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Review

Antidiabetic therapeutics from natural source: A systematic review

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ABSTRACT

Diabetes mellitus (DM) is a common metabolic/endocrine disorder throughout the world and cause serious medical problems to human health. Recent drastic changes over human dietary habits and contemporary lifestyle lead to various chronic disorders/diseases particularly metabolic diseases including obesity. Traditional medicinal plants and their active phyto-constituents have been used throughout the world for the therapy of diabetes and associated secondary complications. Among many medications and other alternative medicines, numerous herbs have been well-known to cure and prevent diabetes. Several traditionally important medicinal plants have been investigated for their beneficial use in different types of diabetes and its complications. The effects of these plants may delay the development of diabetic complications and alter the metabolic abnormalities using a variety of cellular and molecular mechanisms. A considerable number of active medicinal plants and their bioactive compounds were subjected to clinical trials and were found effective. Moreover, during the past few years many phyto-constituents responsible for antidiabetic effects have been isolated from plants showed higher potential than synthetic drugs. As a result, recently, considerable scientific attention has been directed towards classification/identification of traditional medicinal plants with antihyperglycemic ability that may be used for daily consumption along with the food. This review paper mainly focuses on natural phytoextracts with their pharmacological mechanism of action and their preclinical experimental model, which attracts the attention of pharmacologist, phytochemist and pharmocognosist for further scientific research towards endocrine metabolic disorder.

1. Introduction

Diabetes mellitus is a complex and a fast growing medical problem throughout the globe, in both developed and developing countries. As per WHO report, diabetes is a multifarious group of disorders that disturbs the metabolism of carbohydrates, fat and protein and results in a shortage or lack of insulin secretion and/or reduced sensitivity of the tissue to insulin. Despite advances in understanding and management of this metabolic disorder, the rate of morbidity and mortality due to this disorder is increasing every year. Approximately 285 million people have been diagnosed with diabetes mellitus worldwide and this figure is expected to double by the year 2030 [1]. The number of diabetes mellitus (DM) cases is rapidly increasing worldwide and its complications are a major cause of disability and hospitalization, posing a significant financial burden.

Various antidiabetic drugs such as biguanides, sulfonylureas, meglitinides, thiazolidinediones, α-glucosidase inhibitors, incretin mimetics, dipeptidyl peptidase-IV (DPP-IV) inhibitors and insulin are currently available to reduce, control and manage diabetes mellitus. Most classes of these pharmaceutical drugs have serious side/adverse effects. For instance, sulfonylurea results in hypoglycaemia, which though usually mild to moderate, can cause mild headache, fatal complication, weight gain [2,3], increase food intake, gastrointestinal disturbances and cardiovascular mortality. Metformin (under class biguanides) leads to transient nausea, anorexia or diarrhoea, abdominal discomfort, lactic acidosis with severe renal impairment and renal hypoperfusion [4,5]. Thiazolidinediones group of drugs also causes gastrointestinal disturbances, weight gain, anaemia, headache, visual disturbances, dizziness, haematuria, impotence, less commonly fatigue,

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Table 1
List of medicinal plants used for diabetes.

