

## Alternative Therapies of Significance in the Treatment of Diabetes Mellitus: Review Article

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**Abstract:** *Diabetes mellitus (DM) is the most widespread endocrine disorder and by the year 2015, it is projected that more than 200 million people globally will have DM and 300 million will consequently have the disease by 2025. The aim of this review is to summarize and discuss the alternative therapies for controlling diabetes. DM is a chronic and most common metabolic disorder consequential from a defect in insulin action, insulin secretion or both. There are a lot of factors can increase the risk of having type 2DM development, such as obesity, race, family history, ageing, polycystic ovarian syndrome. The most common consensus on medication of type 2 diabetes is that lifestyle management is at the key of therapy options. In addition to weight control, exercise and medical nutrition treatment, oral glucose-lowering agents and insulin injections are the conventional therapies.*

**Keywords:** *Alternative therapies, Diabetes mellitus, lifestyle management, Oral glucose-lowering agents.*

### Introduction

Diabetes mellitus (DM) is a chronic and most common metabolic disorder consequential from a defect in insulin action, insulin secretion or both. The deficiency of insulin leads to chronic hyperglycaemia with carbohydrate disturbances, fat and protein metabolism. DM is the most widespread endocrine disorder and by the year 2015, it is projected that more than 200 million people globally will have DM and 300 million will consequently have the disease by 2025. Due to the disease progresses tissue or vascular injury ensues leading to severe diabetic complications for example neuropathy, retinopathy, cardiovascular, nephropathy complications and ulceration. Therefore, DM covers a wide variety of heterogeneous diseases. DM can be categorized into two major types: type 1 and type 2 DM. Drugs are used mainly to save life and meliorate the symptoms. Secondary aims are to decrease or prevent long-term diabetic complications and, by reducing a variety of risk factors, so as to enhance longevity. Insulin injection therapy is the mainstay for patients who suffer from type 1 DM whereas lifestyle and diet adjustments are considered the keystone for the management and treatment of type 2 DM. Insulin is also vital in type 2 DM particularly when blood glucose

concentrations is difficult be controlled via weight loss, exercise, diet and oral medications. Oral hypoglycaemic drugs are also of use in the treatment of type 2 DM. Oral hypoglycaemic drugs such as *biguanides, sulphonylureas, meglitinide analogues, alpha glucosidase inhibitors, and thiazolidinedione* are also useful. The main goal of these agents is to correct the primary metabolic disorder, for instance inadequate insulin secretion and insulin resistance. However, these agents should be given in combination with a suitable diet and lifestyle changes. Lifestyle and diet therapeutics strategies are to diminish body weight, improve blood glucose levels management and decrease the risk of cardiovascular complications, which account for 70% to 80% of deaths among patients with DM. Diabetes, can be well controlled either by diet alone and exercise, or diet with medicinal plants or oral hypoglycaemic drugs or insulin replacement. The major side effects of DM are increases of body weight and hypoglycaemia with sulfonylureas, gastrointestinal (GIT) disorders with metformin, weight gain, GIT disorders and liver fatty changes with thiazolidinediones, GIT disorders, weight gain and hypersensitivity reactions toward meglitinides and flatulence, diarrhoea and abdominal bloating with alpha-glucosidase inhibitors factors.

### Risk factors

There are a numerous factors that increase the risk of T2DM development, some of which include: ethnicity, weight gain (Obesity), low birth weight, family history, Over aging, polycystic ovarian syndrome, physical immobility, high energy-dense, high-fat diet, low-fiber diet, urbanization, symptoms of insulin resistance, for instance acanthosis nigricans, cardiovascular disease (hypertension), impaired glucose regulation and gestational DM (GDM).

### Require and capacity of alternative medicine

Despite of the type of diabetes, DM patients are needed to control their blood glucose levels with prescription and/or by adhering to dietary plan and exercise program. As a result of modernization of lifestyle, type 2 DM is becoming a main health problem both in developing and under developing countries. Patient with type 2 DM are frequently located on a restricted

diet program and are recommended to exercise which aimed to control weight gain. If exercise and diet fail to control blood glucose levels, pharmacological drugs are then prescribed (Khosla, Gupta, & Nagpal, 1995). These pharmacological drugs have their own disadvantage ranging from development of resistance and unfavorable effects to lack of responsiveness in a wide segment of patient population. Additionally, none of the glucose lowering drugs sufficiently control the hyperlipidemia that commonly met with the DM (Zia, Hasnain, & Hasan, 2001). An inadequacy of presently available oral antidiabetic drugs either in terms of efficiency/safety together with the emergence of the disease into worldwide epidemic have encouraged alternative medicine that can control DM more efficiently and safely.

