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Current Trends of Plants Having Antidiabetic Activity: A Review

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Abstract

Medicinal plants have been proposed as rich yet unexploited potential sources for antidiabetic drugs, even though used since ancient times for the treatment of diabetes mellitus. Many of the synthetic drugs were discovered either directly or indirectly from the plant source. The present study reviews of plants having antidiabetic property. Although many plants are recommendation, further pharmacological and chemical research should be done to elucidate the exact mechanism of hypoglycemic activity.

Keywords: Diabetes mellitus; Medicinal plants; Antidiabetic; Alloxan; Streptozotocin

Introduction

Diabetes mellitus is a metabolic disorder, characterized by chronic hyperglycemia, with disturbances of carbohydrate, fat and protein metabolism, resulting defects in insulin secretion, insulin action, or both [1]. More than 347 million people are affected by diabetes worldwide [2]. The prevalence of diabetes has risen from 2.4% to 6.4% in the last 15 years [3]. Diabetes related deaths are more common in the low and middle-income countries where more than 80% deaths occur [4].The World Health Organization projects that diabetes will be the 7th leading cause of death in 2030 [5].

Traditional, complementary and alternative medicines have been used since ancient times. Yet the use of traditional medicine (TM) remains widespread in developing countries, while use of complementary and alternative medicine (CAM) is increasing rapidly in developed countries. In many parts of the world, policy-makers, health professionals and the public are wrestling with questions about the safety, efficacy, quality, availability, preservation and further development of this type of health care. TM is sometimes also the only affordable source of health care especially for the world's poorest patients [6].

Indian traditional health care system uses a number of medicinal plants traditionally over 1000 years in herbal preparations. Medicinal plants, minerals and organic matter cover a major part of traditional medicines. Most of the Indian traditional medical practitioners formulate and dispense their own recipes. 21,000 plants are listed by the WHO, which are used for medicinal purposes around the world. Among these, 2500 species are in India, out of which, 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called the botanical garden of the world [7-11]. Ethnobotanical information reports about 800 plants which possess anti-diabetic potential [12].

TM/CAM is used to treat 200 million patients annually. WHO Regional office reports that 71% of the population in Chile and 40% of the population in Colombia are using TM. Many developed countries uses CAM 46% in Australia, 49% in France and 70% in Canada [13-17]. Even though plant sources are potential antidiabetic drugs, they have not gained sufficient momentum among the scientific community. The present study reviews the medicinal plants used for antidiabetic activity.

Materials and Methods

A current review was done by selecting 50 research papers with antidiabetic effect from plant sources (Table 1).

Results

Investigations of medicinal plants with different species and families were studied. Different parts of the plants were used for the antidiabetic study. The methanol, ethanol and aqueous solvents were most commonly used for the extractions. The preliminary phytochemical analyses mostly show the presence of terpenoids and flavonoids. Efficacy evaluation of medicinal plants was done by streptozotozine or alloxone induced diabetic modules. Most of the research results showed the hypoglycaemic effects and almost the same effect of standard drugs. Numerous mechanisms of action had been proposed for the plant extracts.

Discussion

Diabetes is a chronic disease that occurs when the body cannot produce enough insulin or cannot use insulin effectively [69]. It is projected that 300 million people will have the disease by the year 2025 [70] and it may reach to 366 million in the year 2030 [71]. Type 2 diabetes is a common condition and a serious global health problem. In most countries, diabetes has increased alongside rapid cultural and social changes: ageing populations, increasing urbanisation, dietary changes, reduced physical activity and unhealthy behaviours [72]. A person's risk of developing Type 2 Diabetes Mellitus has been shown to be highly linked to obesity and any family history of diabetes [73]. Hyperglycaemic condition causes increased glycosylation leading to biochemical and morphological abnormalities due to altered protein structure and develop the neuropathy, retinopathy, neuropathy and cardiomyopathy [74]. Diabetes kills 1.1 million people in 2005 and more than 220 million people worldwide have diabetes, almost 80% of