Number	Plant name	Part(s) extract	Mechanism of action	Experiment model	Reference
1	*Artemisia afra*	Leaves	Regeneration of pancreatic beta cells, thereby stimulating the release of insulin and alleviating the oxidative stress in the pancreas through its antioxidant nature. Enhanced glucose utilization by significantly reducing blood glucose level in the diabetic rats	Streptozotocin-induced diabetic rats	[24,25]
2	*Albizia odoratissima*	Aerial parts	Methanolic extract has effectively protected the vital organs including pancreas, kidney, liver, heart and spleen, thereby regulating blood glucose concentration. An extract of this plant significantly reduced lipid profile and also prevent the diabetic complications	Alloxan-induced diabetic rats	[26,27]
3	*Acacia nilotica*	Leaves	Extract induces hypoglycemic and anti-platelet aggregation activity in diabetic rats. The aqueous methanolic extract showed an antidiabetic effect and diabetic nephropathy complications due to the presence of active phytocompounds such as tannins and polyphenols	Streptozotocin-induced diabetic rats	[28]
4	*Achyranthes rubrofusca*	Leaves	Significant changes of body weight due to protein metabolism, blood glucose level, and lipid profile. The extract has significantly increased in the pancreatic antioxidant enzymes SOD, CAT and glutathione expression and also histological studies of the pancreas showed better protective nature of islets	Alloxan-induced rats	[29,30]
5	*Alangium salvifolium*	Barks	The extract normalizes the blood serum parameters pertaining to liver function test and also reduces blood glucose. Phytochemical analysis of extract revealed the presence of alkaloids, glycosides, terpenoids, steroids and tannins	Alloxan-induced rats	[31]
6	*Boldoa purpurascens*	Leaves	Ethanol and aqueous extracts of leaves effectively reduces the blood glucose due to presence of D-pinitol and other flavonoids. The antidiabetic property of the extract was compared with standard antidiabetic drug, metformin	Alloxan-induced diabetic rats	[32]
7	*Boerhaavia diffusa*	Leaves/roots	The extract maintained the ionic balance, renal Na+-K+ ATPase activity and also renal antioxidant status (GPx, catalase, SOD and GSH) in diabetic condition. Treatment with the leaf extract resulted in significant reduction in serum and tissue cholesterol, free fatty acids, phospholipids, and triglycerides. In addition, it has significantly altered the insulin, hemoglobin, glycosylated hemoglobin and hepatic enzymes. These alterations were compared with standard antidiabetic drug, glibenclamide	Streptozotocin- and alloxan-induced rats	[33–35]
8	*Boswellia serrata*	Gum and resin	Extracts prevent pancreatic islet destruction and consequent hyperglycemia in a diabetic animal model. Inhibition of the production/action of cytokines [pro-inflammatory cytokines (IL-1A, IL-1B, IL-2, IL-6, IFN-γ, TNF-α) in the blood] related to induction of islet inflammation in an autoimmune process	Streptozotocin-induced diabetic mice	[36]
9	*Bougainvillea spectabilis*	Roots and barks	Aqueous extracts showed significant increase in glucose-6-phosphate dehydrogenase activity and hepatic, skeletal muscle glycogen. In addition, regeneration of insulin-producing cells and corresponding increase in the plasma insulin and c-peptide levels with the treatment of methanolic extracts. D-pinitol (3-O-methyl-chiroinositol), an active principle from this plant, and it is claimed to exert insulin-like effects	Streptozotocin- and alloxan-induced diabetic rats	[37,38]

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Table 1 (*Coninued*)

