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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]