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	Scientific Name/ (Family)	Parts Used	Extraction	Diabetic induced by/ Efficacy Evaluation	Active Ingredient	Probable Mechanism of action	References
1	*Acanthopanax senticosus* (Araliaceae)	Whole plant	Aqueous	Alloxan/polysaccharides of this plant decreased the blood glucose, blood lipid (TC and TG), TBARS, GSH, ALT AST, ALP, creatinine, total bilirubin, and urea levels, at the same time it also increased the body weight, liver glycogen formation, and antioxidant enzyme (SOD and GPX) levels as compared with those of diabetic control group.	Polysaccharide.	Potent antioxidant activity leads to antidiabetic activity.	[18]
2	*Acorus calamus* (Acoraceae)	Rhizome	Methanol	Streptozotocin/The crude extract reduced the fasting blood glucose significantly and produce the maximum improvement in glucose tolerance and increase the serum insulin levels.	Phenylpropanoids, sesquiterpenes, monoterpenes, xanthone glycosides, flavones, steroids, lignans, triterpenoidand saponins.	Decrease the activity of glucose -6 phosphates and fructose 1, 6 phosphatase enzymes.	[19]
3	*Adina cordifolia (*Rubiaceae)	Leaves	Hydro-alcoholic	Alloxan/In this study, the extract given to diabetic rats continuously for 15 days, It will produce the dose-dependent reduction of blood glucose level compared to diabetic control rats.	Tannins, saponins and flavonoids.	Increase the insulin secretion or inhibit the intestinal absorption of glucose.	[20]
4	*Cocos nucifera* (Arecaceae)	Spadix	Hydro-methanol	Streptozotocin/Significant reduction in fasting blood glucose level as compared with diabetic control group. Serum enzyme level (SGOT, SGPT, SALP), lipid peroxidation and antioxidant enzyme level such as CAT, GSH, SOD and cholesterol and triglycerides in the *Cocos nucifera* treated groups were restored towards normal level as compared to diabetic control groups and the values were comparable with the standard groups (glibenclamide).	Flavonoid, tannin and saponin.	Potentiating the insulin effect of plasma by increasing either the pancreatic secretion of insulin from the existing β cells or by its release from the bound insulin.	[21]
5	*Afzelia africana* (Fabaceae)	Stem Bark	Aqueous	Streptozotocin/Blood glucose level was significantly reduced (P<0.05). After the plant extract administration the feed and water intake was markedly reduced as compared with the diabetic untreated rats.	Flavonoids, proanthocyanidins, tannins, phenols and flavonols.	Potentiating of insulin from β cells or by increasing peripheral glucose uptake.	[22]
6		Leaves	Alcoholic	Streptozotocin–Nicotinamide/Significant reduction of TG, TC, LDL and increase in HDL level was observed after the administration of plant extract. Significantly increased the SOD and CAT and reduced the TBARS level and conclude that the alcohol leaf extract increase the utilization of glucose uptake increased as similar as biguanides.	Alkaloid , terpenoids, steroids, tannins and phenol.	Improvement in glucose tolerance, restoration of liver glycogen and antioxidant activity to reduce the risk of secondary complication associated with diabetes.	[23]
7		Bark	Methanol	Alloxan/The bark extract significantly reduced the blood sugar level and reduced the serum cholesterol, triglycerides, serum glutamic-oxaloacetic transaminase, serum glutamine-pyruvic transaminase and alkaline phosphate.	Bi flavonoids, triterpene glycosides, saponins, sapogenins and fatty acids.	Insulin secretion and improvement of glycogenesis process.	[24]
8		Leaves	Methanol	Streptozotocin/All the three plants showed significant anti-diabetic activity and anticholesteremic activity.	Flavonoids.	Protect the loss of degradation of structural proteins (which is contributed to the body weight). Presence 20% proteins and 8 essential aminoacids (lysine,threonind and tryptophan), vitamins, calcium and minerals in the plant extract reduce the hyperglycemia.	[25]
9		Stem	Methanol	Streptozotocin/The plant estract significantly reduce the blood glucose level in dose dependent manner and modulated the lipid profile changes in STZ diabetic rates in a dose dependent manner.	Terpenoids, steroids, phenolic compounds, flavonoids and aminoacid.	Decrease the glycated haemoglobin levels and improvement in insulin secretion.	[26]