Number	Plant name	Part(s) extract	Mechanism of action	Experiment model	Reference
10	*Brassica juncea*	Seeds	Ethyl acetate fraction significantly reduced the thiobarbituric acid-reactive substance levels of serum and hepatic and renal mitochondria. It is beneficial in attenuating the oxidative damage involved in diabetes and its complications. Major active flavonoid compounds, isorhamnetin 3,7-di-O-β-d-glucopyranoside (isorhamnetin diglucoside), from mustard leaf effectively reduced oxidative stress during diabetic condition through *in vivo* and *in vitro* studies	Streptozotocin-induced diabetic rats	[39,40]
11	*Bauhinia Variegata*	Whole plant/leaves	Ethanolic extract and its major active constituent roseoside, has enhanced insulin release/concentration through *in vitro* studies. The presence of an insulin-like protein in chloroplasts of plant may indicate its involvement in carbohydrate metabolism during diabetic condition	Streptozotocin- and alloxan-induced diabetic rats	[41,42]
12	*Byrsonima crassifolia*	Fruits and seeds	Extracts from fruits and seeds of *B. crassifolia* increased the levels of SOD, GSH, GSSG and CAT, hepatic glycogen content, glucose-6-phosphatase (G6Pase), plasma insulin and reduced the blood glucose concentration	Streptozotocin-induced diabetic rats	[43]
13	*Coscinium fenestratum*	Stems	Alcoholic extract significantly altered the glycolytic enzymes, gluconeogenic enzyme and various toxicological parameters in treated diabetic rats. In addition, it has a protective action on cellular antioxidant defense against oxidative damage in streptozotocin-nicotinamide induced diabetes. This antidiabetic nature of this plant extract due to its bioactive constituent, berberine	Streptozotocin-induced type 2 diabetic rats	[44,45]
14	*Cistus laurifolius*	Leaves	Ethanolic extract reduced the blood glucose level and inhibit the α-amylase & α-glucosidase. Three known flavonoids (quercetin-3-O-methyl ether, quercetin, genkwanin) were purified from the leaf extract of this plant. These flavonoids were to be potent antidiabetic agent against experimentally induced diabetes and its complications	*In vivo* studies: streptozotocin-induced diabetic rats *in vitro* studies: assays for α-amylase & α-glucosidase inhibitory activity	[46]
15	*Combretum lanceolatum*	Flowers	Crude extract of flowers has antihyperglycemic activity, as well as that quercetin is the major compound in the extract. This activity due to the AMPK activation in the liver by quercetin and also inhibiting hepatic glucose production	Streptozotocin-induced diabetic rats	[47,48]
16	*Cinnamomum zeylanicum*	Whole plant	Cinnamon polyphenols treatments effectively reduced the iNOS, NF-κB expressions and also it can exert the hypoglycemic and hypolipidemic effects through the repairing of pancreatic beta cells in diabetic mice and improving its antioxidative nature	Streptozotocin-induced diabetes	[49]
17	*Dioscorea spp*	Whole plant	Allantoin, an active compound from the extract may improve glucose utilization in skeletal muscle through β-endorphin dependent- and independent-pathways that decrease plasma glucose	Streptozotocin-induced diabetic rats	[50]
18	*Dodonaea viscosa*	Aerial parts	*In vitro* steady state and time resolved studies revealed that extract showed comparable antioxidant ability in steady state and kinetic studies suggesting its potential role in observed antidiabetic and hypolipidaemic activities. The extract and fraction decreased oxidative stress by improving endogenous antioxidant system	Streptozotocin-induced diabetic rats	[51,52]

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Table 1 (*Coninued*)

Number	Plant name	Part(s) extract	Mechanism of action	Experiment model	Reference
19	*Entada phaseoloides*	Seeds	Extract normalizes hyperglycemia, reverses dyslipidemia and tissue steatosis generally associated with diabetes. It was also revealed repressing chronic inflammation response is a possible mechanism contributing to the antidiabetic properties. In addition, it shows anti-inflammatory effect through the alterations of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) and C-reactive protein (CRP) levels and these actions were compared with metformin	High-fat diet and low-dose streptozotocin-induced diabetic rats	[53]
20	*Emblica officinalis*	Fruits	It improves high-density lipoprotein-cholesterol and lowered low-density lipoprotein-cholesterol levels in human patients. The extract also increases in reduced glutathione, glutathione peroxidase, superoxide dismutase, catalase, and decrease LPO level in vital tissues of diabetic rats. A major active component of the fruit of the gooseberry, β-glucogallin was isolated based on the bioactivity	Type 2 diabetic patients and streptozotocin-induced diabetic rats	[54–56]
21	*Ficus amplissima*	Barks	The extract has beneficial effects on blood glucose level and other toxicological parameters. It also normalizes the lipid profile as well as oxidative stress markers. Histological studies showed the regenerative effect of extract on the pancreatic β-cells	Streptozotocin-induced diabetic rats	[57]
22	*Ficus deltoidea*	Fruits	Reduces the blood sugar levels and inhibits the α-glucosidase & α-amylase. Extracts of *F. deltoidea* stimulated insulin secretion and enhanced basal and insulin-mediated glucose uptake into adipocytes cells	Yeast α-glucosidase, rat intestinal α-glucosidase & α-amylase inhibition assay	[58,59]
23	*Gmelina arborea*	Barks	Ethanolic extract increases the blood reduced glutathione levels and increases the free radical scavenger and in the repair of free radical caused biological damage. It increases the plasma insulin level and decreases glucose concentration	Streptozotocin-induced rats	[60]
24	*Gymnema montanum*	Leaves	Its possess the antidiabetic effect by suppressing carbohydrate absorption from the intestine and thereby reducing hyperglycemia	Streptozotocin-induced type 2 diabetic rats	[61]
25	*Gynura procumbens*	Leaves	The extract has exerted its hypoglycemic effect by promoting glucose uptake by the muscles. The bioactive compounds such as chlorogenic acid, rutin, astragalin and kaempferol-3-O-rutinoside were identified in the extract, which is more responsible for antidiabetic properties	Streptozotocin-induced diabetic rats	[62]
26	*Hiptage benghalensis*	Leaves	The methanolic extract effectively regenerate the beta cells of the pancreas and potentiation of insulin secretion from surviving beta cells; the increase in insulin secretion and the consequent decrease in blood glucose level may lead to inhibition of lipid peroxidation and control of lipolytic hormones	Alloxan-induced diabetic rats	[63,64]
27	*Hibiscus sabdariffa*	Whole	The aqueous extract of *H. Sabdariffa*, rich in several polyphenols and it is effectively inhibited α-amylase and α-glucosidase. The antidiabetic and antioxidant properties of this extract due to normalizes the blood glucose level and oxidative markers	Type 2 diabetic rats	[65]
28	*Hyptis suaveolens*	Leaves	It possesses significant antihyperglycemic activity which might be imputed to the stimulating effects on glucose utilization and antioxidant enzyme	Streptozotocin-induced rats	[66,67]

