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Role of antioxidants in diabetes mellitus

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Abstract

Diabetes mellitus (DM), commonly referred to as diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period. Symptoms of high blood sugar include frequent urination, increased thirst and increased hunger. If left untreated, diabetes can cause many complications. Acute complications can include diabetic ketoacidosis, nonketotic hyperosmolar coma, or death serious long-term complications include heart disease, stroke, chronic kidney failure, foot ulcers, and damage to the eyes.

Oxidative stress plays a major role in the pathogenesis and development of complications of both types of DM. However, the exact mechanism by which oxidative stress could contribute to and accelerate the development of complications in diabetic mellitus is only partly known and remains to be clarified. On the one hand, hyperglycemia induces free radicals; on the other hand, it impairs the endogenous antioxidant defense system in patients with diabetes. Endogenous antioxidant defense mechanisms include both enzymatic and non-enzymatic pathways. Their functions in human cells are to counterbalance toxic reactive oxygen species (ROS). Common antioxidants include the vitamins A, C, and E, glutathione (GSH), and the enzymes superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and glutathione reductase (GRx). Many natural antioxidants can be used in lowering blood glucose level. This review describes the importance of natural antioxidants to be included in the diet to reduce the hyperglycemic effect.

Keywords: oxidative stress, reactive oxygen species, antioxidants, diabetic mellitus, free radicals

Introduction

Diabetes is a chronic metabolic disorder with a rapidly increasing prevalence highlighting the importance of continued research and the need for novel methods to both prevent and treat this pandemic. Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced. There are three main types of diabetes mellitus:-

- **Type 1 DM** results from the pancreas's failure to produce enough insulin. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". The cause is unknown.
- **Type 2 DM** begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses a lack of insulin may also develop. This form was previously referred to as "non-insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The most common cause is excessive body weight and not enough exercise.

Gestational diabetes is the third main form and occurs when pregnant women without a previous history of diabetes develop high blood-sugar level.

Effect of Free Radicals in Diabetes Mellitus

Oxidative stress reflects an imbalance between the systemic manifestation of reactive oxygen species and a biological system's ability to readily detoxify the reactive intermediates or to repair the resulting damage. Disturbances in the normal redox state of cells can cause toxic effects through the production of peroxides and free radicals that damage all components of the cell, including proteins, lipids, and DNA. Oxidative stress from oxidative metabolism causes base damage, as well as strand breaks in DNA. Base damage is mostly indirect and caused by reactive oxygen species (ROS) generated, e.g. O_2^- (superoxide radical), OH (hydroxyl radical) and H_2O_2 (hydrogen peroxide). Further, some reactive oxidative species act as cellular messengers in redox signalling. Thus, oxidative stress can cause disruptions in normal mechanisms of cellular signalling.

Role of Antioxidant in Diabetes Mellitus

The inhibition of intracellular free radical formation would provide a therapeutic strategy to prevent oxidative stress and the related diabetic vascular complications. Antioxidants may act at different levels, inhibiting the formation of ROS or scavenge free radicals, or increase the antioxidants defense enzyme capabilities. Supplementation with antioxidants and/or factors essential to nitric oxide (NO) production may potentially improve endothelial dysfunction in T2DM by re-coupling and mitochondrial function, as well as decreasing vascular NAD (P) H oxidase activity. However, in the case of macrovascular/microvascular complications, the antioxidant therapy is beneficial together with blood pressure control, management of dyslipidemia, and optimal glucose concentration. There is large number of natural cellular defense mechanisms as the naturally existing antioxidant components, which neutralizes free radical damage. The enzymatic antioxidant systems, such as copper, zinc, manganese superoxide dismutase, gluthatione peroxidase, gluthathione reductase, and catalase may remove the ROS directly or sequentially, preventing their excessive accumulation and consequent adverse effects. Non-enzymatic antioxidant systems consist of scavenging molecules that are endogenously produced such as glutathione, ubichinol, and uric acid or

derivatives of the diet such as vitamins C and E, carotenoids, lipoic acid, selenium, etc.

Antioxidant Rich Foods

1. Fenugreek

Fenugreek (**Trigonella foenum-graecum**) is an annual plant in the family Fabaceae, with leaves consisting of three small obovate to oblong leaflets. It is cultivated worldwide as a semiarid crop, and its seeds are a common ingredient in dishes.

Chemical Constituents

Fenugreek seeds contain lysine and L- tryptophan rich proteins, mucilaginous fibre and other rare chemical constituents such as saponins, coumarin, fenugreekine, nicotinic acid, sapogenins, phytic acid, scopoletin and trigonelline.

Diabetic Action

Fenugreek seeds are famous for their ability to lower blood sugar in people with diabetes. They contain fiber and help in slowing the digestion process and thus regulate the absorption of carbohydrates and sugar. They also help in improving the way the body uses sugar.

2. Bitter Gourd

Momordica charantia, known as bitter melon, bitter gourd, bitter squash, or balsam-pear. It is a tropical and subtropical vine of the family Cucurbitaceae, widely grown in Asia, Africa, and the Caribbean for its edible fruit. Its many varieties differ substantially in the shape and bitterness of the fruit.

Chemical Constituents

Momordica charantia (Karela) consists the following chemical constituents those are alkaloids-momordicin and charantin. Charine, cryptoxanthin, cucurbitins, cucurbitacins cucurbitanes, cycloartenols, diosgenin, elaeostearic acids, erythrodiol, galacturonic acids, gentisic acid, goyaglycosides, goyasaponins are also present.

