 2045 if current trends continue ³. Maintaining luxuriously low blood sugar levels leads to elevated oxidative stress, long-term inflammation, harm to blood vessel walls, and harm to mitochondria, which are key in the expansion of diabetes-related complications ⁴.

High glucose levels determine the production of harmful substances called reactive oxygen species (ROS), trigger inflammatory processes such as those involving NF- κ B and MAPK pathways, destroy signaling pathways that aid insulin in doing its job. Also, AGEs frame up tissues of public with diabetes and deteriorate injury to blood vessels and nerves ⁵.

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A mix of genetic factors, being plump, abnormal cholesterol levels, high blood pressure, and other environmental impacts all play role in the reason of progression of diabetes. Usual treatments for diabetes involve insulin, sulfonylureas, biguanides, DPP-4 inhibitors, and SGLT2 inhibitors, which are accustomed to managing blood sugar levels ⁶. However, using these treatments for a long moment can lead to various side consequences like low blood sugar, stomach upset, weight gain, liver and kidney damage, and resistance to drugs ⁷. Numerous patients do not pass their target blood sugar levels even when utilizing multiple medications, which exhibits the need for safer and more effective additional treatment options. Because of this, there is a booming concentration on applying medicinal plants and the chemicals found in them as useful additions to diabetes treatment ⁸.

Herbal medications have been study for a long time to help in control of blood sugar, make insulin more effective, reduce stress on the body's cells, and support the wellness of the cells that generate insulin. Active components in plants like flavonoids, alkaloids, terpenoids, polyphenols, glycosides, and saponins, have strong effects in lowering blood sugar through different biological mechanisms ⁹. These substances can help in how the body uses glucose, stop enzymes that break down carbohydrates, increase insulin release, improve how cells take in glucose, and degrade inflammation. Natural compounds alike, such as curcumin from turmeric, berberine from berberis plants, resveratrol from grapes, and epigallocatechin gallate from green tea, have been established to have strong antidiabetic effects in both lab studies and in real-life situations ¹⁰. These plant-based chemicals help regulate important pathways involved in insulin action alike as PI3K/Akt, AMPK, and the movement of glucose transporters (GLUT4), while likewise lowering levels of harmful substances linked to inflammation and oxidative stress. More scientific research shows that using plant-based treatments could be a promising way to better handle blood sugar levels and degrade the difficulty that enter with diabetes ¹¹.

Diabetes Mellitus Prevalence and Patterns: Diabetes mellitus is the most severe public health

issues globally, affecting people in both evolved and developing countries across varied regions such as Asia, Europe, North America, Latin America and the Caribbean, Africa, and Oceania ¹². It owns a major influence on the number of cases, deaths, and the all around health burden. Current global wellness reports exhibit that diabetes is becoming a booming part of non-communicable diseases. In 2021, around 537 million adults possessed diabetes, this number is expected to rise to around 783 million by 2045 ¹³. The quality of diabetes, its comparable deaths, and the collective health effect differ across regions. According to the International Diabetes Federation (IDF), Asia owns highest rates, with 54.0% frequency, 53.2% death, and 55.1% disease burden, followed by Europe (16.4%, 17.1%, 15.8%); North America and the Caribbean (13.2%, 12.4%, 13.0%); Latin America (9.1%, 9.8%, 8.9%); Africa (4.7%, 5.2%, 4.9%); and Oceania (2.6%, 2.3%, 2.3%) ¹⁴. The expensively high rate of diabetes in rural Asia is related to delegates like quick urbanization, lesser operating lifestyles, poor eating habits, obesity, genetic predisposition, and revolt metabolic issues ¹⁵.

India and China are among the homeland with the huge numbers of people in the world living with diabetes. Studies on South and East Asian populations display that numerous people with diabetes evolve insulin resistance and associated difficulty even at lower body mass index positions compared to those in the West ¹⁶. Also, expanding rates of adolescent obesity, lack of physical activity, long-term strain, and older populations are contributing to a rapid rise in the global diabetes burden. As a creator, diabetes has become one of the primary reasons for cardiovascular diseases, kidney failure, blindness, and immediate death worldwide ¹⁷.