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Table 1 (*Coninued*)

Number	Plant name	Part(s) extract	Mechanism of action	Experiment model	Reference
29	*Kigelia pinnata*	Flower	Flower extract have significant antidiabetic effects and also showed improvement in lipid profile and body weight. New iridoid glucoside and nine known compounds were identified from the twigs of *K. pinnata*. These compounds significantly stimulate GLUT4 translocation to the cell surface from intracellular compartments required for the uptake of glucose in the cell	Streptozotocin-induced diabetic rats	[68]
30	*Lantana aculeata*	Mature roots	Roots of *L. aculeata* possess antidiabetic potential due to high concentration of active compound, oleanolic acid present in the roots	Alloxan-induced diabetic rats	[69,70]
31	*Malva parviflora*	Leaves	Hexane extract has significantly altered the blood sugar level; serum biochemical parameters, hepatic enzymes, thiobarbituric acid-reactive substances, glycosylated hemoglobin, advanced glycation end products, and insulin level in diabetic rats	Streptozotocin-induced diabetic rats	[71]
32	*Murraya koenigii*	Leaves	Leaf extract possesses a potent antihyperglycemic, antioxidant and hypolipidemic effects and these extracts was compared with glibenclamide, a standard diabetic drug, by restoring the pancreatic beta cell function	Streptozotocin-induced diabetic rats	[17,18,22,72]
33	*Mirabilis jalapa*	Roots	Trigonelline is the major bioactive component of *M. jalapa* L and it shows better hyperglycemia, hyperlipidemia, and prevent β cell damage and improve the antioxidant nature of pancreas in diabetic rats	Streptozotocin-induced rats	[73–75]
34	*Mucuna pruriens*	Seeds	Oral administration of seed extract also significantly reduced the weight loss associated with diabetes and reduces the blood glucose concentration. Total phenolic content of extract shows better antioxidant and antidiabetic properties	Streptozotocin- and alloxan-induced diabetic rats	[76,77]
35	*Merremia emarginata*	Whole plant	The methanolic extract shows antidiabetic action through pancreatic β-cells regeneration and increase level of insulin	Streptozotocin-induced diabetic rats	[78]
36	*Nigella sativa*	Whole plant/seed	*N. sativa* and its bioactive compound thymoquinone (TQ) protected and preserved beta cell integrity by decreasing oxidative stress and possess the antidiabetic activity *N. sativa* and TQ in ameliorating inflammation through suppression various inflammatory mediators during diabetes and preserving β cells	Streptozotocin-induced diabetic rats	[79,80]
37	*Olea europea*	Leaves	Polyphenolic components of olive leaves on redox homeostasis that may have a role in the maintenance of β-cell physiology. Extract exhibited significantly lower HbA1c and fasting plasma insulin levels and also improved glucose homeostasis in humans	Streptozotocin-induced diabetes/diabetic patients	[81,82]
38	*Opuntia joconostle*	Whole plant	The frequent consumption of *O. joconostle* by humans in the diet may contribute to prevent and control the complications associated with type 2 diabetes mellitus	Streptozotocin-induced diabetes	[83,84]
39	*Phaleria macrocarpa*	Fruit (Pericarp)	A flavonoid-rich sub-fraction effectively reduces the blood glucose. Extract can attenuate hyperglycemia in both in vitro and *in vivo* conditions by inhibiting carbohydrate-hydrolysing enzymes. LC-MS analyses revealed that mangiferin is one of the active compounds, which possess more antidiabetic nature	Streptozotocin-induced diabetic rats	[85,86]
40	*Phoenix dactylifera*	Fruits	Crude extracts have improved the biochemical results, i.e. the serum glucose level and liver functions as well as lipid profiles. Diosmetin glycosides isolated from the extract shows antidiabetic and antioxidant nature	Alloxan-induced diabetic rats	[87]