10		bark	aqueous	Streptozotocin/In this study the bark extract increase the body weight, hemoglobin and decreased blood glucose level.	Flavonoid, tannins, and ellagic acid.	Reversal of insulin resistant by increasing insulin secretion.	[27]
11		Leaves Stem Bark root	Methanol	Alloxan/The leaves and stem bark crude methanol extracts of *Anthocleista djalonensis* gave comparable alpha amylase inhibition of 73.66% and 72.90%, respectively which were quite higher than the 38.93% and 22.90% of the same plant parts given by *Anthocleista vogelii.* The crude stem bark extract of *Anthocleista djalonensis* exhibited significant peak blood glucose reduction on day 6 (72.59%, $p<0.05$) which was higher than the leaves or roots which gave 45.73% and 47.46% ($p<0.05$), respectively the stem bark ethyl acetate fraction of *Anthocleista djalonensis* gave reduction in blood glucose level of 60.86% ($p<0.05$).	-	Alpha Amylase inhibitory activity.	[28]
12		Root	Ethanol	Alloxan/The extract fraction casused a significant ($P<0.001$) reduction in fasting blood glucose of the diabetic rats both in acute and study and prolonged study (2 weeks). The overall activities of the plant extraction were more than that of the reference drug, Glibenclamide.	Alkaloids, flavonoids, tannins, terpenes, saponins, anthraquinones, reducing sugar and cardio glycoside.	Potentiating the insulin effect by increasing the pancreatic secretion of insulin from the cells of islets of langerhans.	[29]
13		Leaf	Methanol	Alloxan/Leaf extract compresses at all the doses (250, 500 and 1000 mg/kg) used caused a respective time dependent and significant ($p<0.0001$) reduction (by 31.5%, 19.8% and 24.5%) of the blood glucose levels in the diabetic rats when compared to the negative control group at the 6^{th} hour. However, the reference drug (glibenclamide, 2 mg/kg) decreased the blood glucose levels by 69.9% and the tween 20 solution (negative control) increased the blood glucose level by 15.2% at the 6^{th} hour.	Glycoside, flavonoids and tannins.	Stimulation of surviving β cells to release more insulin just like glibenclamide.	[30]
14		stembark	Ethanol	Streptozotocin/The plant extract significantly reduced the blood sugar at doe level 353 mg/kg from 2 to 24 hours while compared to glibenclamide (5 mg/Kg)	Alkaloids, flavonoids, steroids, glycosides, saponins, tannins and terpenoids.	Increases the level of insulin secretion.	[31]
15		Stem bark	Ethanol	Alloxan/Steam bark extract exhibit significant hypoglycemic activity at different doses and intervals and 22.2% more potent than the standard oral hypoglycemic drug glibenclamide 0.2 mg/kg.	Flavonoids, Tannins, alkaloids, cardio glycoside, anthraquinones, saponines and triterpenes.	The mode of action like glinenclamide and extra pancreatic effects. Pytochemical screening showed the presence of cardiac glycosides, flavonoids, saponins and tannins in the extracts and the many researched documented the hypoglycemic properties of falvonoids may be the reason for antdiabetic properties.	[32]
16		seeds	Ethanol/ Butanol	Streptozotocin/Administration of both extract significantly ($P<0.5$) lower the fasting blood glucose leve in daiabetic rats by 55%, 64%, and 56%. Similarly serum superoxide dismutase activity was significantly ($P<0.5$) enhanced by treating the both extract. At the same time both the extract significantly decresed the elevated serum creatinine, urea, total cholesterol, triglyceride and thiobarbituric acid reactive species (TBARS) products in diabetic rats.	Cardioglycoside, saponines, alkaloids, anthraquinones, flavones, glycosides and tannins.	By stimulation of few surviving β cell to release more insulin.	[33]
17		root	Alcohol	Streptozotocin/The dose dependent reduction in fasting blood glucose level and glucose tolerance test showed better tolerance of glucose in treated rats. Decrease in lipid peroxides and increase in superoxide dismutase and catalase. Significant reduction in triglycerides, total cholesterol and high density lipo-protein cholesterol.	Tannins phenolics and triterpinoids.	Over production and decreased utilisation of the tissues.	[34]

