

Herbal Drugs used for the Management of Diabetes: A Review

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Abstract:

An abnormal increase in blood glucose level leads to diabetes, which is characterized as major metabolic disorder. Risk of various serious complications like diabetic retinopathy, diabetic neuropathy, diabetic non-healing foot ulcers and multi-organ failure increases in patients present with uncontrolled diabetes. Diabetes can be managed in patients by using various marketed conventional anti-diabetic drugs which are expensive and lead to multiple severe side-effects in patients. Considering this, various cost-effective herbal medicines are developed that can be used for the effective management of diabetes with a lower risk of severe side effects. Investigation of various herbal plants has been conducted in past few years to evaluate their efficacy in the treatment of Type 1 and Type 2 diabetes. Findings of experimental studies provide evidence that presence of natural antioxidants, flavonoids, and tannins as secondary active metabolites is responsible for the significant anti-hyperglycemic activity of various herbal plants which are associated with considerable potential to regenerate beta-cells activity and reduce blood glucose levels. Providing detailed information about the herbal plant's utility as anti-diabetics in various conventional medicines is the major objective of this review article. These include *Coriandar Sativum*, *Aloe Vera*, *Zingiber Officinale*, *Tinospora Cardifolia*, *Ferula Asafoetida*, and *Andrographis Paniculata*.

Keywords: Diabetic retinopathy, Diabetic non-healing foot ulcers, secondary metabolites.

1. INTRODUCTION

Severe impairment in glucose metabolism occurs majorly due to deficiency of insulin or due to severe autoimmune pancreatic beta cell destruction which leads to diabetes, a chronic metabolic disorder.¹ Severe complications of uncontrolled diabetes like diabetic neuropathy, diabetic nephropathy, and diabetic retinopathy are reported in patients due to the chronic rise in oxidative stress, dyslipidemia, and alterations in the body's antioxidant defense system.² International diabetes foundation provided report suggest that around 451 million (aged 18–99 years) people are present with diabetes worldwide. By 2045, these figures are expected to rise to 693 million. In 2017, worldwide, in the 20-99 years age range, approximately 5 million deaths worldwide were reported due to diabetes. Finding of various studies suggested the diabetes mellitus complications prevalence varying from 20 to 90.5³⁻⁶

Generally, diabetes mellitus can be classified into four types: gestational GDM, Type II DM, type I DM, and DM-specific types (monogenic diabetes, cystic fibrosis diabetes, latent autoimmune diabetes in adults , and drug-induced diabetes).⁷ The major reason of tissue damage, cellular injury and organ

dysfunctioning is oxidative stress which is usually associated with diabetes complications. Oxidative stress is characterized as the rise in the level of reactive oxygen species that induce chronic impairment in various biological molecules like proteins, lipids and DNA.⁸ Oxidative stress can be reduced by using various antioxidant enzymes including glutathione peroxidase, superoxide dismutase, glutathione reductase and catalase.⁹

Risk of various acute complications like ketoacidosis and hyperosmolarity increase in patients present with uncontrolled diabetes¹⁰ Various chronic complications like renal impairment, foot ulcer, cardiovascular disorder and retinopathy are also reported in patients with diabetes mellitus.¹¹ Insulin, diet modifications and oral anti-diabetic agents can be used for the diabetes management, however, no successful therapeutic intervention for diabetes mellitus has been reported. Medicinal plants have emerged as an alternative therapeutic option for diabetes management in an effective manner.¹²