Pathophysiology of Diabetes Mellitus: Diabetes mellitus mostly consist of two kinds: Type 1 diabetes mellitus (T1DM) and Type 2 diabetes mellitus (T2DM). T1DM is an autoimmune condition where the immune network assaults and destroys the beta cells in the pancreas, which causes in a comprehensive lack of insulin ¹⁸. On the other hand, T2DM is originally related to insulin resistance, where the body's cells don't react appropriately to the insulin, along with diminished

insulin output and phased decline in the function of beta cells¹⁹. The reason for T2DM affects various molecular result such as challenges with insulin receptor signaling, long-term inflammation, increased oxidative stress, impaired mitochondrial function, and irregular glucose transport²⁰. Insulin resistance determines the weight's muscles and fat tissues to absorb less glucose, lead to higher blood sugar levels. At the same time, the liver creates too much glucose, which deteriorates the health of high blood sugar. Inflammatory chemicals such as TNF- α , IL-1 β , and IL-6 trigger pathways such as NF- κ B and JNK, which interfere with the acceptable functioning of insulin receptor substrates and destroy the insulin signaling procedure²¹. Too much oxidative stress caused by an overproduction

of reactive oxygen species (ROS), injuries beta cells because these cells have a restricted capability to safeguard themselves against like damage. Additionally, issues with mitochondria and the endoplasmic reticulum contribute to the death of beta cells and metabolic imbalance²². Advanced glycation end products (AGEs) and trigger of protein kinase C pathways similarly play a role in harmful blood vessels and determinant difficulty of diabetes including kidney disease, nerve damage, eye problems, heart disease. These facility procedures highlight the many factors involved in diabetes mellitus and emphasize the significance of treatments that target multiple aspects of the disease²³ **Fig. 1.**

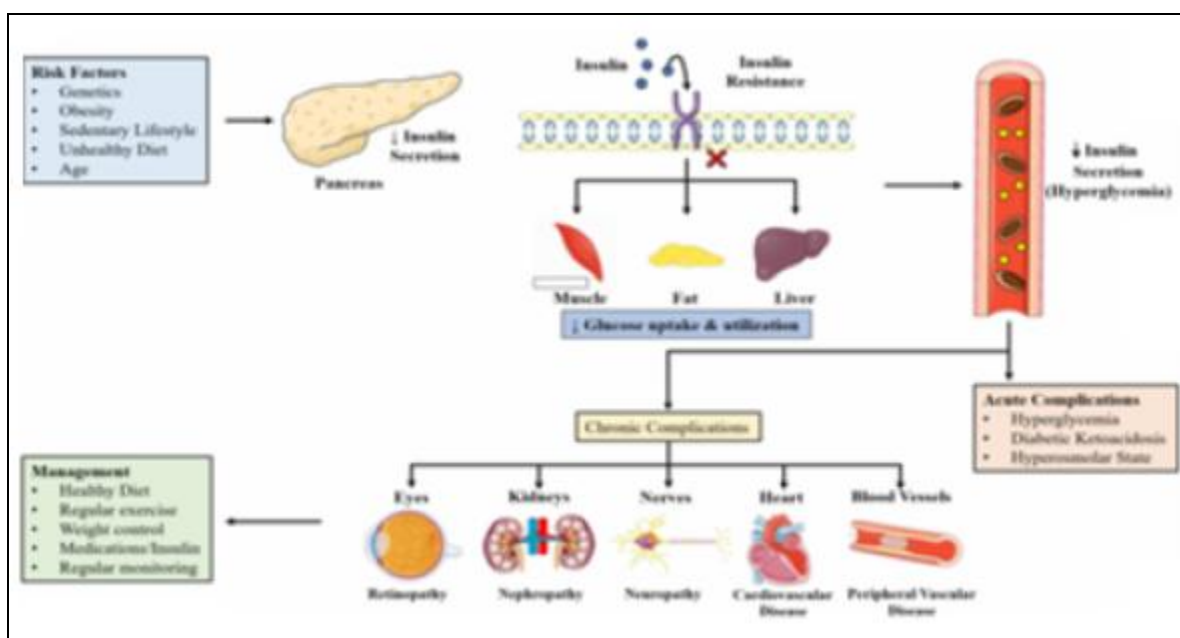


FIG. 1: PATHOPHYSIOLOGY OF DIABETES MELLITUS

Conventional Treatments for Diabetic Mellitus:

Conventional treatment for diabetes mellitus mainly aims to keep blood sugar levels within a normal range and prevent complications related to diabetes. The usual methods of treatment involve insulin therapy and oral medications like metformin, sulfonylureas, thiazolidinediones, and DPP-4 inhibitors. These treatments work by either improving insulin release, making the body more responsive to insulin, or decreasing the amount of glucose produced. While these treatments are effective, they can also have certain drawbacks, such as causing low blood sugar, leading to weight gain, causing stomach issues, being expensive, and having difficulty in being followed over time.