18		leaves	Isolation flavones	Streptozotocin/Significant blood glucose lowering effects and compared to standard glibenclamide.	Flavonoids	Blood glucose lowering by the regeneration of pancreatic islets and probably insulin release.	[35]
19		leaves	Aqueous infusion	Streptozotocin/Exhibited significant (P<0.05), dose-dependent and marked hypoglycaemic and antihyperglycaemic activities with quick onset. These effects did not differ with respect to agroclimatic elevation, although there were differences in the content of phyto-constituents.	Poly phenols, caffeine, theaflavins and thearubigins.	Inhibited intestinal glucose absorption and impaired α-glucosidase and α -amylase activities. Increasing the Insulin/ glucose ratio.	[36]
20		Fruits	Methanol	Alloxan/Significantly lowered the elevated blood glucose levels by 48% (p<0.001) and 64.5% (p<0.001) respectively at dose level of 400 mg/kg per oral after 24 h as compared to diabetic control. The polyphenolic and flavonoid content of methanol extract and its ethyl acetate soluble fraction were found to be 15.8 ± 1.2mg and 18.55 ± 0.34mg (gallic acid equivalent/g extract) and flavonoid content 2.92 ± 0.03mg and 1.534 ± 0.30mg (rutin equivalent/g extract) respectively.	Polyphenolic, flavonoid and flavanone.	Increase in degree of polymerization and segregation of secondary metabolites .	[37]
21		Polysaccharides	Isolation Polysaccharides	Streptozotocin/Significant decrease in the concentrations of blood glucose, total cholesterol (TC), triglycerides (TGs), low-density lipoprotein-cholesterol (LDL-C) and maleic dialdehyde (MDA). Significant increase in the concentrations of high density lipoprotein-cholesterol (HDL-C) and the activities of antioxidant enzymes.	Polysaccharides.	Polysaccharides may stimulate pancreatic release of insulin and/ or reduce insulin metabolism.	[38]
22		fruits	Methanol	Streptozotocin/The extract treat to the diabetic rats were the doses of 50 and 100 mg/kg bw for 14 days. BG, TC, TG, HDL-C, ALT, AST and AChE levels were significantly reduced at the same time antioxidant levels were significantly increased in the treated groups.	Bioactive triterpenes such as oleanolic acid and ursolic acid. Bioactive phenolic acids vitamin and flavonoids.	Inhibition of glucose transporter, α-glycosidase, α-amylase, lipase and strong antioxidant potential.	[39]
23		Aerial part	Ethanol	Cell Culture/The extract increased insulin secretion in β cells as well as glucose uptake in adipocytes and skeletal myotubes. It also displayed hypoglycemic activity in the diabetic sand rat.	Flavonoids.	Reduction in hepatic lipids is associated with the decrease in glucose absorption or due to an independent mechanism.	[40]
24		leaves	Aqueous	Streptozotocin/Blood glucose levels decreased by ethanol extract at of 250 and 500 mg/kg doses as compared to control group (16%–34%). It has the potent inhibitor of a-glucosidase and a-amylase, possibly due to several polyphenolic compounds present within the extract.	Tannins (ellagic acid), sterols, phenolic acids, lignan glycosides, phenolic compounds and flavonoids (apigenin, quercetin and kaempferol).	Potent inhibitor of α -glucosidase and α-amylase.	[41]
25		barks	Methanol	Streptozotocin/While compared to the standard glibenclamide it shows the significant decrease in blood glucose and significant increase in plasma insulin and liver glycogen levels in treated diabetic rats. Further antilipidemic activity as evidenced by significant decrease in serum TC, TG, LDL-C levels and significant increase in HDL-C level in treated diabetic rats. SCBe also restored the altered plasma enzymes (SGOT,SGPT and ALP), total protein, urea and creatinine levels to near normal.	Steroids, Triterpenoids and phenolic compounds.	Potentiation of the pancreatic secretion of insulin from regenerated β -cells, or its action to release bound insulin from regenerated β cells by inhibiting the ATP sensitive K+ channels like glibenclamide.	[42]

