



Emerging role of herbal drugs in the management of diabetes mellitus

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Abstract

Diabetic mellitus and associated complications are the foremost reason of morbidity and mortality in word wide. Insulin therapy and oral hypoglycemic agents are currently employed to treat patients with diabetic mellitus, but these agents are considered to be inadequate to control the DM and progression into its complications such as diabetic nephropathy, diabetic retinopathy, diabetic neuropathy etc. Therefore, the role of various herbal preparations and their active phytoconstituents has been shown to treat DM with advantages such as lesser adverse effects, toxic effects, low cost and great potential to treat disorder. In the present status around 400 experimentally established medicinal plants having anti-diabetic property out of which detailed mechanism of anti diabetic is on hand only for about 100. In the present editorial, we have discussed the novel therapeutic role of some important herbal drugs along with active phytoconstituents in preventing the pathogenesis of diabetic mellitus patient.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia which transpires mainly due to lack of insulin secretion from β -cell of pancreas or else by development of insulin resistance due to peripheral load, results alteration in carbohydrate, fat and protein metabolism. The Diabetes Mellitus (DM) can be classified into three types Type 1 Diabetes mellitus/Insulin dependent DM/Juvenile onset DM, Type 2 Diabetes mellitus/Non insulin dependent DM/ Maturity onset DM and Gestational diabetes. Type 1 DM is exemplified by beta-cell obliteration caused by an autoimmune process leading to absolute insulin deficit, whereas type 2 DM is a complex heterogeneous group of metabolic condition characterized by elevated levels of serum glucose resulting from a defect in both insulin secretion and insulin sensitivity. In addition, gestational DM recognized as any degree of glucose intolerance with onset or first recognition during pregnancy. Further, the important symptoms of DM are polyuria, polydipsia, polyphagia, weight loss, blurred vision, slow-healing cuts or infections, persistent itching of the skin etc. If DM remains untreated for a long time, often leads to serious complications, which are further categorized into micro vascular, macro vascular, acute and other complications. In microvascular, the complications are diabetic nephropathy, neuropathy, retinopathy, cardiomyopathy and in macro vascular complications includes coronary artery disease, peripheral vascular disease, cerebrovascular disease and diabetic necrosis. In addition acute complications such as diabetic ketoacidosis, hypoglycemia, diabetic coma and other complications such as depression and hypertension may emerge [1]. Therefore, requires an immediate care and treatment of patients suffering from DM sooner than advancement into its complications. Furthermore, the treatment of diabetes mellitus includes insulin therapy (Short acting insulin therapy (regular insulin), intermediate insulin (insulin zinc and suspension) and long acting insulin therapy (protamin zinc insulin), oral hypoglycemic agents such as sulphonylureas, rapaglinide, nateglinide, biguanides, thiazolidinediones, alpha-glucosidase inhibitors, somatostatin, diazoxide etc [2]. The numbers of pharmacological agents are useful to treat DM but 100% curative effect is not practicable. Therefore, the roles of various herbal drugs and their active constituents are come into existence to treat DM and synergize the effect.

Potential herbal interventions to have ameliorative effect in the progression of Diabetes Mellitus