In addition, these treatments mainly focus on controlling the symptoms of diabetes rather than stopping the disease from getting worse, which shows the need for safer and more effective treatment options.

Insulin Therapy: It is quite a primary treatment for type 1 diabetes and severe type 2 diabetes. It helps control blood sugar levels by permitting cells to take in glucose and promoting the generation of glucose by the liver. Diverse groups of insulin, such as rapid-acting, short-acting, intermediate-acting, and long-acting, are chosen based on the patient's needs. Using intensive insulin therapy helps lower high blood sugar levels and can slowly

reduce the growth of diabetes-related complexity²⁴. Although the insulin treatment is efficient, it has many disadvantages. Patients frequently require holding insulin injections regularly, which can make it challenging to succeed with the treatment plan and may lower their overall quality of life²⁵. One of the utmost steady and severe side outcomes is hypoglycemia, especially in older people. Utilizing insulin over a long time can likewise lead to weight gain, a modification in body fat redistribution at the injection location, and a higher risk of heart and blood vessel challenge²⁶. Additionally, insulin treatment does not fully quell the oxidative stress and inflammation that are associated with difficulty from diabetes²⁷.

Biguanides (Metformin): Metformin is admired as the selected oral medication for severe type 2 diabetes mellitus because it is both effective and safe²⁸. It works by decreasing the count (up to) of glucose generated by the liver and by making body tissues further sensitive to insulin, which is achieved by the trigger of AMP-activated protein kinase (AMPK)²⁹. Additionally, metformin helps in handling lipid balance and may lower the risk of heart-related issues³⁰. Long-term use of metformin is frequently accompanied by to gastrointestinal consequences like nausea, diarrhoea, stomach discomfort, and a metallic taste³¹. In certain cases, extended treatment may cause in a lack of vitamin B12 and a buildup of lactic acid, particularly in people with kidney problems³². Furthermore, as diabetes progresses, metformin independently may not be sufficient to handle blood sugar levels effectively due to the decreasing work of the pancreatic cells that generate insulin³³.

Sulfonylureas: Sulfonylureas like glibenclamide, glimepiride, and gliclazide cause the closing of ATP-sensitive potassium channels in pancreatic β -cells, which assist in expanding insulin release³⁴. These medications are usually accustomed to because they are efficient in lowering blood glucose levels and are expenditure-efficient³⁵. The foremost disadvantage of sulfonylureas is the chance of serious low blood sugar levels, specifically in elderly grown-ups and those with kidney problems³⁶. Utilizing these medicines for an elongate time can similarly cause the pancreas's beta cells to become less effective, which reduces their capability to regulate blood sugar over time.

Furthermore, weight gain and concerns about heart health have formed these medication less usually accustomed to conventional diabetes treatment approaches³⁷.

Thiazolidinediones: Thiazolidinediones, like pioglitazone, assist the bulk use of insulin further efficiently by exciting the peroxisome proliferator-activated receptor gamma (PPAR- γ)³⁸. These drugs increase the capability of fat and muscle tissues to swallow glucose and also lower insulin resistance³⁹. Thiazolidinediones are related to various side consequences, such as fluid retention, swelling, weight gain, and a higher chance of heart failure⁴⁰. Overlong utilize has similarly been associated to an elevated danger of bone fractures and potential damage to the liver. Because of these safety issues, their use in treating diabetes has become limited for numerous patients⁴¹.

DPP-4 Inhibitors: Dipeptidyl peptidase-4 (DPP-4) obstacles such as vildagliptin, sitagliptin, and linagliptin assist regulate blood sugar levels by boosting the body's realistic incretin hormones⁴². These drug promote insulin release in reaction to glucose and degrade the discharge of glucagon, while not frequently leading to low blood sugar levels⁴³. While these medication are normally source tolerated, they can create side effects like colds, headaches, pancreatitis, and joint pain in certain public⁴⁴. Their capability to lower blood sugar is not as powerful as some other treatments. Furthermore, the expense of these drug can be a barrier to spell in low- and middle-income countries⁴⁵.