26		gum resin	Ethanol	Streptozotocin/At the end of experimental period of 60 days, showed an increase in body weight. A significant antihyperglycemic effect was evident from 15 days onwards and the decrease in plasma glucose was 76.22% and significant increase in insulin level. Showed a significant decrease in plasma total cholesterol (20.73%), triglycerides (19.76%), LDL-cholesterol (41.66%), VLDL cholesterol (22.22%) and atherogenic index (33.32%) and a significant increase in HDL-cholesterol (14.81%).	Sterols, sugars (sucrose, fructose), aminoacids, camphorene, Cembrene, allylcembrol, resin, oil and several steroids.	Improvement in insulin levels.	[43]
27		fruit	Aqueous	Streptozotocin/Significant increase in the body weight, liver glycogen and serum insulin level and decrease in the blood glucose, glycosylated hemoglobin levels, total cholesterol and serum triglycerides. HDL cholesterol level was significantly increased when treated with the extract.	Carbohydrates, proteins and amino acids.	Increasing the pancreatic secretion of insulin from the existing β-cells.	[44]
28		root	Methanol	Alloxan/Significantly reduced the blood glucose, serum total cholesterol, triglyceride, AST and ALT levels. At the same time increased liver glycogen content. OGTT was performed by administration of 200 mg and 400 mg and 7 mg of glibenclamide to different groups respectively which significantly lower at all time points that blood was sampled after oral glucose load.	Flavanoids, sterols, triterpenoids, alkaloids and phenolics.	Promote insulin secretion by closure of K^+-ATP channels, membrane depolarization and stimulation of calcium influx, an initial key step in insulin secretion.	[45]
29		Leaves	Methanol	Alloxan/Oral administration of the extract (250 and 500 mg/kg body weight) produce beneficial effects of blood glucose level ($P<0.001$) while compare the drug (glibenclamide 10 mg/kg). Enhance the serum insulin level and body weight and there are no histopathological changes.	Poly phenols.	Stimulation of insulin secretion.	[46]
30		Berries	Methanol	Alloxan/Significantly increase in bodyweight, reduced the elevated plasma glucose, glycosylated haemoglobin and pro-inflammatory mediators (interleukin 6 and tumour necrosis factor α). Also decreased the elevated malondialdehyde, restored depleted glutathione, antioxidant enzymes, superoxide dismutase and catalase in liver.	Embelin.	Antidiabetic activity may be due to its potent antioxidant properties. Potent antidiabetic action of *Embelia ribes* observed earlier by many studies may be due to the presence of embelin in the extract.	[47]
31		leaves	Hydro-methanol	Streptozotocin/Oral administration extract 100, 200, 300 and 400 mg/kg b.w. daily for 45 days showed a significant ($P<0.05$) decrease in fasting blood glucose and increase insulin level as compared with the diabetic rats. Also it significantly ($P<0.05$) reduced all biochemical parameters (serum creatinine, serum urea, SGOT, SGPT and lipid profile). The treatment also resulted in a significant ($P<0.05$) increase in reduced glutathione, glutathione peroxidase, superoxide dismutase, catalase, and decrease LPO level in the liver and kidney of diabetic rats.	Tannins, phenolic compounds, and flavonoids.	Stimulation of insulin secretion and absorbed restoration of metabolic activity.	[48]
32		Seeds	70% ethanol	Streptozotocin/Reduced fasted blood glucose and serum insulin levels and oxidative stress in type 2 diabetic mellitus rats. Moreover, a significantly hypolipidemic effect and an improvement in tissue steatosis could be observed after the extract administration.	Saponins.	Improving peripheral insulin resistant rather than protecting pancreas islet β-cells and stimulating insulin secretion.	[49]