### **Alternative Treatments for Type 2 Diabetes**

#### **Conventional Therapies**

The common consensus on medication of type 2 diabetes is that lifestyle management is at the key of therapy options. In addition to weight control, exercise and medical nutrition treatment, oral glucose-lowering agents and insulin injections are the conventional therapies. While the most important pathological changes during the development of diabetes include three key organs for example, liver, pancreatic islets, and skeletal muscle, approximately all anti-diabetic agents are aimed at these organs. Pharmacological treatment is prescribed if fasting glucose concentration exceeds 140 mg/dL, the postprandial glucose concentration exceeds 160 mg/dL or HbA1c exceeds 8.0 percent (Clark, 1998).

#### **Pharmacological Treatment**

##### **Glucose lowering drugs**

There are five categories of oral drugs approved for the treatment of type 2 diabetes. With conventional standard, oral therapy is approved in any patient who suffers from type 2 diabetes if the exercise and diet fail to accomplish acceptable glycemic control (Clark, 1998). Although the initial responses may possibly good, oral hypoglycemic drugs may possibly lose their efficiency in a significant proportion of patients. The drug groups include biguanides, sulfonylureas, alpha-glucosidase inhibitors, meglitinide and thiazolidinediones.

Sulfonylureas are including both first generation of antidiabetic drugs such as tolbutamide and second generation such as glyburide. Sulfonylureas activate the pancreatic beta-cells and increases secretion of insulin. A considerable side effect of these drugs is hypoglycemia. Sulfonylurea treatment is also frequently associated with weight gain due to hyperinsulinemia (Goksel et al., 1998). hyperinsulinemia is implicated to be as a cause of secondary drug failure (Borissova et al., 1991).

### **Complementary and Alternative Medicine Approach**

Complementary and alternative therapies are the treatments that neither extensively taught in medical faculties nor commonly practiced in hospitals. The use of complementary and alternative medicine (CAM) in the worldwide is increasing. In 1997, more than 42% Americans used CAM therapy. Total visit of DM patients to complementary practitioners (629 million) exceed total visit to US primary care physicians (386 million) (Eisenberg et al., 1998). In Canada, a modern epidemiological survey reported that 75% people with DM used nonprescribed supplements (for example medicinal plants, vitamin, mineral, or others) and alternative medications (Ryan, Pick, & Marceau, 2001). Overall research point out that the majority of people who use CAM therapies do so additionally to, rather than in place of conventional medical treatment (Astin, 1998; Ryan et al., 2001). Although some of them do not receive any simultaneous conventional medical care (Eisenberg et al., 1993). CAM for DM has become gradually accepted in last several decades. Alternative therapies together with antidiabetic activity have been studied relatively and predominantly in India. Perfect therapies should have a similar degree of efficiency without adverse effects. The mode of action of some CAM agents used for reducing the blood glucose is presented.

#### **Medicinal herbs**

There are more than 800 medicinal plants which are found to have antidiabetic beneficial (Eddouks & Maghrani, 2004). The surveys of ethnopharmacology indicated that more than 1200 medicinal plants are used in herbal medicine for their association with hypoglycemic activity (Kesari, Kesari, Singh, Gupta, & Watal, 2007). The indigenous diet might not be valuable in lowering the blood glucose to the same extent like insulin and other hypoglycemic drugs do, however it has some other effects, which may be functional for the management of the diabetes and its complications (Pandey, Tripathi, Pandey, Srivatava, & Goswami, 2011). In diabetes, a number of herbal alternatives are confirmed to give symptomatic relief and help in the prevention of the secondary complication of the disease. Some herbs have also been proven to help in regeneration of  $\beta$ -cells and in overcoming resistance. In addition to maintaining normal blood sugar level, some herbs are also reported to possess antioxidant activity and cholesterol lowering action. The management of type 2 diabetes mellitus is possible with drug that can lower the blood sugar level in one hand and restore the liver glycogen level on the other hand. In modern system of medicine, there is no drug, which is reported to possess both of the properties (Chakrabarti et al., 2003). However, the hypoglycemic effect of some herbal extracts have been confirmed in human and animal models of type 2 diabetes and conventional drugs have been derived

from the active molecule of these medicinal plants. Metformin, a less toxic biguanide and potent oral glucose lowering agents, was developed from *Galega officinalis* and used to treat diabetes (Bailey & Day, 1989; Fabricant & Farnsworth, 2001). To the date, over 400 traditional plant treatments for diabetes have been reported (Bailey & Day, 1989) although only a small number of these have received scientific and medicinal evaluation to assess their efficacy. The following is a summary of several of the most studied and commonly used medicinal herbs.