SGLT2 Inhibitors: Sodium-glucose cotransporter 2 (SGLT2) inhibitors, like dapagliflozin and empagliflozin, assist in degrading blood glucose levels by promoting the excretion of glucose through urine⁴⁶. This occurs because these medications block the reabsorption of glucose in the kidneys⁴⁷. In addition to manipulating blood sugar, these medications similarly offer safeguards for the heart and kidneys in individuals with diabetes⁴⁸. SGLT2 inhibitors may increase the danger of urinary tract infections, genital fungal infections, dehydration, and diabetic ketoacidosis⁴⁹. Losing overly significant glucose through urine can also lead to electrolyte differences and low blood pressure in certain patients.

The long-term protection of these medications is quietly being studied⁵⁰.

GLP-1 Receptor Agonists: GLP-1 receptor agonists like semaglutide and liraglutide aid in enhancing insulin release, degrade glucagon secretion, slow down the motion of food from the stomach into the intestines, and promote weight loss⁵¹. These treatments have been exhibited to offer positive effects on blood sugar regulation and heart-related consequences⁵². Usual side effect that

people may experience include nausea, vomiting, diarrhea, and stomach discomfort⁵³. Some investigations likewise signify that there could be a danger of developing pancreatitis or gallbladder outcome⁵⁴. Furthermore, the high cost of these medications and the requirement for injections can create it challenges for patients to succeed with the treatment strategy constantly and access the therapy effortlessly⁵⁵. **Table 1** provided list of conventional treatment in diabetic activity).

TABLE 1: LIST OF CONVENTIONAL TREATMENT WITH ANTI-DIABETIC ACTIVITY

Category	Drug name	Common brands	Mechanism of Action	Side effects	Ref.
Insulin analog	Insulin (Lispro, Regular, Glargine)	Huminsulin, Novorapid, Lantus	Increase glucose uptake in muscle and fat, inhibits hepatic glucose production	Hypoglycemia, weight gain	56
Biguanide	Metformin, phenformin	Glucophage	Decrease hepatic gluconeogenesis, increases insulin sensitivity	GI upset, vitamin B12 deficiency	56
Sulfonylurea (2nd generation)	Glibenclamide, Glimepiride, Gliclazide	Daonil, Amaryl, Diamicon	Stimulates insulin secretion from pancreatic beta cells by closing K ⁺ channels	Hypoglycemia, weight gain	57
Thiazolidinedione	Pioglitazone, Rosiglitazone	Actos, Avandia	Increases insulin sensitivity in adipose tissue and muscle	Edema, heart failure risk	58
DPP-4 inhibitor	Sitagliptin, Vidagliptin	Januvia, Galvus	Inhibits DDP-4 enzyme – prolongs incretin action	Headache, nasopharyngitis	59
SGLT2 inhibitor	Empagliflozin	Jardiance	Blocks SGLT2 in kidney – reduces glucose reabsorption	UTI, dehydration, ketoacidosis	60
Alpha- glucosidase inhibitor	Acarbose	Glucobay	Delays carbohydrate absorption in intestion	Flatulence, abdominal discomfort	61

Herbal Treatment for Diabetic Mellitus: Herbal medicines have been widely studied as alternative and complementary treatments for diabetes mellitus because they are effective and have fewer side effects compared to some conventional treatments. Many medicinal plants, such as Bitter melon (*Momordica charantia*), Gymnema (*Gymnema sylvestre*), Aloe vera (*Aloe barbadensis* Miller), Fenugreek (*Trigonella foenum-graecum*), and Jamun (*Syzygium cumini*), have shown strong antidiabetic effects. These plants help by increasing insulin production, improving the body's ability to use glucose, reducing insulin resistance, and protecting the pancreatic β-cells from damage caused by oxidative stress. These properties suggest that herbal therapies could be valuable for managing diabetes over a long period.