33		stem bark	Alcoholic and Aqueous	Alloxan/Significantly decreased the blood glucose level (BGL) in a dose dependent manner after repeated administration for 7 days. In alloxan-induced diabetic rats, both the extracts decreased blood sugar levels with significant improvement in glucose tolerance and body weight at the end of 1st, 2nd and 3rd week after test extract treatment.	carbohydrates, alkaloids, flavonoids, saponins, phytosterols, phenolics, tannins, proteins, amino acids, fixed oils and fats.	Insulin mimetic activity or improved glucose utilization.	[50]
34		bark	Methanol	Streptozotocin/Significant reduction in blood glucose levels and effect is more in the dose 50 mg/kg and 100 mg/kg than 150 mg/kg. Also showed significant increase in serum insulin, body weight, and glycogen content in liver, skeletal muscle, total protein contents were markedly increased. The significant anti-lipid peroxidative effect in the pancreas.	Lup-20(29)-en-3-yl acetate, lupeol, myristicacid,1,3,4,5-tetrahydroxylcyclohexane carboxylicacid, stearicacid,phytol, sitosterol, and lanosterolacetate.	Potentiation of pancreatic secretion of insulin from existing β-cells of islets by the significant increase in the level of insulin.	[51]
35		stem	Alcohol	Streptozotocin/Significant reduction in blood glucose levels and improvement in plasma insulin levels. The effect was more pronounced in 100 and 200 mg/kg than 50 mg/kg. The extract showed significant increase in hexokinase, Glucose-6-phosphate dehydrogenase and glycogen content in liver of diabetic rats and significant reduction in the levels of glucose-6-phosphatase and fructose-1,6-bisphosphatase.	Gymnemosides and gymnemic acid.	Potentiation of pancreatic secretion of insulin from existing β -cells of islets and significant increase in the level of insulin.	[52]
36		suspension cell	Ethanol	Alloxan/ Oral administration of the extracts reduced the glucose content in blood and urine, sugar and lipids in serum significantly ($P<0.5$) at the same time the extract increase the body weight, total hemoglobin and plasma protein content.	Triterpene, saponins and gymnemic acids (I-XVIII and gymnemosaponins (I-V).	Potentiating the insulin effect of plasma by increasing either the pancreatic section in insulin form β-cell or its release bound form.	[53]
37		Whole plant	Alcohol	Streptozotocin/ Significant increase in the body weight and decrease in blood glucose level with higher antioxidant capacity ,good reducing power, scavenger of reactive oxygen like DPPH, nitric acid, hydrogen peroxide and deoxyribose.	Tannins, Flavonoids, vitamin-C and vitamin-E.	Enhance the peripheral utilisation of glucose.	[54]
38		leaves	Ethanol and Aqueous	Streptozotocin/In showed an outstanding hypoglycaemic effect at 500 and 1000 mg/kg doses, 1–4 h after the administration. In oral glucose tolerance test, glucose solution was loaded to normal rats just after 30th minute measurement. The ethanol extract, given in 1000 mg/kg, was found more effective (3.2– 11.7%).	Terpenoids, fatty acids and other hydrocarbons.	Effect in insulin secretion or insulin like activity. Rising sensitivity of PPAR- γ receptors by increasing the release of insulin from β cells of pancreas.	[55]
39		flowers	Petroleum ether	Streptozotocin/21 days of oral administration of extract significantly reduced the blood glucose, serum cholesterol and triglycerids levels. At the same time the high density lipoprotein level was found to be improved ($P<0.01$).	Iridoids, flavonoids, naphthoquinones, and volatile constituent.	Enhance insulin activation.	[56]
40		Whole plant	Methanol	Streptozotocin/ Significant decrease in blood glucose and glycosylated hemoglobin with a significant increase in plasma insulin level, body weight and food intake. Furthermore γ-sitosterol showed anti-hyperlipidemic activity as evidenced by significant decrease in serum total cholesterol, triglycerides and very low density lipoprotein-cholesterol levels coupled with elevation of high density lipoprotein-cholesterol levels. A significant decrease in the alanine aminotransaminase, aspartate aminotransaminase, alkaline phosphatase and acid phosphatase in γ-sitosterol treated rats when compared to diabetic control rats indicated its protective role against liver damage.	Glycosides, lippiflorin A and B, nodiflorin A and B, alkaloids, essential oil, resin, stigmasterol, beta-sitosterol, sugars, mono and diflavone sulphates of neptin, jaceosidin, hispidulin and 6-hyfroxy- luteolin.	Regeneration of β-cells.	[57]