### ***Acacia arabica* (Babhul)**

It is distributed all worldwide particularly India mainly in the wild habitat. The aqueous extract of the plant acts as an antidiabetic agent via acting as secretagogue to enhance insulin release from pancreatic beta cells. It induces hypoglycemia in control experimental rats but not in alloxan-induced rats. 2- 4 g/kg body weight of powdered of *Acacia Arabica* seeds administrated to normal rabbits induced hypoglycemic effect via initiating release of insulin (Wadood, Wadood, & Shah, 1989).

### ***Aloe vera* and *Aloe barbadensis***

Aloe, well known indoor plant, has a long history as a multi-use folk remedy. It can be separated into two vital products: latex and gel. *Aloe vera* gel is the mucilage or leaf pulp while aloe latex, generally referred to as "aloe juice," is a bitter yellow exudate from the pericyclic tubules just beneath the outer skin of the leaves. Aqueous extracts of aloe gum significantly increases glucose tolerance in both diabetic and normal rats (Al-Awadi & Gumaa, 1987). Treatment of *Aloe barbadensis* leaves exudates showed hypoglycemic effect in alloxan-induced diabetic rats. Single and chronic doses of bitter extract of the same plant also demonstrated hypoglycemic effect in diabetic rats. The hypoglycemic action of *Aloe vera* and its bitter principle is may be due to the stimulation of insulin synthesis and/or release from pancreatic beta cells (Ajabnoor, 1990). Moreover, this plant also has anti-inflammatory properties in a dose dependent manner and improves healing of wound in diabetic mice (Davis & Maro, 1989).

***Aegle marmelos***: (Bengal Quince, Bel or Bilva) *Aegle marmelos*, universally known as bael, golden apple, Bengal quince, stone apple, Japanese bitter orange, wood apple, bhel and bili, is a species of tree native to India. It is distributed throughout Southeast Asia as naturalized specie. Administration of aqueous extract of leaves reduces blood sugar, improves digestion and reduces serum urea, cholesterol in alloxan-induced rats when compared to control. In addition of its hypoglycemic activity, this plant extract also prevented blood sugar rises one hour in oral glucose tolerance test.

### ***Allium sativum*: (garlic)**

This is a permanent herb cultivated all over India. Allicin, a sulfur-containing compound is accountable for its pungent odour and it has been made known to have important hypoglycemic activity (Sheela & Augusti, 1992). This effect could be due to increased insulin release from pancreatic beta cells, insulin sparing effect or hepatic metabolism (Patel, Prasad, Kumar, & Hemalatha, 2012). Aqueous extract of garlic (10 ml/kg/day) given orally to sucrose fed rabbits (10 g/kg/day) significantly increased free amino acid content, increased hepatic glycogen, decreased fasting blood glucose levels, and serum triglyceride concentrations compared to controls (Nasri, 2013).

S-allyl cystein sulfoxide (SACS), the principle of garlic oil and allicin, is a sulfur containing amino acid that controls lipid peroxidation better than insulin and glibenclamide. Thus, it improved diabetic conditions. SACS also stimulated secretion of insulin *in vitro* from rat's isolated normal beta cells (Augusti & Sheela, 1996). Apart from this, *Allium sativum* shows cardioprotective, antimicrobial and anticancer activities.

### ***Allium cepa*: (onion)**

The onion, also known as the bulb onion or common onion, is a vegetable and is the most widely cultivated species of the genus *Allium*. Various ether soluble extracts as well as insoluble fractions of dried onion powder reveals anti hyperglycemic activity in diabetic rabbits. *Allium cepa* is also acknowledged to have hypolipidaemic and antioxidant activity. The treatment of a sulfur containing amino acid from *Allium cepa* such as S-methyl cysteine sulphoxide (SMCS) to alloxan induced diabetic rats was significantly controlled blood glucose levels. In addition, it regulated serum lipids and tissues profiles, as well as it normalized the activities of liver glucose 6-phosphatase, hexokinase and hydroxymethylglutary Co A reductase (Kumari, Mathew, & Augusti, 1995; Roman-Ramos, Flores-Saenz, & Alarcon-Aguilar, 1995) If diabetic patients were given single oral dose of 50 g of onion juice, it significantly controlled postprandial glucose levels (Mathew & Augusti, 1975).