In the recent era, interest in various natural products has been increasing. Findings of recent studies suggested that anti-diabetic activity can be possessed by various dietary natural products. Underlying mechanisms and antidiabetic effects induced by various natural products can be summarized based on the findings from clinical, experimental and epidemiological studies. In the prevention and therapeutic management of diabetes, a significant role can be played by various medicinal herbs (*e.g.*, *Aloe vera* leaf and *Nigella sativa*), vitamin C and carotenoids, some fruits (*e.g.*, grape, blueberry, and cherry), grains (oat, rye, and brown rice) and vegetables (*e.g.*, bitter melon and *Lycium barbarum* leaves). Anti-diabetic drugs ongoing development underscores the significance of safety and efficacy in finding new components with no side-effects. Due to various side-effects associated with chemical drugs, plants or herbal plants have been utilized as alternative medicines. Various bioactive natural components are present in the plants which are having marked pharmacological effects in human body.¹³ Their underlying anti-diabetic mechanisms include exerting anti-glycation, anti-inflammatory and antioxidant effects, modulating insulin action, potentiating the gut microbiota and inhibiting carbohydrate-hydrolyzing enzymes. This review article's major focus is to demonstrate the multiple herbal medicinal plants that can be used for diabetes management and the mechanism by which the isolated components present in plants manage the increased glucose level in diabetic patients.

2. MEDICINAL PLANTS IN THE MANAGEMENT OF DIABETES MELLITUS

In the large proportion of patients, diabetes mellitus is effectively managed by using herbal medicines¹⁴ More than 1200 medicinal plants have been clinically used for the effective treatment of diabetes mellitus, as suggested by Ethno botanical studies findings. Findings of Ethno botanical studies demonstrated that for diabetes mellitus management, at least 1200 medicinal plants have been utilized. Chronic progression of diabetes complications and metabolic abnormalities may be corrected by plant-derived medicines.¹⁵ In the previous studies, in comparison to conventional medicines, more significant anti-diabetic effects have been reported with the various bioactive constituents isolated from plants.^{16,17} Globally, multiple medicinal plant extracts have been utilized for the effective management of diabetes mellitus, and these are associated with multiple advantages like fewer side effects, and being inexpensive compared to conventional medicines. Multiple bioactive components isolated from plant extracts were utilized as a lead compound. In Ethiopia, various medicinal plant

parts were used experimentally. Various phytoconstituents like coumarins, phenolic components and flavonoids are present in plant-based products demonstrating significant blood-glucose-lowering efficacy. Certain traditional medicines utilized for diabetes mellitus management include the *Aloe vera* (Aloaceae), *Momordica Charantia* Linn (Cucurbitaceae), *Moringa Oleifera* (Moringaceae), *Trigonellafoenum-Graecum*L (Fabaceae), *Euphorbia sp. Gmel*, (Euphorbiace) and *AlliumSativum* (Amaryllidaceae)

POTENTIAL MEDICINAL PLANTS WITH ANTIDIABETIC ACTIVITY

CORIANDAR SATIVUM L

Marked nutritional and medicinal properties are present in herbal medicinal plant due to presence of various phytoconstituents like vitamins, phytosterols and polyphenols. *Coriander (Coriandrum sativum L.)* which belongs to *Apicea* family.¹⁸ Investigation of antidiabetic, anti-inflammatory and antioxidant effect of Polyphenolic fraction of *Coriander sativum* seeds demonstrated potent antihyperglycemic activity of 9 polyphenols present in medicinal plant extract.¹⁹ *Coriander sativum* seed extract was administered to animals at 40 mg/kg dose which leads to marked antihyperglycemic effect in streptazocin-induced (STZ) diabetic rats.²⁰ Further, in another study, after inducing the diabetes in Wistar rats by alloxan, *Coriander (Coriandrum sativum L.)* leaf extract and ethanolic stem extract was administered, which leads to the significant hepatoprotective, hypolipidemic and hypoglycaemic effect.²¹ Improvement in various parameters such as insulin resistance, decline in level of triglycerides, blood glucose level in normal range was achieved on *Coriander sativum* seeds aqueous extract administration.²²