41		Leaves	Aqueous Methanol (90%)	Alloxan/Significant (P<0.05, P<0.001) dose related reduction in blood glucose concentration when compared to glibenclamide.	Glycosides, flavonoids, proteins , resins, oils, steroids , terpenoids , alkaloids tannins and saponins.	Immunostimulatory effect and protect the pathological damages secondary to the diabetic complications. The antidiabetic activity is evidently due to flavonoid content of the plant.	[58]
42		Aerial part	Aqueous	Alloxan/Significant effect antidiabetic and antihyperlipidemic (dose-dependent effect). A decrease in blood glucose by 50% for the dose 100 mg/kg and more than 60% for doses 200 and 300 mg/kg twice daily for 2 weeks showed the best decrease in the blood glucose level comparable to the effects of glibenclamide, as well as a significant lowering of total lipids, triglycerides, and total cholesterol levels in treated animals, compared with diabetic controls group (p<0.001), have been observed.	5-O-caffeoylquinic, apigenin 6,8 di-C-glucoside, ballotetroside, verbascoside-pentoside, verbascoside-pentoside, alyssonoside, luteolin O-glucuronide , apigenin O-glucoside, crysoeriol O-glucuronide, ladanein, flavonoids and cinnamic acid.	Stimulation of insulin secretion from β cells of islets by inhibition of insulin degradation processes.	[59]
43		Leaves	Ethanol	Alloxan/Significant reduction in fasting blood glucose (P<0.001) in acute and prolonged treatment (2 weeks). The activities of extract more than the reference drug glibenclamide. The extract also significantly reduced the levels of serum, total cholesterol, LDL, VLDL, and triglycerides, at the same time increase in HDL levels.	Terpenes, saponins, tannins and alkaloids.	Hypoglycaemic action by potentiating the insulin effect, either by stimulating the pancreatic secretion of insulin from the cells of islets langerhans or its release from bound insulin.	[60]
44		Whole plant	Methanol	Streptozotocin/Significant decrease in blood glucose, serum urea and serum creatinine and increases in body weight insulin and protein level and total hemoglobin level. Significantly decrease the glucose -6 phosphates, fructose-1, 6- bi-phosphates. Histology of diabetic rated trated with the plant extract showed the pancreatic β cell regeneration.	Terpenes, steroids, polyphenols, glycosides, flavanoids, carbohydrates and proteins.	Stimulates insulin secretion from the remnant β-cells or from regenerated β-cells	[61, 62]
45		root	Aqueous	Streptozotocin/The antidiabetic effects were compared with glibenclamide and the plant extract produced the more significant reduction of blood glucose in the dose 100 and 150 mg/kg then 50 mg/kg. It also produce significant reduction in the levels of serum triglyceride and total cholesterol.	Flavonoids, diosmetin, luteolin and 7-O-β-D-glucosides.	Potentiating the pancreatic secretion of insulin from existing β-cells of islets by increasing the level of insulin.	[63]
46		Whole plant	Ethanol	Streptozotocin/Administration of 5 mg/kg of plant extract, blood glucose levels of the non insulin dependent diabetes mellitus rats showed 62.00 and 76.29% decrease in the blood glucose levels on day 0 and day 30 respectively. Damages caused to the kidney tissue were negligible or not seen. Serum urea and creatinine levels showed 61.49 and 70.96% decrease on day 30. LPP levels of kidney and pancreas showed 70.58 and 77.41% decrease respectively.	-	Regeneration of epithelium, expansion of glomeruli, disappearance of haemorrhages and cytoplasmic debris, decrease in the levels of serum urea and creatinine were the major changes observed besides lowering blood glucose	[64]
47		Oligosaccharides of the plant	Isolation of oligosaccharides	Streptozotocin/Increase body weight, decrease organ related weights of liver and kidney, reduce fasting blood glucose level, and improve oral glucose tolerance in diabetic rats. Moreover, increased glycogen content in liver and skeletal muscle, reduced urinary protein excretion, higher hepatic GCK enzyme activity, lower hepatic PEPCK enzyme activity, enhanced GLP-1 level, decreased glucagon level and alleviated histopathological changes of pancreas occurred in extract treated diabetic rats by comparison with untreated diabetic rats.	Oligosaccharides.	Increase the β-cell mass by inhibiting apoptosis. Stimulates insulin synthesis and release.	[65]

