

REVIEW ARTICLE

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Natural remedies for diabetes mellitus

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ABSTRACT

Diabetes is a metabolic disorder and a progressive disease that needs proper attention as uncontrolled diabetes can lead to various acute and chronic complications such as retinopathy, nephropathy, neuropathy, gastropathy etc. Pharmacological management of diabetes is costly and has certain side effects. There is a need for the usage of natural diet in the management of diabetes, as it will be cost effective, easy to use and having no side effects. Healthy individuals must also be aware of healthy eating routines. The purpose of this review article is to highlight the importance of dietary management of diabetes. More than 81 plant species have anti-diabetic activities. In this review article, some of the most commonly used natural anti-diabetic sources are mentioned, some of which have already been used for management of diabetes since ancient times.

Key Words: Hyperglycemia, Diet, Spice, Obesity, Insulin, Metabolism.

INTRODUCTION

Diabetes mellitus (DM) being a metabolic disorder is characterized by a defect in insulin secretion, its action, or both (Bastaki, 2005). Deficiency of insulin leads to chronic hyperglycemia (increased fasting and postprandial blood sugar (glucose) levels) as well as protein, fat and carbohydrate metabolism are also disturbed (Joseph and Jini, 2011).

Diabetes mellitus is classified based on its cause and clinical signs and symptoms. In general, diabetes is classified into 4 types, that are type 1 diabetes mellitus or noninsulin dependent diabetes mellitus, type 2 diabetes or insulin dependent diabetes mellitus, gestational diabetes, and other specific types. Non-insulin dependent diabetes mellitus is the major type of diabetes in younger age groups. Though the prevalence of type 1 diabetes is increasing all over the world, yet it accounts for a minority. Children of earlier age groups are more prone to type 1 diabetes mellitus (Piero *et al.*, 2015).

Diabetes is a complex disease that can lead to various complications; it demands a multifarious therapeutic approach. Drug therapy is provided to patients whose cells do not respond to insulin whereas insulin deficiency is managed by insulin injections in patients who show a total lack of insulin (Joseph and Jini, 2011).

TYPES OF DIABETES MELLITUS

Diabetes mellitus has following types:

Type 1 or Insulin Dependent Diabetes Mellitus (IDDM)

Younger people (Children and adolescents) are most vulgar to Type 1 or IDDM also known as ketosis-prone or juvenile onset diabetes. IDDM is characterized by insulin deficiency and patient needs exogenous insulin for survival (Plotnick, 1994). Failure of pancreas to discharge enough insulin for the body requirements to be met is the main cause of type 1 diabetes. Glucose intolerance occurs because of progressive destruction of β -cells, as diabetes is a progressive disease. It takes months or years for enough demolishment of β -cells for the insulin dependent diabetes mellitus to appear. This destruction might be autoimmunemediated (in most cases) or it could be idiopathic destruction (Maahs *et al.*, 2010).

Risk Factors

Only liability to Type 1 diabetes is inherited, not the disease itself. Type-1 Diabetes has a strong genetic factor. The risk of developing type 1 diabetes in children with diabetic father is 4-6%, whereas those with diabetic mother it is 2-3%. If one of the parents is diabetic, then the risk is 5% (Gorrell *et al.*, 2003).

Pathophysiology of IDDM

Insulin secretion is reduced because of the damage to pancreatic β -cells, which could be in the form of autoimmune destruction. In addition, α -cells start performing their functions abnormally as well, which cause increased discharge of glucagon in Type-1 diabetics. Blood glucose level is inversely proportional to glucagon secretion but in such patients, hyperglycemia does not suppress glucagon's secretion (Ozougwu *et al.*, 2013).

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Non-Insulin Dependent Diabetes Mellitus

In type 2 diabetes mellitus, the first abnormality detected is abnormal sensitivity to insulin. Insulin is being produced by the pancreatic cells but their ability to produce high levels of insulin to meet the bodily demands is decreased thus causing insulinopenia, which in turn causes the development of impaired glucose tolerance and eventually the patient has to face diabetes mellitus (DeFronzo, 1992).

Clinical Features

The symptoms of Non-insulin-dependent diabetes mellitus progress slowly with the patient being asymptomatic in the beginning. Patient might face conditions like polyuria and polydipsia. Non-insulin-dependent diabetes mellitus is diagnosed during physical examination of the patient. Major symptoms include lethargy, dizziness, tiredness, leg cramps, mood swings, skin infections, itching, blurred vision and headache (Surya *et al.*, 2014).