ALOE VERA

Aloe Vera, another medicinal plant belongs to the family *Liliaceae* known for its marked pharmacological effect against various ailments like hyperlipidemia, oxidative stress, cancer, hypercholesteremia, and various other skin infections.²³ Acute oral toxicity, antidiabetic and antioxidant activity evaluation of *Aloe vera* flowers methanolic extract (AVFME) was evaluated in alloxan-induced diabetic rats. Findings of study suggest that in the management of Type 2 diabetes mellitus, AVFME can be utilized as novel antidiabetic supplement.²⁴ Investigation of antidiabetic potential of methanolic extract of *Aloe Vera* proposed that it inhibit the formation of advanced glycation end products and may inhibit the increase in postprandial glucose.²⁵ Findings of systematic review and meta-analysis study of eight trials carried out to investigate the effect of *Aloe vera* on glycemic control suggested that *Aloe vera* significantly increase the fasting plasma glucose level with little effect on HbA1c.²⁶

ZINGIBER OFFICINALE

Zingiber officinal Roscoe, commonly named ginger associated with enormous health benefits and belongs to the *Zingiberaceae* family which is used for the management of various conditions like hypertension, diabetes, arthritis, and sore throat from many years.²⁷ Evaluation of in-vitro antidiabetic activity of rhizome extract of *Zingiber officinale* revealed that herbal plant rhizome extract modulates the uptake of glucose at 400 ug/ml.²⁸ On the administration of 200mg/kg/b.w of gingerol, an active phytoconstituent present in *Z.officinale* modulates insulin secretion and further, also facilitates the

glucose uptake by skeletal muscles by binding with GLUT4 (Glucose transporters) and modulating the enzyme named glycogen synthase secretion.²⁹ Marked improvements in the glycaemic index and antioxidant status in patients present with type 2 diabetes was reported on the administration of powdered ginger (3g/day).³⁰ Furthermore, the uptake of glucose in peripheral cells and modification in the glycolytic process in the liver and kidneys occurred with ginger extract oral administration in diabetic rats.³¹

FERULA ASAFOETIDA

Ferula Asafoetida, another traditional medicinal plant, is used in the treatment of various disorders like Asthma, bronchitis, influenza, and various other neurological conditions.³² Administration of oleo-gum resin extract of *Ferula Asafoetida* at the dose of 150 mg/kg for a duration of 3-6 weeks leads to a reduction in the hyperglycaemia while no change in blood glucose concentration was seen on the administration of 250 mg/kg of Ole-gum resin extract of *Ferula Asafoetida*.³³ In another study, in-vitro antidiabetic activity of *Ferula Asafoetida* seed extract was evaluated through alpha-glucosidase and dipeptidyl peptidase IV inhibitory activity. Findings of study provide evidence that various alpha-glucosidase and dipeptidyl peptidase IV inhibitors are present in *Ferula Asafoetida* methanolic extract and it could be a potential source for the management of Type 2 diabetes.³⁴ Evaluation of antidiabetic activity of Asafoetida extract in alloxan-induced diabetic rats suggested the antidiabetic efficacy of Asafoetida due to its preserving beta-cell integrity potential.³⁵

KIGELLA GENUS

Kigela pinnata, traditional medicinal plant, belonging to family *Bignoniaceae*, known for its various pharmacological activities such as antineoplastic, antioxidant, analgesic, antidiarrheal, and antiprotozoal.³⁶ In alloxan-induced diabetic rats, antidiabetic activity of *Kigella African* aqueous and alcoholic extract antidiabetic effect was investigated out. Findings of the study demonstrated the marked hypoglycemic effect of *Kigella African* ethyl extract.³⁷ In STZ-induced diabetic rats, on the administration of 250 and 500 mg/kg of *Kigella pinnata* flower extract (KPFE), marked reduction in blood glucose level was seen. Dose-dependent antidiabetic effect of KPFE was reported in the findings of the study.³⁸

PHYLLANTHUS EMLICA L (INDIAN GOOSEBEERY)

In the ayurvedic medicine system, *Pyallanthus emblica L* regarded as a medicinal plant with huge importance, also known as Amla. Phenolic constituents present in this medicinal compound are known for the anti-cancer, anti-hyperglycemic and anti-inflammatory activities possessed by the plant. Furthermore, tannins and flavonoids present in it potentiate glucose metabolism and also potentiate glucose homeostasis.³⁹ Therapeutic in-vitro and in-vivo antidiabetic activity of *E. officinalis* fruit juice and gallic acid was evaluated in fructose-induced diabetic rats and in 3T3-L1 preadipocytes. Gallic acid in *E. officinalis* delineate the upregulation of pAkt, PPAR- γ and Glut4.⁴⁰ Marked reduction in fasting serum glucose level in type 2 diabetic rat was reported after the *E. officinalis* aqueous extract administration.⁴¹