Momordica charantia: *Momordica charantia*, usually specified as the bitter melon, is the most systematically investigated medicinal plants used to address diabetes mellitus because of its powerful

ability to lower blood sugar position⁶². This plant involves various functioning substances like charantin, vicine, momordicosides, polypeptide-p, and flavonoids, which assist in its capability to regulate diabetes⁶³. Research shows that bitter melon assists the body utilize glucose further effectively by moving GLUT4 to the cell surface and by activating the AMP-activated protein kinase (AMPK) path in muscle cells⁶⁴.

It likewise demote the yield of glucose in the liver and avoid the immersion of glucose in the intestines, which aid to lower high blood sugar levels after meals⁶⁵. Bitter melon assist protect the pancreas's beta cells by increasing antioxidant activities like those of superoxide dismutase (SOD), glutathione and catalase⁶⁶. Additional studies exhibit that *M. charantia* reduces inflammatory factors like TNF-α and IL-6 by blocking the NF-κB signaling pathway, which assists in enhancing insulin sensitivity and collectively metabolic control⁶⁷.

Gymnema sylvestre: *Gymnema sylvestre*, frequently referred to as "gurmar," has been used for a long time in Ayurvedic medicine to help manage diabetes⁶⁸. This plant holds various combinations like gymnemic acids, saponins, flavonoids, and alkaloids, which possess muscular abilities to lower blood sugar position⁶⁹. Gymnemic acids cause the immersion, the cessation of glucose immersion in the small intestine, and the promise of the release of insulin from the pancreas. Studies suggest that extracts

from this plant may help repair damaged pancreatic cells and support the body's own insulin production⁷⁰. Furthermore, the antioxidants found in *Gymnema* assist in degrading oxidative stress and prevent injury to cells caused by high blood sugar levels over time. Laboratory research has also found that using *Gymnema* extracts can lead to exceeding glucose storage in the body, lower levels of blood sugar when fasting, and enhance capability to handle blood sugar levels after meals⁷¹.

TABLE 2: LIST OF HERBAL PLANT WITH ANTI-DIABETIC ACTIVITY

Herbal medicinal plant	Common name	Family	Part used	Bioactive constituents	Mechanism of action	Ref.
<i>Gymnema slyvestre</i>	Gurmar	Apocynaceae	Leaves	Gymnemic acids, saponins	Stimulates insulin secretion and regeneration of β -cells	72
<i>Momordica charantia</i>	Bitter melon	Cucurbitaceae	Fruits	Charantin, vicine, polypeptide-p	Enhances glucose uptake and insulin sensitivity	73
<i>Trigonella foenum-graecum</i>	Fenugreek	Fabaceae	Seeds	Trigonelline, galactomannan	Delays glucose absorption and stimulates insulin release	74
<i>Syzygium cumini</i>	Jamun	Myrtaceae	Seeds	Jamboline, ellagic acid	Reduces blood glucose level	75
<i>Azadirachta indica</i>	Neem	Meliaceae	Leaves	Nimbidin, flavonoids	Exhibits hypoglycemic and antioxidant activity	76
<i>Curcuma longa</i>	Turmeric	Zingiberaceae	Rhizome	Curcumin	Suppresses inflammation and oxidative stress	77
<i>Tinospora cordifolia</i>	Giloy	Menispermaceae	Stem	Berberine, tinosporaside	Enhances glucose metabolism	78
<i>Allium sativum</i>	Garlic	Amaryllidaceae	Bulb	Allicin, sulphur compound	Improves insulin secretion	79
<i>Aloe barbadensis</i> Miller	Aloe	Asphodelaceae	Leaf gel	Aloin, phytosterols	Lowers fasting blood glucose	80
<i>Camellia sinensis</i>	Tea plant	Theaceae	Leaves	EGCG, catechins	Improves insulin sensitivity	81
<i>Ocimum sanctum</i>	Tulsi	Lamiaceae	Leaves	Eugenol, ursolic acid	Enhances pancreatic β -cell function	82
<i>Pterocarpus marsupium</i>	Indian kino	Fabaceae	Heart-wood	Pterostilbene, marsupsin	Regenerates pancreatic cells	83
<i>Mangifera indica</i>	Mango	Anacardiaceae	Leaves	Mangiferin	Reduces intestinal glucose absorption	84
<i>Murraya koenigii</i>	Curry leaf	Rutaceae	Leaves	Carbazole alkaloids	Improves insulin activity	85
<i>Phyllanthus emblica</i>	Amla	Phyllanthaceae	Fruits	Vitamin C, tannins	Reduces oxidative stress and hyperglycemia	86
<i>Zingiber officinale</i>	Ginger	Zingiberaceae	Rhizome	Gingerols, shogaols	Enhances glucose uptake	87
<i>Cinnamomum verum</i>	Cinnamon	Lauraceae	Bark	Cinnamaldehyde, polyphenols	Mimics insulin action	88
<i>Ficus religiosa</i>	Peepal	Moraceae	Bark and leaves	Flavonoids, sterols	Decreases blood glucose levels	89
<i>Berberis aristata</i>	Daruharidra	Berberidaceae	Roots	Berberine	Activates AMPK pathway	90
<i>Aegle marmelos</i>	Bael	Rutaceae	Leaves	Marmelosin, aegeline	Improves glucose tolerance	91