Pathophysiology of NIDDM

Type 2 DM is characterized by both improperly functioning β -cells as well as α -cells. Insulin insensitivity is the major factor in type 2 diabetes mellitus. Insulinopenia caused by destruction of β -cells result in reduced transport of glucose into the fat cells, liver and muscle cells. During fasting, breakdown of fat in increased causing hyperglycemia. The hepatic glucose and glucagon levels that increased during fasting are not suppressed with a meal. Patient faces hyperglycemia due to reduced secretion and increased resistance of insulin (Olokoba *et al.*, 2012).

Gestational diabetes

Gestational diabetes mellitus (GDM) being firstly recognized during pregnancy is defined as glucose intolerance of variable severity (Kim *et al.*, 2011). About 5% of pregnant females are affected by gestational diabetes mellitus and its frequency is expected to increase as the obesity increases. In the years following the pregnancy, the affected females are more vulnerable to type-2 diabetes mellitus. In addition, their children are vulnerable of getting obese as well as developing type-2 diabetes mellitus early in their life (Kampmann *et al.*, 2015).

Majority cases of gestational diabetes mellitus can be controlled with lifestyle modifications alone. Insulin is not transferred from pregnant woman to her fetus, thus it is employed as initial line medical care. Both Metformin & Glyburide are considered efficacious and safe, although we have no evidence of safety for their chronic use. According to ACOG, oral agents and insulin have same efficacy, so either can be employed as initial line medical care whereas NICE prefers metformin to insulin therapy (Kelley *et al.*, 2015).

Other types of Diabetes Mellitus

Diabetes can be classified into other types based upon their etiology.

- Maturity onset diabetes in youth is characterized by abnormally functioning β-cells and this defect is genetic.
- Less than 10% are those having pancreatic disorders caused by infections, chemicals or drugs.
- Those having faulty insulin action.
- Those having cystic fibrosis or pancreatitis.
- Those having diseased endocrine gland (Baynest, 2015).

COMPLICATIONS OF DIABETES

In diabetes mellitus, either small blood vessels are damaged (micro-vascular disease) or arteries are damaged (macro-vascular disease). Micro-vascular complications include neuropathy, retinopathy and/or nephropathy. Common macro-vascular complications include cerebrovascular disease and myocardial infarction (Forbes and Cooper, 2013).

Generally, diabetic complications can be classified into 2 groups:

- a) Acute metabolic complications: Short-term complications including ketoacidosis, hyperosmolar nonketonic coma and hypoglycemia.
- b) Late systemic complications: Long lasting complications including retinopathy, diabetic nephropathy, atherosclerosis, diabetic neuropathy, microangiopathy and infections (Ullah *et al.*, 2015).

CURRENT MANAGEMENT OF DIABETES MELLITUS

- Agents like Voglibose, acrabose and miglitol are used to manage post-prandial hyperglycemia. These agents decrease glucose absorption by the cells and thus manage diabetes at digestive level.
- Different therapies used to manage diabetes mellitus do have some limitations, as they are not cost effective and can show certain side effects like liver toxicity, weight gain, gastrointestinal disturbances as well as hypoglycemia.
- Biguanide such as metformin is used to potentiate glucose uptake by peripheral cells. Sulphonylureas like glibenclamide act as insulinotropic and work as secretagogue for pancreatic cells (Joseph and Jini, 2011).

DIETARY MANAGEMENT OF DIABETES MELLITUS

Dietary management of diabetes pursue to attain most favorable blood lipid concentrations, suitable energy for equitable weight, normal growth and development during pregnancy and lactation, to avoid diabetic complications, and for improvement of health by consuming well balanced nutrition (Asif, 2014).

In most developed countries, 4th or 5th leading cause of death is diabetes mellitus which can reach to epidemic proportions in most developing and newly industrialized countries. Due to traditional lifestyle, a very few rural people are affected by type 2 diabetes mellitus (Stevn et al., 2004). To obtain good glycemic control, low intake of calories and weight loss is important. The ideal proportion of carbohydrates, fats, and proteins that should be recommended remains unclear (Ajala et al., 2016). To prevent, manage or lower the rate of development of complications of diabetes, medical nutrition therapy is important (Bantle, 2008). In case of type 1 diabetes mellitus the role of diet is doubled, it helps in maintaining the glucose level in blood almost steady as well as reduces long-term complications. When we talk about the management of diabetes with diet, the principles are same for both type 2 as well as type 1 diabetes mellitus (Bastaki, 2005).