PSIDIUM GUAVJA

Psidium Guavja is a traditional medicinal plant having significant antioxidant, analgesic and anti-inflammatory potential and it is utilized in the treatment of diarrhoea and diabetes.⁴² A study was designed with the objective to investigate the anti-diabetic activity of *Psidium guajava* L (Guava) ethanolic extract on streptazocin-induced type 2 diabetic rats. Findings of study suggested that administration of plant ethanolic extract leads to significantly reduction in serum glucose level by 18%.⁴³ Evaluation of the antihyperglycemic potential of *Psidium Guavja* leaves aqueous extract demonstrated that it leads to a marked reduction in hyperglycemia in diabetic animals as compared to animals of the control group at the administration of 400 mg/kg dose. Alpha-glucosidase enzyme activity is significantly inhibited by PG leaves and Bark ethanolic extract as evidence supported by the study.⁴⁴ Investigation of anti-diabetic activity of polysacchrides isolated from *Psidium guavja* leaves in streptazocin-induced diabetic rats suggested the marked antidiabetic activity of plant isolated polysacchrides.⁴⁵

CITRUS COLOCYNTHIS

Citrullus colocynthis (L.) Schrad medicinal plant distributed over the southern and Sudan parts of Asia used for the management of leprosy, diabetes, cancer, arthritis, joint pain, asthma and bronchitis, belongs to the *Cucurbitaceae* family⁴⁶ *Citrullus colocynthis* pulpy flesh seeds hydro-ethanolic extract antidiabetic activity was evaluated in vitro by using DPPH inhibition assay, alpha-glucosidase enzyme assay and in vitro by Streptazocin induced diabetic rats. Findings of study demonstrated the time-dependant hypoglycemic effect of medicinal plant extract due to its alpha-glucosidase enzyme inhibition potential.⁴⁷ A clinical study was carried out with the objective to demonstrate the anti-diabetic efficacy of *C. colocynthis* on HbA1c and fasting blood sugar in 70 patients present with type II diabetes. Fasting blood sugar level and HbA1c marked reduction with the administration of 125 mg *C. colocynthis* once per day for 2 months was seen.⁴⁸

Biophytum Sensitivum

The Biophytum genus, belongs to the *Oxalidaceae* family is quite rich in various phytoconstituents like tannins, flavonoids, saponins, polysaccharides, essential oil, pectin, amino acids and steroids used in the management of arthritis, wounds, inflammation, stomach ache, tumors, asthma, cough, and diabetes.⁴⁹ Anti-diabetic activity of aqueous, ethanolic and ethyl acetate extract of *Biophytum sensitivum* was evaluated in streptazocin induced diabetic rats at a dose of 200 mg/kg. Marked blood glucose level decline and rise in the insulin level was seen after providing the treatment for 45 days.⁵⁰ Furthermore, antidiabetic activity of aqueous solution of *Biophytum sensitivum* leaf extract (BSEt) was determined in streptazocin-nicotanimide induced diabetic rats. Promising antidiabetic efficacy of plant extract on STZ-nicotanimide induced diabetic rats.⁵¹

ANDROGRAPHIS PANICULATA

Andrographis paniculata, an anti-bacterial and anti-inflammatory herb possessed diverse pharmacological activities like anti-obesity, anti-diabetic, anti-inflammatory due to presence of Andrographolide, major active constituent present in medicinal plant.⁵² In a study, *Andrographis paniculata* and *Andrographis echiodis* herbal plants ethanolic extracts antioxidant and antidiabetic activity were compared by alpha amylase inhibitory activity and alpha glucosidase inhibitory in-vitro tests. Both medicinal plants exhibited the significant antidiabetic effect in a dose-dependent manner,

however antidiabetic efficacy of *Andrographis paniculata* was observed more in comparison to *Andrographis echinoides*.⁵³ In another study, antidiabetic activity of 200 mg/kg BW of *Andrographis paniculata* was investigated on an obese diabetic animal. Finding of study demonstrate the marked antidiabetic activity of plant extract.⁵⁴