48		Cladodes	80% ethanol	Streptozotocin/Significantly decreased (P<0.05) the fasting levels of blood glucose (BG), total cholesterol (TC), triglycerides (TGs), plasma urea nitrogen (PUN), and malondialdehyde (MDA); and the activity of glucose-6-phosphatase (G-6-Pase). In contrast, it significantly increased (P<0.05) the body weights, hepatic glycogen (HG) levels, high-density lipoprotein cholesterol (HDL-C) levels, and the hepatic superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) activity in diabetic mice.	Polysaccharides, betalains, phenolic compounds, organic acids, lipids, minerals, vitamins, amino acids and taurine.	Overproduction of excessive hepatic glycogenolysis, gluconeogenesisand decreases the utilization of glucose by the tissues.	[66]
49		Whole plant	Chloroform	Streptozotocin/Significant lowering (p<0.05) of the final blood glucose level compared to the pretreatment level. No significant differences in the plasma insulin levels post-treatment compared to the pretreatment levels and significantly increased (p<0.001) the glucose uptake by the rat diaphragm muscle.	Isopimarane-type diterpenes, orthosiphols A-E, monoterpenes, triterpenes, saponins, flavonoids, hexoses, organic acids, rosmarinic acid, chromene, myo-inositolm flavonoids and terpenoids.	Direct insulin-like effect on the utilization of glucose by increasing the membrane transport of glucose in peripheral tissues.	[67]
50		Root	Ethanol and aqueous	Streptozotocin/Significantly (P<0.001) reduced the blood glucose at the dose 250 mg/kg.	Carbohydrates, proteins, aminoacids, saponins, tannins,phenolic compounds, alkaloids and flavonoids.	The mechanism of these hypoglycemic effects of the extracts is not elucidated in this study.	[68]

Table 1: Review of medicinal plants with antidiabetic potential.

diabetes deaths occur in low- and middle-income countries [75]. Anti-diabetic drugs used as mono-therapy or in combination to achieve better glycemic control. Each of the oral antidiabetic agents is however, associated with a number of serious adverse effects [76,77] and none of the antidiabetic drugs could give a long term glycaemic control without cousin the side effects [78]. Plant based drugs have been known to be safe and cheaper and the plant play the major role to manage the diabetes mellitus [79-81]. World health organisation (WHO) has recommended the evaluation of traditional plant treatments for diabetes as they are effective, non-toxic, which less or no side effects and are considered to be a valuable source for the investigation of hypoglycaemic agents [82,83]. According to world ethnobotanical information reports, almost 800 plants possess antidiabetic potential [84]. Several reviews on the plants used in the management of diabetes have been reported in the past [85-92].The current review showed that plants possessed antidiabetic property and may of the study not properly mention the precise mechanism of the plant and the active compound responsible for the antidiabetic effect. This may be explained by the nature of extracts and lack of in vivo methods. Most of the authors explained that the mechanism of the plant extract is the same as that of standard drugs and that the antidiabetic effect is due to the antioxidant property of the plants [18,23,39,47]. Some other authors had mentioned the mechanism of the plant is by increasing the insulin secretion by stimulating the β cell [51-55,62-65]. However the exact mechanism is very challenging to identified and explained in proper manner. Streptozotocin and alloxan induced diabetes model is used as a screening method for anti-diabetic drugs and many other animal models have been developed and described for the screening of anti-diabetic drugs, but none of them is exactly equivalent to human diabetes [93]. Plant products are known to be rich in phenolic compounds, flavonoids, terpenoids, coumarins and other constituents which reduce blood glucose levels [94,95]. In the current review most of the plants have the flavonoid, and terpenoids may be the reason for reducing the blood glucose level in animals. In Africa, hundreds of plants are used traditionally for the management of diabetes mellitus, but only few of the plants have been scientifically validated [96,97]. The variety of phytoconstituent classes and the wide differences in the molecular structure of the isolated compounds suggest the possibility of different mechanisms of action in lowering blood glucose [98]. So, the identification of phytochemical is not only enough, at the same time prove the exact mechanism and clinical trial is essentially need to use the plant drug clinically.

Conclusion

The study found that since the antidiabetic evaluation is done using extracts. It may be difficult to find the exact mechanism responsible for the hypoglycemic effect. Studies are needed to identify the active compound responsible for the hypoglycemic effect. Although numerous medicinal plants have anti diabetic effect, phytochemical and clinical research work on the discovered plant species is yet to be done. Every plant material is not safe, so need to investigate the toxic effect of these plants before consumption. Isolate and test the active components from the potent active antidiabetic plant and there is the essential need for clinical research on the new drug available in the market with less side effects.

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