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Table 1 (*Coninued*)

Number	Plant name	Part(s) extract	Mechanism of action	Experiment model	Reference
41	*Piper longum*	Roots	The plant extract is capable of managing hyperglycemia and complications of diabetes in streptozotocin-induced diabetic rats. Piperine, a bioactive compound isolated from the extract shows better antidiabetic and antioxidant nature through various protective nature of pancreatic beta cells	Streptozotocin-induced diabetic rats	[88,89]
42	*Psidium guajava*	Leaves	Inhibits the activity of alpha-glucosidase and stimulated glucose metabolic enzymes in liver tissue. Treatment with freshly prepared leaf extracts significantly reduced blood glucose and lipid profile levels. Extract protected pancreatic tissues, including islet β-cells, against lipid peroxidation and DNA strand breaks induced by diabetogen, and increases insulin secretion. In addition, it inhibited pancreatic nuclear factor-kappa B protein expression	Alloxan-induced diabetic rats	[90,91]
43	*Pongamia pinnata*	Whole parts	Pongamol, Karanjin, active compounds isolated from the fruits of *P. pinnata* and it is increase in glucose uptake in L6 myotubes is the result of an increased translocation of GLUT4 to plasma membrane associated with activation of AMPK pathway, in a PI-3-K/AKT-independent manner	Streptozotocin- and alloxan-induced diabetic rats	[92–94]
44	*Parquetina nigrescens*	Whole plants	Decreases the blood glucose due to increased level of insulin and lowering lipogenesis	Alloxan-induced diabetic rats	[95]
45	*Potentilla discolor bunge*	Whole plants	Antidiabetic and hypolipidemic properties of extracts through strong antioxidant nature and a protective action on pancreatic beta cells	Streptozotocin-induced diabetic rats	[96]
46	*Ricinus communis*	Leaves	The extract has a significant antidiabetic effect and this effect may be due to the presence of saponins, flavonoids, and other constituents present in the leaves. In addition, it has a significant effect on liver and kidney function	Streptozotocin-induced diabetic rats	[97]
47	*Salvia miltiorrhiza*	Roots and rhizome	The total polyphenolic acids fraction could ameliorate hyperglycemia, hyperlipemia and improve insulin resistance in diabetic rats. Salvianolic acid A (SalA) is one of the active compounds of *S. miltiorrhiza* and its shows suppressive effect on oxidative stress and AGEs-induced endothelial dysfunction	Streptozotocin-induced diabetic rats	[98,99]
48	*Sphaeranthus indicus*	Flowers	Decreases the blood glucose level and improves the glucose metabolism in type 2 diabetes due to changes of liver glycogen and insulin level	Streptozotocin- and alloxan-induced diabetic rats	[100,101]
49	*Selaginella tamariscina*	Whole plant	It shows the antidiabetic nature due to increase the level of insulin. Extract and total flavonoids show significant antioxidant and antihyperlipidaemic activity, which finally elevated the insulin sensitivity of the liver	Streptozotocin-induced diabetic rats	[102,103]
50	*Sida cordifolia*	Aerial parts	Improve the antidiabetic nature due to reduce the serum glucose level, insulin and cholesterol	Streptozotocin-induced diabetic rats	[104]
51	*Solanum surattense*	Leaves	Improve the plasma insulin level and reduce the blood glucose concentration. β-sitosterol, a phytosterol from *S. surattense*, showing antioxidant property in diabetes-induced oxidative damage. It also decreases glycated hemoglobin, serum glucose, and nitric oxide, with concomitant increases in serum insulin levels	Streptozotocin-induced diabetic rats	[105,106]
52	*Solanum xanthocarpum*	Leaves	The results indicate that extracts effectively reduce the blood glucose level and oxidative stress markers. Its contain various chlorophyll, carotenoids, total sugar, protein, amino acid and mineral contents and it is helpful for treatment of diabetes	Alloxan-induced diabetic rats	[107]