TINISPORA CARDIFOLIA

Tinospora cordifolia, potent herbal plant, belonging to family *Menispermaceae*, is quite rich in various phytoconstituents like alkaloids, terpenoids, lignans and steroids due to which it is utilized in urinary problem, skin diseases, leprosy, diabetes, fever and dysentery.⁵⁵ Anti-diabetic activity of *Tinospora Cardifolia* was evaluated in alloxan induced diabetic rats. After the administration of both low dose (200 mg/kg) and high dose (400mg/kg) administered to animals, dose dependant hypoglycemic action of plant extract was seen.⁵⁶ In another study, methanolic extract anti-diabetic activity evaluation of stem of medicinal plant demonstrated that *Tinospora cardifolia* possessed leads to marked reduction in level of fasting glucose level in streptozocin-induced diabetic rats. Further, marked improvements in the level of C-peptide and insulin was also observed in the finding of the study which demonstrate about the effect of medicinal plant on the beta cell regeneration.⁵⁷

RAUWOLFIA SERPENTINA

Rauwolfia serpentina, also known as endangered medicinal plant possessed diverse pharmacological properties like antihypertensive, antiproliferative, anti-inflammatory and antifungal, belonging to family *Apocynaceae*.⁵⁸ To demonstrate the therapeutic effect of methanolic extract of *R. serpentina* in the treatment of type 2 diabetes, a study was carried out in fructose induced diabetic mice. Plant extract oral administration for 14 days leads to marked improvement in various parameters like glycaemic change, total cholesterol, fasting insulin resistance, glycosylated haemoglobin and hepatic glycogen. From the findings of the study, it was suggested that medicinal plant effectively modulates the metabolism of carbohydrates and lipids by effecting the intestinal absorption of fructose.⁵⁹ In another study, antidiabetic activity of *Rauwolfia serpentina Benth* methanolic root extract was carried out in Alloxan-induced diabetic rats. In the finding of study, marked improvement in insulin/glucose ratio, glucose and insulin level was observed in test group animals in comparison to diabetic control animal.⁶⁰

TAMARINUS INDICA

Tamarindus Indica, an important traditional medicinal plant belongs to the family *Leguminosae*, widely utilized for the management of cough, stomach disorder, diarrhoea jaundice, bacterial and parasitic infections, malaria and rheumatism.⁶¹ Hydroethanolic extract of seed coat extract of *Tamarindus Indica* was prepared with the objective to investigate its antidiabetic activity in alloxan-induced diabetic rats. Phytochemical analysis of hydroalcoholic extract of medicinal plant revealed the presence of flavonoids in the hydroethanolic extract. Marked blood glucose level decline was also seen on providing the treatment with single and multidose of *Tamarindus Indica*. Further, histopathological findings revealed the protective effect induced by plant extract on pancreatic beta-islets cells.⁶² In another study, anti-diabetic potential evaluation of *Tamaranus Indica* leaf aqueous methanolic extract at 200 mg/kg suggested the significant anti-diabetic activity of plant extract.⁶³

ANACARDIUM OCCIDENTALE L

Anacardium occidentale L, belongs to the family *Anacardiaceae* is utilized in tropical countries for the management of various inflammatory conditions, diarrhoea and skin diseases. ⁶⁴ Antidiabetic activity of ethyl acetate, 80% methanol, chloroform and petroleum ether extract was evaluated for hyperglycemic and oxidative activity. Finding of study suggested that *A. occidentale* root extract possessed effective antioxidative and antihyperglycemic activity. ⁶⁵ Anti-diabetic activity of leaves of *Anoacardium occidentale* Linn was evaluated with the medicinal plant leaves ethanolic extract in neonatal streptazocin induced diabetic rats. In the results of experimental study, 8.01 % and 19.25% blood glucose level decline was observed on providing the treatment for 15 days and 30 days with 100 mg/kg of medicinal plant extract. Antidiabetic effect produced by medicinal plant extract was quite same as that produced by standard drug Pioglitazone. ⁶⁶