Curcuma longa: *Curcuma longa*, typically named as turmeric, has illustrious antidiabetic properties primarily because of curcumin, which is its main polyphenolic compound⁹². Curcumin assists the body in using insulin more efficiently by triggering the PI3K/Akt and AMPK pathways⁹³. At the same time, it degrades inflammation by restricting the conditioning of the NF- κ B and JNK pathways. Also, curcumin avoids formation of advanced glycation end products (AGEs), which can damage the tissues and leads to diabetes-related complications⁹⁴. The compound likewise acts as a strong antioxidant by neutralizing harmful reactive oxygen species and boosting the activity of natural antioxidant enzymes comparable as catalase, glutathione peroxidase, and superoxide dismutase⁹⁵. In investigation utilize animal models with diabetes, curcumin has been display to considerably low high blood sugar levels and degrade conditions like diabetic nephropathy, neuropathy, and cardiovascular issues. Newer nanoformulations of curcumin have improved its ability to be immersed by the body and its validity in address diabetes⁹⁶. **Table 2** provided list of major plants in diabetic activity.

Trigonella foenum-graecum: Fenugreek, scientifically specified as *Trigonella foenum-graecum*, has been universally recognized for its capacity to low blood sugar levels and enhance the body's response to insulin⁹⁷. The seeds of fenugreek hold various favorable compounds such as soluble fibers, trigonelline, diosgenin, galactomannan, and 4-hydroxyisoleucine, which simultaneously aid in managing diabetes⁹⁸. The soluble fibers in fenugreek slowly down the emptying of the stomach and the absorption of carbohydrates, which aid in degrade unexpected expand in blood sugar after meals⁹⁹. Besides, 4-hydroxyisoleucine promotes the release of insulin from the beta cells in the pancreas in reaction to glucose¹⁰⁰. Fenugreek also assist the body's cells respond exceed to insulin and use glucose further efficiently¹⁰¹. The antioxidants introduce in fenugreek assist reduce oxidative stress and inflammation, which are related to complexity of diabetes¹⁰². Research from clinical studies has exhibit that hold fenugreek can lead to distinguished decreases in fasting blood sugar levels, hemoglobin A1c, and the levels of certain fats in the blood¹⁰³.

Tinospora cordifolia: *Tinospora cordifolia*, generally specified as Guduchi, is an important medicinal plant that has conventionally use in Indian medicine to manage various metabolic conditions¹⁰⁴. It holds several active compounds similar to tinosporaside, berberine, alkaloids, diterpenoid lactones, and cordifolioside, which show strong antidiabetic and antioxidant properties¹⁰⁵. Research suggests that *T. cordifolia* assists in the release of insulin, enhance the body's capability to hold in glucose, also reduces the production of glucose in the liver¹⁰⁶. The plant also assist in lowering oxidative stress by boosting the levels of natural antioxidant enzymes like catalase and superoxide dismutase¹⁰⁷. Its anti-inflammatory effects are owing to its ability to block the NF- κ B signaling pathway and degrade levels of inflammatory markers such as TNF- α and IL-6, which in turn improve insulin sensitivity and defend the pancreas¹⁰⁸. Animal studies exhibit that Guduchi helps preserve the structure of the pancreas and slow down the progression of complexity related with diabetes, such as kidney disease and nerve damage¹⁰⁹.