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Table 1 (*Coninued*)

Number	Plant name	Part(s) extract	Mechanism of action	Experiment model	Reference
53	*Sansevieria roxburghiana*	Whole plant	Potential antidiabetic action is plausible due to modulation of endogenous antioxidant status and increase the level of insulin	Streptozotocin-induced diabetic rats	[108]
54	*Sapindus trifoliatus*	Fruits	The extract has insulin-like activity and the antihyperglycemic effect of the extract due to an increase in peripheral glucose consumption as well as protection against oxidative damage	Alloxan-induced diabetic rats	[109]
55	*Scoparia dulcis*	Whole plant	Crude extracts significantly improve the level of blood glucose and antioxidant nature. Scoparic acid D, a diterpenoid isolated from the extract of *S. dulcis* and its stimulate the insulin secretion from isolated islets, indicating its insulin secretagogue activity. Further, it is protected diabetogen mediated cytotoxicity and nitric oxide (NO) production in RINm5F cells	Streptozotocin- and alloxan-induced diabetic animal	[110,111]
56	*Syzygium cordatum*	Leaves	Antidiabetic nature of this plant extract due to decrease the blood glucose level and insulin concentration. Oleanolic acid and ursolic acid were isolated from the extract and its treatment lowered the blood glucose with concomitant restoration of glycogen. It is suggested that oleanolic acid may have a role in improving type 2 diabetes	Streptozotocin-induced diabetic rats	[112,113]
57	*Terminalia bellerica*	Fruits	Extracts/phytocompounds might have augmented the secretion of insulin by the modulation of cAMP and intracellular calcium levels in the β cells of the pancreas. In addition, it normalizes the altered biochemical parameters in experimental diabetic rat models	Streptozotocin-induced diabetic rats	[114]
58	*Terminalia chebula*	Fruits	Improves the insulin secretion from the pancreatic islets as well as glucose metabolism and reduces the blood glucose. In addition, the extract significantly improved the antioxidant nature due to increase level of enzymatic antioxidants	Streptozotocin-induced diabetic rats	[115]
59	*Teucrium orientale*	Stems, leaves and flowers	The effect of extracts on antioxidant enzyme activity due to the high contents of flavonoids and polyphenol components, which were involved in the healing process of free radical-mediated diseases, including diabetes and its complications	Streptozotocin-induced diabetic rats	[116]
60	*Zizyphus spina-christi*	Leaves	Improves glucose utilization in diabetic rats by increasing insulin secretion due to both saponin and polyphenols content and controlling hyperglycemia through attenuation of meal-derived glucose absorption that might be attributed to the total polyphenols	Streptozotocin-induced diabetic rats	[117]

SOD: superoxide dismutase; GSH/GSSH: glutathione: CAT: catalase; LPO: lipid peroxidation; GLUT4: glucose transporter type 4; AMPK: 5' AMP-activated protein kinase; AGEs: advanced glycation endproducts; cAMP: cyclic adenosine monophosphate.

insomnia, vertigo, hypoglycaemia and proteinuria [6,7]. These scenarios drive researchers in search of a new class of therapeutic antidiabetic compounds that is essential to overcome diabetic problems including various secondary complications [8].