Momordica charantia

Traditionally bitter melon is utilized in the management of diabetic complications. Resistance of insulin at cellular level is the most rudimentary defect in NIDDM patients. This resistance of insulin at cellular level causes hypertriacylglycerolaemia, increased VLDL secretion and hyperinsulinemia (Nerurkar *et al.*, 2008). *Momordica charantia* exert its anti-diabetic effect by improving glucose tolerance and decreasing blood glucose levels. For diabetic patients, obesity is a major issue. *Momordica charantia* checks obesity as well. In addition to increasing insulin sensitivity, *Momordica charantia* also improves the secretion of insulin by improving the condition of damaged β -cells i-e their preservation and protection (Cummings *et al.*, 2004).

Cinnamon (Cinnamomum zeylanicum and C. verum)

Cinnamon belongs to the Lauraceae family. Cinnamon has been used as spice in normal routine as well as medicinally since ancient times (Medagama, 2015). Cinnamon is antiinflammatory, disease lowering compound, lipid lowering, antioxidant, antimicrobial, anti-diabetic, anticancer as well as effective in neurological disorders, like Alzheimer's disease and Parkinson's disease (Rao and Gan, 2014).

Cloves (Eugenia Caryophyllata or Syzygium aromaticum) It belongs to Myrtaceae family. Clove has the potential to control blood glucose level. Clove can also be used to prevent blood clots due to the presence of eugenol in it (Milind and Deepa, 2011). The major phenolic constituents present are caffeic acid, gallic acid, kaempferol, isoquercitrin and ellagic acid. Upon usage of powder of clove buds in rats, it is proved that this powder exhibits many useful actions like hypoglycemic activities, antioxidant activities, anti-hyper-lipidemic and anti-hepatotoxic activities. It slows down digestion of carbohydrates and also checks oxidative stress (Rizvi *et al.*, 2014).

Capsicum annum

It belongs to Solanaceae family. Serrano and Fresno are 2 different varieties of red chili powder having antihypercholesterolemic and antihyperglycemic properties. Therefore, red chili powder can be recommended for use by diabetic patients (Magied *et al.*, 2014).

A factor that is involved in hypoglycemia might be the hindrance of reabsorption of intestinal glucose. Postprandial hyperinsulinemia could be achieved by the regular usage of chili pepper (Fathima, 2015).

Coccinia indica

Coccinia indica belongs to Cucurbitaceae family, which is abundantly grown in India and is being used traditionally for managing diabetes mellitus. In alloxan diabetic rats, *Coccinia indica* has proved to be hypoglycemic as well as hypolipidemic (Manjula and Ragavan, 2007). Safety and effectiveness of various parts of this plant and their derived formulations having anti-diabetic effects have also proven by various clinical trials. *Coccinia indica* also possess antiinflammatory, antipyretic, hepatoprotective, hypolipidemic and analgesic activities (Deokate and Khadabadi, 2011).

Vaccinium myrtillus

A natural source to maintain lower levels of blood sugar is blue berry (D Jini, 2011). Wild berries boost various health conditions, as they are anti-microbial, anti-inflammatory, anti-aging, anti-cancer, as well as anti-diabetic. High contents of phytochemicals like proanthocyanidins, flavonols, anthocyanins and phenolic acids are found in blue berries (Parmar and Rupasinghe, 2013).

Trigonella foenum graecum

It belongs to the family Fabaceae. It can prove beneficial for both type 2 as well as type 1 diabetes mellitus. Anti-diabetic and anti-hyperlipidemic effect of fenugreek is because of diosgenin and saponins. In laboratory animals and human beings, fenugreek can be used as a hypoglycemic herb (Aher *et al.*, 2016).

Anti-diabetic activity of fenugreek seeds could be due to galactomannan-rich soluble fiber fraction. Pancreatic β -cells are directly stimulated by amino acids, thus the presence of amino acid 4-hydroxyisoleucine might be

responsible for the anti-diabetic and insulinotropic properties. Delayed stomachic voidance and inhibition of aldohexose transport even have been postulated as potential mechanisms (Rashmi *et al.*, 2011).

Prunus dulcis

A Seventh Day Adventists study was conducted in which it was noticed that almonds have a potential to lower postprandial blood glucose levels as well as oxidative damage in normal healthy humans. Jenkins *et al.* (2006) also claimed the same effect of almonds. Almond has a sweet and a bitter variety having special dietary values. They are used in cakes and biscuits as floor, as they practically contain no starch. So diabetic patients can use these cakes and biscuits (Jini, 2011).