MOMRDICA CHARANTIA

Momordica charantia (MC) belongs to family *Cucurbitaceae* has been utilized as an medicine in many regions and Asian countries from ancient times. ⁶⁷ Various studies have demonstrated the anti-inflammatory, anti-tumour, antioxidative activity of MC. A study was carried out with the objective to demonstrate the effect of *Memordica charantia* saponins (MCS) on insulin signaling pathway, oxidative stress, and on lipid metabolism in type 2 diabetic rats. In the study findings, significant reduction in the various important parameters like fatty acid, triglycerides, total cholesterol and fasting blood glucose level was seen in the group of animals treated with MCS. Furthermore, marked rise in the level of various antioxidant enzymes such as SOD (Superoxide dismutase) and catalase was seen after the administration of MCS for 4 weeks. Considering the study results, it was concluded that MCS possessed significant antidiabetic activity due to its potential to reduce oxidative stress, marked improvement in lipid metabolism disorder and regulation of pathway mediated by insulin signalling. ⁶⁸ In another study, antidiabetic activity of saponins from *Momordica charantia* was evaluated in type 2 diabetic rats. Findings of study suggested that plant saponins can increase glucose tolerance, lowers fasting blood glucose level and can modulate the insulin sensitivity index, insulin content in rats. ⁶⁹

CINNAMOMUM CASSIA

Cinnamomum Cassia widely used traditional herbal medicine used for the management of various conditions like peptic ulcer disease, ischemic brain injury and dyspepsia. ⁷⁰ A study was conducted with the aim to investigate anti-diabetic potential of *Cinnamomum Cassia* Oil in alloxan-induced diabetic rats. Finding of study demonstrate the antidiabetic activity of plant oil either due to its potential to stimulate the remaining beta-cells or due to modulation of glucose cellular utilization. ⁷¹ In another study, four major commercial cinnamon types *Cinnamomum cassia* [CC], Indonesian; *C. burmanii* [IC], Vietnamese; *C. loureirii* [VC], and Ceylon; *C. zeylanicum* anti-hyperglycemic activities were compared. Results of study demonstrate the significant anti-hyperglycemic activity of Cinnamon with most marked antidiabetic activity was seen with Ceylon Cinnamon. ⁷²

GARCINIA INDICA

Garcinia indica, also commonly known as Kokum is used in conventional medicine to treat dermatitis, diarrhea, inflammation and to potentiate digestion, belongs to the Clusiaceae family ⁷³. Garcinol is an antioxidant benzophenone compound isolated from *Garcinia Indica*, possessed hepatoprotective, anti-inflammatory, anticancer and antioxidant properties. A study was carried out with the aim to demonstrate the antidiabetic effect possessed by garcinol in streptazocin induced-diabetic rats. Therapeutic administration of garcinol at three different dose (25, 50 and 100 mg/kg) was provided to rats for 28 days. Marked decline in certain parameters glycosylated haemoglobin, lipid level and blood glucose was seen in group of animals treated with garcinol in comparison to group of animals provided treatment with standard anti-diabetic metformin drug. ⁷⁴ In another study, antidiabetic, renal protective and antihyperlipidemic activity of *Garcinia Indica* fruits rinds aqueous and ethanolic extract was investigated in alloxan-induced diabetic rats. Study findings suggest the significant antihyperglycemic activity of plant extract. ⁷⁵