In spite of prevention and management of diabetes, identification of active compounds with no/minimal adverse effect is still a major challenge to the biomedical and scientific community. Researchers utilize various animal models, especially murine models [9,10] to understand regulatory as well as metabolic pathways, for genomic studies on target genes for obesity, diabetes and insulin resistance and for discovery of novel therapeutic agents. They were also used for subsequent screening test on efficacy and toxicity of novel compounds/candidates in order to minimize adverse effects [11] in the future translational studies.

In this review article, we discussed the available experimental model found to possess potential antidiabetic therapeutics from natural source and enlisted various important medicinal plants for diabetic management and treatment based on scientific evidences that will enrich researchers' knowledge on natural sources of diabetic drugs and existing systemic exploration on its mechanism of action against diabetes.

2. Importance of natural products for diabetes treatment

Herbal medicines have long been used effectively in treating diseases/disorders in Asian communities and throughout the world. The mechanism of most of the herbs used has not been scientifically determined. Many traditional plants and their derived

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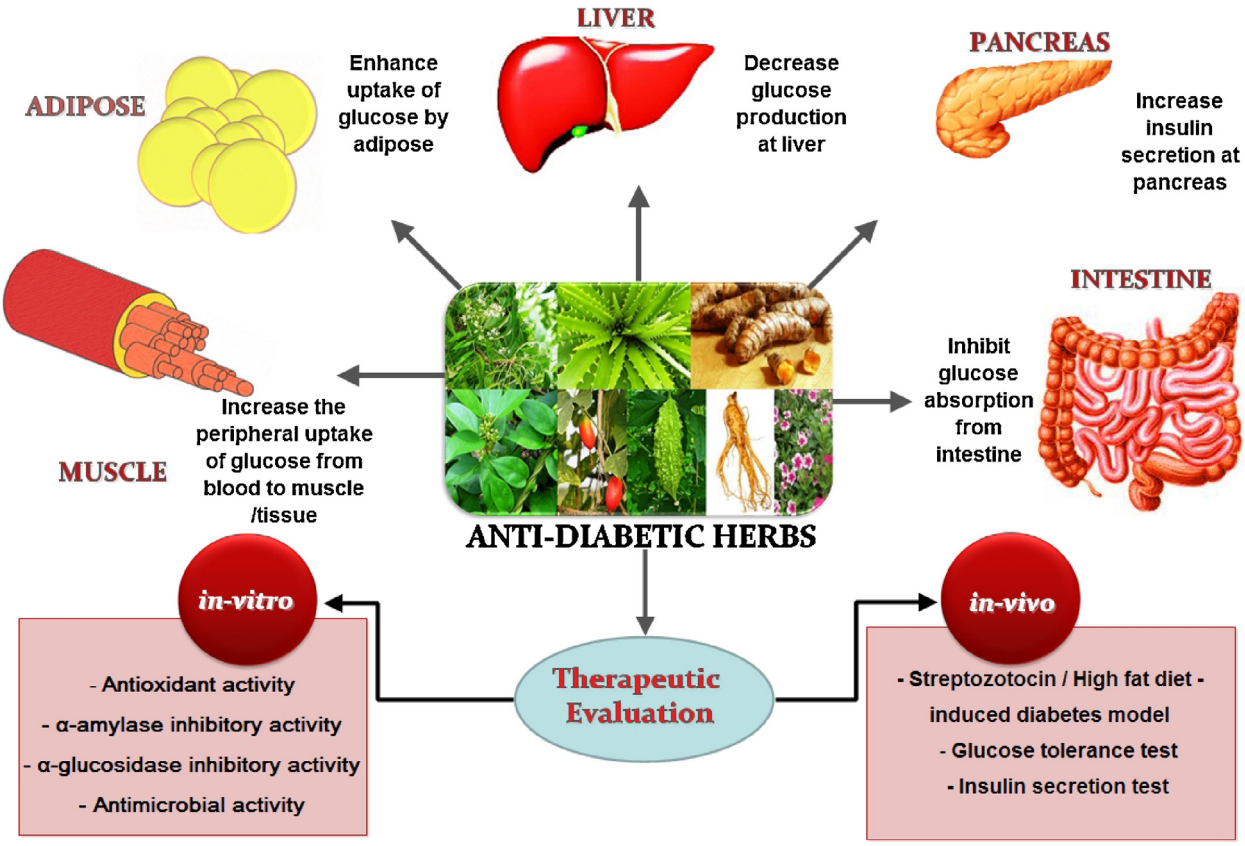