Ficus religiosa

Common name is Peepal tree. It belongs to the Moraceae family having active constituent like β -sitosterol-D-glucoside, which has blood sugar lowering effect in rabbits that are made diabetic by Alloxan and in pituitary-diabetic rats (Chandrasekar *et al.*, 2010). Nearly every part of this plant has various medicinal uses but we are concerned with hypoglycemic effects of the plant. Bark can be used for the management of diabetes. FRAE additionally showed vital increase in serum insulin and polyose content in skeletal muscles and liver of STZ-evoked diabetic rats whereas a vital depletion within serum triglyceride level and entire cholesterin was seen (Panchawat, 2012).

Emblica officinalis

Amla fruit has various therapeutic applications in heart diseases, hepatic disorders, cancer and diabetes as well as it is an anti-inflammatory agent. It also shows memory effects (Dasaroju and Gottumukkala., 2014). *Emblica officinalis* fruit has anti-diabetic effect in both healthy as well as diabetic individuals. In diabetic rats, oxidative stress was reduced, so was the neuropathic pain. It can enhance oxidative stress and glycemic status in non-insulin dependent diabetic rats. Anti-diabetic property of this fruit has also reported by many articles. The exact mechanism of its hypoglycemic activity is not yet clear (Fatima *et al.*, 2015). Amla fruit has various health benefits. It can be used in conditions like heart diseases, ulcer prevention, cancer, and hepatotoxicity as well as in diabetes (Dasaroju and Gottumukkala, 2014).

Onion (Allium cepa)

Onion being cultivated in India, China and United States, is a part of Amaryllidaceae family. It is used as a spice in home. It contains many essential nutrients and can be used in asthma, cholera, hepatitis and stomach disease (MSH Akash *et al.*, 2014). Its anti-diabetic properties could be due to the active constituent allyl propyl disulfide (Andallu *et*

al., 2001). Utilization of glucose and its cellular uptake in rats, insulin release and action might be enhanced due to onion extract like glibenclamide (Ozougwu, 2011). Due to its anti-hyperglycemic and anti-hyperlipidemic effect, non-insulin dependent diabetic patients can use onions. Onions have various health benefits. It is useful in hypertension, as hypocholesterolemic, hypoglycemic, cardiovascular diseases, as well as anti-carcinogenic (Lee *et al.*, 2013).

Areca catechu

Arecoline is the active constituent having hypoglycemic activity. Subcutaneous administration of alkaloid content of *Areca catechu* can have hypoglycemic activity lasting for 4/6 hours (Patel *et al.*, 2009). It has effective glucose lowering activity in streptozotocin induced diabetic rats (Mondal *et al.*, 2012). *Areca catechu* flowers caused hyperglycemic effect in fasting as well as decreased weight in controlled rats (with diabetes) compared to normal rats (Ghate *et al.*, 2014).

Camellia Sinensis

Green tea shows various health benefits as it is antibacterial, anti-inflammatory, anti-mutagenic, anti-diabetic, antiviral as well as anti-carcinogenic. Its aqueous extract mainly contains catechins like EC, EGC, ECG, EGCG (Rani *et al.*, 2014). By its consumption, blood glucose level was lowered in diabetic mice but it did not affect insulin level in them. If used for long time, not only it enhances insulin sensitivity but it can also prevent insulin resistance issues, anti-hypoglycemia and other metabolic defects in rats fed by fructose (Namita *et al.*, 2012). *Camellia sinensis* enhanced insulin activity in STZ diabetic rats. Experiments proved that its lower doses exhibit insulinotropic effect (Patel *et al.*, 2012).

Phaseolus vulgaris

The exact mechanism of *Phaseolus vulgaris* seeds is still unknown but various authors suggest that it stimulate β -cells of pancreas and hence insulin secretion is increased. Two possible mechanisms have been proposed and both of them focus on the role of α -amylase inhibitors and phytohaemagglutinin inhibitors (Atchibri *et al.*, 2010).

Syzygium cumini

In streptozotocin (STZ) induced diabetic rats, seed extract of *Syzygium cumini* has shown anti-diabetic effect. Blood glucose levels were reduced by the compounds 'Mycaminose' and methanol and ethyl acetate extract was found to reduce the blood glucose level (Kumar *et al.*, 2014).

CONCLUSION

It was concluded that by the usage of natural diet, one could keep his blood glucose levels steady. It has been concluded that the above-mentioned natural remedies can be used for the management of diabetes. Natural plants and their extracts have effective hypoglycemic activity. Further research work is required on this aspect of diabetic management because natural diabetic management is convenient as well as more effective than using medicines.

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Rehan Tariq is a fourth year Pharm. D student in Faculty of Pharmacy, University of Central Punjab, Lahore, Pakistan. He has keen interest in research topics related to community health issues and is actively involved in various Public Health Awareness Campaigns being conducted through platform of different NGOs.

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