Allium sativum: *Allium sativum*, ordinarily named as garlic, exhibit hopeful potential in managing diabetes owing to its sulphur-rich compounds like allicin, diallyl disulphide, and S-allyl cysteine¹¹⁰. These compounds support better glucose metabolism by support insulin release, increase body's response to insulin, and reduce glucose production in the liver¹¹¹. Garlic also owns strong antioxidant activity, which help in neutralize damaging free radicals and lower the level of fat oxidation in the body¹¹². Its anti-inflammatory effects come from inhibiting the NF- κ B signaling pathway and degrade the levels of inflammatory substances, which helps avoid difficulty associated to diabetes¹¹³. Studies from both laboratory experiments and clinical trials have establish that hold garlic can lower fasting blood sugar levels, degrade cholesterol and triglyceride levels, and decrease signs of oxidative stress. Furthermore, garlic offers heart-protective benefits for people with diabetes by improve the act of blood vessel walls and helping to lower high blood pressure¹¹⁴.

Camellia sinensis: *Camellia sinensis*, usually named as green tea, hold a large amount of catechins, specifically epigallocatechin gallate

(EGCG) ¹¹⁵. These compounds have mighty antidiabetic and antioxidant properties. EGCG aid the body utilize insulin more efficiently and enhance how the body procedure glucose by activating the AMPK pathways and enhance the movement of GLUT4 to cell surfaces ¹¹⁶. The polyphenols found in green tea also aid degrade the absorption of glucose in the intestines and lower the increase of fats in the liver ¹¹⁷. Additionally, EGCG assist degrade oxidative stress and inflammation by blocking NF- κ B signaling pathway and lowering also the levels of damaging inflammatory chemicals ¹¹⁸. Studies on animals exhibit that hold green tea can lower blood sugar levels after fasting, enhance the body's metabolism of lipids, and protect the cells in the pancreas that produce insulin from damage caused by oxidation ¹¹⁹. People who frequently drink green tea have similarly been found to have a lower risk of developing type 2 diabetes as well as related heart problems ¹²⁰.

***Azadirachta indica*:** *Azadirachta indica*, typically specified as neem, has powerful antidiabetic properties because it boast compounds like limonoids, flavonoids, tannins, and glycosides ¹²¹. When taken as an extract, neem helps lower blood sugar by potential insulin receptors further sensitive and by enhance how glucose is used in the body's tissues ¹²². It similarly works by blocking the action of α -amylase and α -glucosidase enzymes, which are complicated in breaking down carbohydrates in the intestines and absorbing glucose into the bloodstream ¹²³. Neem also has significant antioxidant and anti-inflammatory effects that aid defense the pancreatic beta cells from injury caused by oxidative stress and inflammation ¹²⁴. Research has establish that giving neem extracts to diabetic animals leads to better glycogen storage, lower levels of sugar in the blood, and heightened antioxidant levels in the body ¹²⁵.

***Syzygium cumini*:** *Syzygium cumini*, ordinarily named as jamun, has been conventionally used to serve diabetes owing to the presence of mixture like jamboline, ellagic acid, anthocyanins, and flavonoids in its seeds ¹²⁶. These compounds aid expand insulin output and reduce the conversion of starch into glucose, which in turn helps lower blood sugar levels ¹²⁷. Extracts from jamun seeds also have antioxidant activities, which help to reduce

the oxidative stress and boost body's natural defense mechanisms against free radicals ¹²⁸. Also, the anti-inflammatory effects of these extracts assist protect the pancreatic β -cells and support the body's insulin signaling processes ¹²⁹. Research investigations have shown that utilize *Syzygium cumini* extracts can enhance glucose tolerance, lower levels of glycated hemoglobin, and degrade the risk of complications interrelated with diabetes ¹³⁰.

***Aloe barbadensis Miller*:** Aloe vera contains compounds similar to polysaccharides, anthraquinones, flavonoids, and phytosterols, which have powerful antihyperglycemic and antioxidant properties ¹³¹. Research exhibits that aloe vera aids the body in becoming further sensitive to insulin, promotes the absorption of glucose, and inspire the release of insulin from the pancreas ¹³². It also lowers oxidative stress by boosting exertion of antioxidant enzymes and degrades the damage caused by lipid peroxidation ¹³³. The plant's anti-inflammatory effects come from its capability to degrade production of pro-inflammatory cytokines, which assist in maintaining better metabolic balance ¹³⁴. Clinical studies have found that taking Aloe vera can lower the position of fasting blood sugar, triglycerides, and cholesterol. Furthermore, it has been exhibited to protect from kidney damage and liver injury associated with diabetes ¹³⁵.