1. ***Ocimum Sanctum (Tulsi)***: The ethanolic extract of leaves *Ocimum sanctum* increased the secretion of insulin via closing of KATP channels there by depolarizing the membrane and increasing Ca^{2+} which may be exhibited by activation of Adenylate cycle or PI3 pathway. In addition, administration of alcoholic extract of *Ocimum sanctum* leaves showed fall in the level of blood glucose. Moreover, the ethanolic extract of leaf powder of *Ocimum sanctum* increases the level of insulin and enhances glucose tolerance in normal and diabetic rats which subsequently resulted in fall of fasting blood glucose and also improves the lipid profile by lowering the increased levels of total amino acids, total cholesterol, triglycerides, phospholipids and total lipid levels [3].
2. ***Trigonella foenum (Fenugreek/Methi)***: The extract of fenugreek in streptozotocin (STZ)-induced hyperglycemic rats prevented the increased blood glucose level, reduced lipid profile. In addition, fenugreek prevented the increased levels of glucose by stimulating the process of glycolysis and inhibiting gluconeogenesis via stimulating enzymes such as hexokinase and inhibiting enzymes such as glucose 6-phosphatase and fructose 1, 6-biphosphatase and subsequently increasing the secretion of insulin [4].
3. ***Emblica officinalis (Amla)***: The plant extract at the dose of 100mg/kg reduce the blood glucose and subsequently increased insulin levels, which may be due to restoration of beta cell of pancreas. In addition, Amla powder at a dose of 2g or 3g daily for 21 days in diabetic patients decreased glucose level and altered lipid profile by decreasing the levels of low density lipoprotein and subsequently increasing the levels of high density lipoprotein [5].
4. ***Bauhinia variegata (kachnar)***: The oral administration of ethanolic, aqueous and hydro-alcoholic extract of leaves and stem bark of *Bauhinia variegata* reduced the elevated blood glucose level by increasing glucose metabolism at 200 and 400 mg/kg in streptozotocin (STZ) and alloxan-induced diabetic rats. Further, ethanolic extract of plant leaves lowered the blood glucose level and improved lipid profile. Moreover, in vitro study that ethanolic extract of leaves of *Bauhinia variegata* and roseoside (active constituent) increased the release of insulin in beta-cell line [6].
5. ***Camellia sinensis (Tea)***: Tea contains flavonoids mainly catechins which are effective in reducing the blood glucose levels by reducing reactive oxygen species and

cytokine levels results an preservation of pancreatic beta cells. Moreover, there is also increased uptake of glucose i.e. stimulated by insulin and basal membrane. Further, scavenging of reactive oxygen species (ROS) by tea catechins reduces oxidative stress induced β -cell destruction. In addition, lipid peroxidation at its maximum levels causes over production of cholesterol and related products such as triglycerides, VLDL, LDL etc., and causes tissue and organ damage, resulting increased complications of diabetes mellitus. Hence, inhibition of lipid peroxidation by green tea catechins causes decrease in levels of cholesterol and other related products in plasma and improves lipid profile. The inducible nitric oxide synthase (iNOS) causes generation of nitric oxide (NO) within the cell and produces cytokines induced pancreatic β -cell damage, demonstrated that green tea catechins reduced the levels of nitric oxide by inhibiting iNOS gene expression and lead to reduction in level of cytokines. Thus, green tea catechin prevents the diabetes mellitus progression [7].

6. **Allium Cepa (Onion):-** It is most common herb used in the kitchen and traditionally used in the treatment and prevention of many disorders. The phytochemistry of *Allium cepa* revealed that it contains phenolic acids, quercetin, glycosides, flavonol and flavone aglycones. In addition, active constituents such as S-methylcysteine and quercetin have shown to normalize the activities of liver hexokinase. Further, it exhibit anti-diabetic effect by decreasing the lipid profile and thereby inhibiting glucose-6-phosphatase and HMG-CoA reductase in alloxan induced diabetic rats [8].
7. **Allium Sativum (Garlic):** It contains carbohydrates, reducing sugars lipids flavonoids, ketones, alkaloids, steroids and triterpenes. The main constituent such as Allicin, a sulphur containing compound of garlic is majorly responsible for anti-diabetic activity. In vitro analysis has shown the stimulatory effect on the secretion of insulin from beta cells isolated from rats, which is due to allicin precursor (S-allyl cysteine sulfoxide) [9].
8. **Azadirachta indica (Neem):** The leaves of the plant extract and seeds oil were administered to both normal and diabetic rats for 4 weeks and the results showed a marked fall in blood glucose levels and were comparable with the

effectiveness of glibenclamide. Further, it was observed that *A. indica* leaf extract significantly reduced the total cholesterol, LDL and VLDL-cholesterol, triglycerides and total lipids of serum in streptozotocin-induced diabetic rats [10].