Fig. 1. Antidiabetic herbs – various mechanisms of actions and persisting models of its therapeutic evaluation.

bioactive compounds are used for treatments of diabetes through various mechanisms of actions (Fig. 1). But most of the scientific evidence for their beneficial effects is anecdotal [12]. Traditional antidiabetic plants might provide new oral hypoglycemic lead compounds, which can counter the high cost and poor availability of the current medicines/present day drugs for many rural populations particularly in developing countries. However, detailed studies on the efficacy, mechanism of action and safety of phytoextracts are needed for further translational investigations.

The World Health Organization Expert Committee on diabetes recommended that traditional medicinal plants be further investigated as they are frequently considered to be free from toxic and side effects [13]. Therefore, search for safe and more effective bioactive agents has continued to be an important biomedical drug development research. The ethnobotanical information reports state that about 800 plants and their active extracts may possess antidiabetic potential [14]. Recently, the medicinal values of various plants extracts and their bioactive compounds have been studied by numerous biomedical scientists in the field of diabetic research [8,15–22].

Various pharmacological studies have emphasized the potential health-promoting and disease-preventing effects of fruits and vegetables in the regular diet. Fruits and vegetables contain a multitude of flavonoids and related phenolic compounds that also act as natural antioxidants, hence, natural antioxidants showed very significant antidiabetic potential against various pharmacological experimental systems [21]. Recently, spices and other natural products have been used in the prevention and treatment of diabetes mellitus and its associated complications. In addition, spices are also considered more natural, economical and safe in the treatment of diabetes mellitus. Control of diabetes by spices is becoming more popular and is more appropriate for use in developing Asian countries. These spices and its derived active compounds may have a direct role in the prevention and control of diabetes. Yeast extract had insulin-potentiating property and this is the first evidence that natural products have insulin-potentiating activity in 1929. Further scientific reports on the several plant species possess antidiabetic properties [23]. In this review manuscript, we have provided the details of antidiabetic medicinal plants and their mechanism of action with specific experimental model (Table 1) for further translational biomedical research.

3. Conclusion

Although, the great strides that have been made in the understanding the pathophysiology of diabetes and management of diabetes, the disease and disease associated complications are increasing. Despite the presence of known antidiabetic medicine on the pharmaceutical market, therapeutic remedies from medicinal plants are used with success to treat this disorder and its ramifications. Medicinal plants derived drugs and herbal preparations are often considered to be less toxic and free from side effects than synthetic ones. Most of the worldwide available medicinal plants, the effective treatment of diabetes with bioactive phytochemicals has not been scientifically validated which may support their substitution for the current therapeutics.

Based on the WHO recommendations, antihyperglycemic agents of natural plant origin used in traditional medicine are important. The attributed antidiabetic potential of herbal plants is due to their ability to restore the function of pancreatic tissues by causing an increase in concentration of insulin. The research for alternate remedies (from the plant kingdom) for diabetes mellitus will continue all over the world as the disease poses many challenges not only to the physician but also to the researcher.

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In conclusion, this review paper has presented a list of antidiabetic plants used in the treatment of diabetes mellitus and their mechanism of action.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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