***Vitis vinifera*:** Grapes, scientifically named *Vitis vinifera*, boast compounds such as resveratrol, quercetin, catechins, and proanthocyanidins, which have important antidiabetic and antioxidant properties ¹³⁶. Resveratrol aid by triggering two major signaling pathways, SIRT1 and AMPK, which in turn improve insulin sensitivity and support exceed mitochondrial function ¹³⁷. Furthermore, it assists in reducing oxidative stress, inflammation, and issues with blood vessel function that are connected to long-term high blood sugar levels ¹³⁸. The polyphenols established in grapes also support blocking the NF- κ B signaling pathway, which involved in inflammation, lower production of inflammatory substances like TNF- α and IL-6 ¹³⁹. Research examinations have exhibited that hold grape extracts can also improve the body's capability to handle glucose, lower insulin resistance, and give protection against heart-related

complications that often come with diabetes. These results suggest that *Vitis vinifera* could be an applicable extension to the treatment draws on for

managing diabetes mellitus¹⁴⁰. **Table 3** provided major phytoconstituents in diabetic activity.

TABLE 3: LIST OF MAJOR PHYTOCONSTITUENTS SHOWING ANTI- DIABETIC ACTIVITY

Individual compound	Cell lines	Animal model	Mechanism of action	Ref.
Gymnemic acid	INS-1, STZ diabetic rats	STZ- induced diabetic rats	Promotes regeneration of pancreatic beta-cells and insulin secretion	141
Charantin	L6 myotubes, diabetic mice	STZ- induced diabetic mice	Increase glucose uptake and glycogen synthesis	142
Curcumin	HepG2, STZ diabetic rats	Acetaminophen-induced liver injury mouse model	Suppresses NF-Kb pathway and oxidative stress	143
Berberine	3T3-L1 adipocytes, HepG2	Gestational diabetes mellitus rat model	Activates AMPK pathway and improves insulin sensitivity	144
Quercetin	INS-1 cells, diabetic rats	STZ- induced diabetic rats	Protect beta- cells from oxidative damage and apoptosis	145
Trigonelline	Pancreatic beta- cell models	Nicotinamide- STZ induced diabetic rats	Enhances insulin secretion and glucose tolerance	146
Jamboline	Experimental diabetic models	Alloxan- induced diabetic rabbits/ rats	Reduces conversion of starch into glucose	147
Luteolin	HepG2	HFD/STZ diabetic mice	Reduces insulin resistance and inflammation	148
Catechin	3T3-L1 adipocytes	Diabetic mice	Enhances glucose metabolism and antioxidant enzymes	149
Apigenin	INS-1 cells	STZ diabetic rats	Preserves β -cell mass and lowers blood glucose	150
Gallic acid	INS-1E β -cells	STZ rats	Protects β -cells from oxidative stress, enhances insulin secretion	151
Rutin	L6 skeletal muscle cells	STZ rats	Enhances glucose uptake, antioxidant enzymes	152

CONCLUSION: Diabetes mellitus remain to be a major generic metabolic condition because of its widespread occurrence, long-term complications, and massive impact on society and economics. Although conventional diabetes medicine like metformin, insulin, sulfonylureas, DPP-4 inhibitors, SGLT2 inhibitors, and GLP-1 receptor agonists are efficient in managing blood sugar levels, continued use frequently leads to side effects and exceptional limited capability to avoid diabetes-related complications.

These disadvantages have created surge of interest on phytotherapy as a safe and effective treatment. Many medicinal plants, such as *Gymnema sylvestre*, *Momordica charantia*, *Curcuma longa*, *Trigonella foenum-graecum*, *Tinospora cordifolia*, and *Syzygium cumini*, contain active components that aid lower blood glucose, reduce oxidative stress, fight inflammation, and defend pancreatic beta cells. These are mediated through various biological pathways, involve AMPK, PI3K/Akt, GLUT4, and NF- κ B. Progress in nanotechnology and innovative drug delivery methods has further

improved the strength of these plant-based compounds. Nevertheless, additional clinical research, safety testing, and standardization of herbal products are needfulness to verify their long-term benefits and safety.

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