9. **Eugenia jambolana (Jamun):** The seeds of ethanolic extract of *Eugenia jambolana* at dose of 100 mg/Kg of body weight given to streptozotocin induced diabetic rats showed reduction in the blood glucose level, blood urea and cholesterol. There is also increase in glucose tolerance and levels of total proteins and liver glycogen and also the reduction in activities of glutamate oxaloacetate transaminase and glutamate pyruvate transaminase. Hence, shows hypoglycemic activity [11].
10. **Momordica charantia (bitter melon) /Kerala:** Bitter melon has mostly used for lowering blood glucose levels in patients with diabetes mellitus. Oral administration of the fruit juice or seed powder causes reduction in fasting blood glucose and improves glucose tolerance in normal and diabetic animals and in humans. Further, the fruit of the plant exhibits both insulin secretagogue and insulinomimetic activity. Moreover, antidiabetic effect of plant has shown to decrease insulin resistance and increase of GLUT 4 protein content in the plasma membrane of the muscle [12].

CONCLUSION

All drugs which we have discussed in this editorial column have a noteworthy in their approach to treat diabetes mellitus. These drugs have easy available and accessible to the people who are incapable to procure the costly synthetic drugs. Hence herbal drugs may be an emerging alternative of synthetic drugs to curing diabetes mellitus. The control and maintenance of normal blood sugar level and blood pressure are essential to prevent the progression of DM. Although, number of therapeutic agents includes herbal preparations are used to treat this menacing disorder. The combination of pharmacological agents along with the herbal preparations has been suggested to be a hopeful therapeutic preference to manage patients with DM. Therefore, more focused research on herbal drugs and their phytoconstituents is necessary to explore the detailed mechanism of action at molecular levels, which may be further employed in clinical studies.

REFERENCES

1. Balakumar P, Arora MK, Ganti SS, Reddy J, Singh M. Recent advances in pharmacotherapy for diabetic nephropathy: Current perspectives and future directions. *Pharmacol Res* 2009; 60:24-32.
2. Padwal R, Majumdar SR, Johnson JA, Varney J, McAlister FA. A systematic review of drug therapy to delay or prevent type 2 diabetes. *Diabetes Care* 2005; 28:736-744.
3. Singh H, Sharma M, Kaur J, Bedi PMS, Khan MU. Diverse role of *ocimum sanctum*: A magic remedy of nature. *Indo American J Pharma Res* 2013; 3: 4396:4406.
4. Kaur J, Singh H, Khan MU. Multifarious therapeutic potential of fenugreek: A comprehensive review. *Int J res pharma bio sci* 2011; 2:863-871.
5. Kaur J, Kaur D, Singh H, Khan MU. *Emblica Officinalis*: A meritocratic drug for treating various disorders. *Indo American J Pharma Res* 2013; 3:4477:4496.
6. Kaur J, Singh H, Kaur D, Khan MU. Pharmacological potential of *bauhinia variegata*: A comprehensive review. *World j pharmacy and pharmaceutical sci*, 2014, 3:447-459.
7. Zaveri NT. Green Tea and its polyphenolic catechins: Medicinal uses and non cancer application. *Life Sciences*, 2006; 78:2073-2080.
8. Mathew PT, Augusti KT. Hypoglycaemic effects of onion, *Allium cepa* Linn. on diabetes mellitus - a preliminary report. *Indian J Physiol Pharmacol*, 1975; 19: 213-217.
9. Eidi A, Eidi M, Esmaeili E. Antidiabetic effect of garlic (*Allium sativum* L.) in normal and streptozotocin-induced diabetic rats. *Phytomedicine*, 2006; 13: 624-629.
10. Atawodi SE, Atawodi JC. *Azadirachta indica* (Neem): A plant of multiple biological and pharmacological activities. *Phytochemistry Reviews*, 2009; 8:601-620.
11. Sharma SB, Nasir A, Prabhu KM, Murthy PS. Anti-hyperglycemic effect of the fruit-pulp of *Eugenia jambolana* in experimental diabetes mellitus. *J Ethanopharmacol*, 2004; 104:367-373.
12. Raman A, Lau C. Anti-diabetic properties and phytochemistry of *Momordica charantia* L. (Cucurbitaceae). *Phytomedicine*, 1996; 2:349-362.