S. No	Plant Botanical Name	Part used in the study	Findings of the study	References
1	<i>Abelmoschus esculentus (L.)</i>	Fruits extract	The study findings demonstrated that the fruit extract of <i>Abelmoschus esculentus (L)</i> exhibit anti-diabetic activity by various mechanisms like modulating sensitivity of insulin, modulating the insulin release and inhibiting the intestinal absorption of carbohydrate at a dose of 50mg/kg.	W Aligita et.al ⁷⁶
3	<i>Ceasalpinia Bonducella</i>	Leaf extract	Marked hypoglycemic and anti-hyperglycaemic activity was reported in normal and alloxan-induced diabetic rats respectively in the study findings conducted with the ethanolic leaf extract of medicinal plant.	Aswar PB et. al ⁷⁷
4	<i>Ficus religiosa L</i>	Bark	Results of the study conducted proposed that <i>Ficus religiosa bark</i> aqueous extract at 50 and 100mg/kg exhibited a marked rise in the insulin and glycogen content in the liver in streptazocin-induced diabetic rats.	Pandit R et.al ⁷⁸
6	<i>Swertia chirayita (Roxb.)</i>	Whole plant	Findings of the study proposed that three major phytoconstituents mangiferin, swertiamarin and their derivatives present in the medicinal	Phoboo S et al ⁷⁹

			plant are responsible for mild anti-hyperglycaemic activity as suggested by positive findings of 2,2-diphenyl-1-picrylhydrazyl radical inhibitory activity and alpha-glucosidase inhibitory activity.	
8	<i>Annona squamosa</i> L	Aqueous leaf extract	In the findings of the study, significant decline in plasma glucose level in group of animals treated with aqueous leaf extract of herbal plant <i>Annona Squamosa</i> L demonstrate its anti-diabetic activity.	Saeed F et.al ⁸⁰
10	<i>Beta vulgaris</i> L. root	Root methanolic extract	Marked decline in the insulin, fasting glucose level in pre-established type 2 diabetic rats was observed in rats treated with plant extract as demonstrated by study finding.	Al-Harbi LN et.al ⁸¹
11	<i>Brassica juncea</i> (L.) Czern	Plant methanolic extract	Significant decline in blood glucose level was seen in streptazocin-induced diabetic rats on 21th day demonstrate the plant methanolic extract anti-diabetic activity.	Kumar A et.al ⁸²
12	<i>Bombax ceiba</i> L	Leaf and flower ethanolic extract	Findings of the study demonstrate the high alpha-amylase and alpha-glucosidase inhibitory activity of 95% ethanolic flower extract of medicinal plant in comparison to the leaf extract	Kriintong N and Katisart T ⁸³
14	<i>Cajanus cajan</i> (L.) Millsp	Leaf extract	Marked decline in the fasting blood glucose level was seen with leaf extract of plant in dose dependant manner, in the findings of study.	Ezike AC et.al ⁸⁴
16	<i>Capparis decidua</i> (Forssk.) Edgew	Leaves ethanolic extract	In the study finding, marked decline in the blood glucose concentration was seen with the plant aqueous and methanolic extract administration in alloxan-induced diabetic rats.	Rathee S et.al ⁸⁵
18	<i>Thymus schimperi</i>	Aqueous and 80%	In the findings of the study, blood glucose level was seen decline in	Melesie Taye G et.al ⁸⁶

		methanolic extract	diabetic mice treated with aqueous and 80% methanolic extract of plant.	
20	<i>Vitex negundo</i> L.	Hydroethanolic extract of leaves	Out of different hydroethanolic extracts of <i>V. negundo</i> , maximum alpha-glucosidase inhibitory activity was reported with 60% ethanolic extract of plant which suggest that <i>Vitex negundo</i> can be utilized for its potent antidiabetic activity.	Nadeem M et.al ⁸⁷
22	<i>Solanum Indicum</i>	Methanolic fruit extract	Findings of study demonstrates dose dependant a alpha-glucosidase and alpha-amylase inhibitory activity of fruit extract of medicinal plant. Furthermore, marked decline in blood glucose level was seen with oral administration of plant extract with more pronounced effect was seen at 200 mg/kg.	Gadewar M et.al ⁸⁸
24	<i>Securinerga virosa</i>	Methanolic Leaf extract	In comparison to the animal of control group, plant extract administration at two doses (50mg/kg b. w. and 100mg/kgb.w.) leads to marked decline in blood glucose level after oral administration for 21 days.	Yeldu, MH et.al ⁸⁹
25	<i>Origanum floribundum</i> Munby	Leaves aqueous extract	Due to presence of various bioactive components present in the plant having significant anti-diabetic potential, blood glucose level reduced significantly in alloxan-induced diabetic rats on the administration of 200 and 400 mg/kg of aqueous leaf extract of plant.	Nasri M et.al ⁹⁰
26	<i>Vinca rosea</i>	Ethanolic whole plant extract	In comparison to the whole plant extract at low dose (300 mg/kg), marked antidiabetic effect is possessed by whole plant ethanolic extract at high dose (500 mg/kg) in diabetic rats. Furthermore, marked improvements in various parameters like lipid profile, body weight and	Liak R and Nandy SK ⁹¹