### ***Caesalpinia bonducella***

*Caesalpinia bonducella* is broadly distributed all over the coastal region of India and used racially by the ethnic groups of India for management of blood sugar. Both the ethanolic and aqueous extracts showed strong hypoglycemic activity in chronic type II diabetic patients. These extracts also found to increased glycogenesis thus increasing liver glycogen deposition (Chakrabarti et al., 2003). Two fractions BM 169 and BM 170 B may increase insulin secretion from isolated islets. Both ethanolic and aqueous extracts of *Caesalpinia bonducella* seeds revealed hypolipidemic

and antihyperglycemic activities in STZ-induced diabetic rats (Sharma, Dwivedi, & Swarup, 1997). The antihyperglycemic effect of the seed extracts could be due to the blocking of glucose absorption. The drug has the potential to act as antidiabetic in addition to antihyperlipidemic (Kannur, Hukkeri, & Akki, 2006).

### ***Coccinia indica***

Its native range extends from Africa to Asia, including India, Cambodia, the Philippines, China, Malaysia, Indonesia, Thailand, Myanmar, eastern Vietnam, the Northern Territories, Papua New Guinea, and Australia. Its documented introduced range includes Fiji, Federated States of Micronesia, Guam, Saipan, Hawaii, Samoa, the Marshall Islands, Tonga, and Vanuatu. *The administration of Coccinia indica* (*C. indica*) dried extracts (500 mg/kg body weight) to diabetic patients for 6 weeks restored the activities of lipoprotein lipase that was reduced and lactate dehydrogenase and glucose-6-phosphatase, which were raised in untreated diabetic patients (Kamble, Kamlakar, Vaidya, & Bambole, 1998). Oral administration of 500 mg/kg of *C. indica* leaves also found to induce significant hypoglycemia in alloxan-induced diabetic dogs and increased glucose tolerance in normal and diabetic dogs.

### ***Ficus religiosa***

*Ficus religiosa*, commonly known as peepal in India, It has been reported to be used in the traditional medicine of Ayurveda for the medication of diabetes. *F. religiosa* has also been shown to possess a broad spectrum of *in vivo* and *in vitro* pharmacological activities: antidiabetic, anticonvulsant, hypolipidemic, anti-inflammatory, analgesic, antioxidant, antimicrobial, antiviral, antiulcer, antitumor, antianxiety, antiasthmatic, immunomodulatory, estrogenic, anthelmintic, endothelin receptor antagonist, cognitive enhancer, apoptosis inducer, and antihypertensive (Singh, Singh, & Goel, 2011).

The concentrated preparation from the bark is used in treatment of diabetes. The plant is supposed to contain a number of bioactive principles including saponins, tannins, flavonoids, polyphenolic compounds and sterols. Sitosterol-d-glucoside is found to be present in the bark of *Ficus religiosa*. And it is believed to possess hypoglycemic activity in rabbits (Chandrasekar, Bhanumathy, Pawar, & Somasundaram, 2010).

***Eugenia jambolana***: (Indian gooseberry, jamun)

*Capparis deciduas*

*Capparis decidua* is one of the traditional medicinal plants used for a variety of medicinal treatments in Pakistan and India particularly in dry areas. All plant extracts prominently rich in glucosinates and phenolics, and they showed powerful antidiabetic activity. In alloxanized rats, the administration 30% extracts of *Capparis decidua* (*C. decidua*) powder for 3

weeks significantly reduced blood glucose. The extract also significantly decreased alloxan induced lipid peroxidation in kidney, erythrocytes and heart. Moreover, *C. decidua* was also found to change superoxide catalase and dismutase enzyme levels to reduce oxidative stress (Yadav, Sarkar, & Bhatnagar, 1997). *C. decidua* additionally showed hypolipidaemic activity (Chahlia, 2009).

### **Conclusion**

In conclusion, DM is considered one of the most chronic widespread community disease in the world, many factors play role in developing the diseases such as gene, obesity, family history, high fat diet ..etc. There are many alternative complementary treatments has proven to control the disease these alternative medicinal plants include *Ficus religiosa*, *Capparis decidua*, *Caesalpinia bonducella* and others.

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