			pancreatic beta cells regeneration is possessed by plant ethanolic extract.	
27	<i>Emblica officinalis</i>	Dried fruits ethanolic extract	Findings of in-vivo study provide evidence that dried fruit extract of herbal plant administration at 80 mg/kg led to marked decline in glucose level in diabetic rats. Based on the findings, it was concluded that fruit ethanolic extract of plant can be used as potent antidiabetic and antioxidant agent.	Bashir A et.al ⁹²
29	<i>Punica granatum L.</i>	Aqueous and alcoholic extract of leaves	Due to presence of flavonoids as major bioactive constituents in both aqueous and alcoholic extract of medicinal plant, it exhibits significant alpha-amylase and glucose uptake inhibitory activity	Cheurfa M et.al ⁹³
30	<i>Cocos Nucifera</i>	Husk boiling water extract	Glucose level was reduced in animals treated with <i>Cocos Nucifera</i> husk extract as demonstrated by study findings. Furthermore, regenerative potential of medicinal plant extract was also revealed by findings of histopathological analysis.	Victor E and Jeroh E ⁹⁴
31	<i>Camellia sinesis</i>	Leaves hot water extract	Isoquercitrin and rutin, phenolic constituents present in extract of plant modulate the secretion of insulin from pancreatic beta cells in concentration dependant manner and also led to rise in glucose tolerance.	Ansari P et.al ⁹⁵
33	Terminalia Chebula	Ethanolic extract	Findings of investigation of antidiabetic potential of 5 different concentration of ethanolic extract of medicinal plant revealed that plant extract inhibitory activity increases with the direct increase in concentration.	Priya SK et.al ⁹⁶

CONCLUSION

Persistent increase in glucose level or chronic impairment in insulin synthesis or insulin resistance leads to diabetes which is severe metabolic disorder. In the last few years, a huge rise in the cases of diabetes is observed even after the huge development of various new pharmaceutical agents like biguanides and thiazolidinediones. Diabetes can be managed in quite effective way by using these drugs, however, certain severe side effects and complications are induced by these drugs. Conventional medicinal plants have emerged as a safer and effective treatment for diabetes mellitus. In this review article, around 15 herbal medicinal plant antidiabetic activity and their mechanism of action as the anti-diabetic agent has been discussed. Due to the presence of various active phytoconstituents, major herbal medicinal acts in diabetes by potentiating the secretion of insulin from pancreatic beta-islets cells, regenerating the beta-islets cells and by inhibiting alpha-glucosidase enzyme activity. All these marked anti-diabetic effects possessed by medicinal plants triggered the research on herbal medicinal plants to find suitable alternatives which are associated with no side effects and work as effective therapeutic agents. To conclude, more investigations that focused on phytoconstituents isolation from these medicinal plants can modulate the newer anti-diabetic drug development.

LIST OF ABBREVIATIONS

1. **ABAE**- Averrhoa Billimb aqueous extract
2. **GLT**- Glucose transporters
3. **KPFE**- Kigella pinnata flowers extract
4. **PG**- Psidium Guavja
5. **STZ**- Streptazocin

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