Diabetic Action

The fruit contains at least three active substances with anti-diabetic properties, including charantin, which has been confirmed to have a blood glucose-lowering effect, vicine and an insulin-like compound known as polypeptide-p. These substances either work individually or together to help reduce blood sugar levels. It is also known that bitter melon contains a lectin that reduces blood glucose concentrations by acting on peripheral tissues and suppressing appetite - similar to the effects of insulin in the brain. Lectin is thought to be a major factor behind the hypoglycemic effect that develops after eating bitter melon.

3. Spinach

Spinach (Spinacia oleracea) is an edible flowering plant in the family Amaranthaceae native to central and western Asia. Its leaves are eaten as a vegetable.

Chemical Constituents

Spinach leaves contain considerable amount of calcium but unfortunately it cannot be completely digested because spinach also contain oxalates that bind with the calcium. It is rich in iron, potassium and vitamin (A, B2, B9 and C).

Diabetic Action

It contains antioxidant alpha lipoic acid that increase insulin sensitivity and prevent oxidative stress induced changes in diabetic patient.

4. GARLIC

Allium sativum, commonly known as garlic, is a species in the onion genus, Allium.

Chemical Constituents

Alliin, a sulfur-containing compound found in garlic. Fresh or crushed garlic yields the sulfur-containing compounds alliin, ajoene, diallyl polysulfides, vinyldithiins, S-allylcysteine, and enzymes, saponins, flavonoids, and Maillard reaction products, which are not sulfur-containing compounds.

Diabetic Action
It has medicinal properties to prevent or diminish the effects of some of the complications of diabetes. Some complications of diabetes that garlic has an effect on are: Lowers the level of sugar/glucose in the blood, increase the insulin production and due to the formation of a colloidal type suspension in the stomach and intestines when the mucilaginous fiber of garlic is hydrated, therefore affecting gastro-intestinal transit and slowing glucose absorption.

5. Red Kidney Bean

The kidney bean is a variety of the common bean (Phaseolus vulgaris). It is named for its visual resemblance in shape and color to a kidney.

Chemical Constituents
It consist of calcium, sufur containing amino acid,vitamin C,carotenoids.

Diabetic Action
It contains soluble fibers that reduce metabolism of carbohydrates.

6. Amla

Phyllanthusemblica, alsoknownas emblic, emblicmyrobalan, myrobalan, Indian gooseberry, Malacca tree, or amla from Sanskrit amalika is a deciduous tree of the family Phyllanthaceae. It is known for its edible fruit of the same name.

Chemical Constituents
Fruits are reputed to contain high amounts of ascorbic acid (vitamin C), high density of ellagitannins such as emblicanin A (37%), emblicanin B (33%), punigluconin (12%) and pedunculagin (14%). It also contains punicafolin and phyllanemblinin A, phyllanemblin other polyphenols: flavonoids, kaempferol, ellagic acid and gallic acid. Emblicanins are a type of polyphenolic antioxidant found in Amla. Emblicanins one of the best free radical scavenging antioxidant property.

Diabetic Action
Amla is the fruit of the Indian gooseberry tree and is a traditional remedy to control high blood sugar levels. It also contains mineral called chromium which regulates carbohydrate metabolism and helps in making body more responsive to insulin. The tannoids of E. officinalis are potent inhibitors of Aldose Reductase (AR). Emblica and its tannoids counter the polyol pathway-induced oxidative stress as there was a reversal of changes with respect to lipid peroxidation, protein carbonyl content, and activities of antioxidant enzymes. Emblica also preventing aggregation and insolubilization of lens proteins caused by hyperglycemia.

7. Drumstick

Moringa oleifera is the most widely cultivated species of the genus Moringa, which is the only genus in the family Moringaceae.. It is a fast-growing, drought-resistant tree, native to the southern foothills of the Himalayas in northwestern India, and widely cultivated in tropical and subtropical areas.

Chemical Constituents
Main chemical components are pterygospermin, moringine, moringinine spirochin, behenic acid, moringic acid, niazinin A & B, niazimicin, campesterol, stigmasterol, beta sitosterol and amino acids.

Diabetic Action
The aqueous extract of the leaves has some direct effect by increasing the tissue utilization of glucose by inhibiting hepatic gluconeogenesis or absorption of glucose into the muscles and adipose tissues.

8. Guava

Guavas are common tropical fruits cultivated and enjoyed in many tropical and subtropical regions. Psidium guajava (common guava, lemon guava) is a small tree in the Myrtle family (Myrtaceae).

Chemical Constituents
Guava leaves contain both carotenoids and polyphenols like (+) gallocatechin and leucocyanidin. As some of these phytochemicals produce the fruit skin and flesh color, guavas that are red-orange tend to have more polyphenol and carotenoid content than yellow-green ones.

Diabetic Action
Due to the rich fibre content and low glycaemic index, guavas prevent the development of diabetes. While the low glycemic index inhibits a sudden spike in sugar levels, the fibre content ensures the sugar levels are well regulated. Eating guava without its skin can reduce the sugar absorption in your blood.Since guava is rich in dietary fiber helps ease constipation (a common diabetic complaint) and can even lower the chance of developing type two diabetes.

9. Cinnamon

Cinnamon is a spice obtained from the inner bark of several tree species from the genus Cinnamomum. Cinnamon is used in both sweet and savoury foods.

Chemical Constituents
Most species contain significant amounts of cinnamaldehyde, usually as much as 60-75% in the volatile oil. Other bioactive compounds comprise coumarin, styrene, cinnamic acid, cinnamate, linalool, procyanidins and catechins. Eugenol is mostly found in the leaves of cinnamon trees, but usually in high concentrations.

Diabetic Action
Cinnamon can be an effective tool in managing the disease.Cinnamon can help manage disease in two different ways.It can reduce blood pressure and have a positive effect on blood markers for those with Type 2 diabetes and cinnamon can also reduce insulin resistance.Cinnamon works directly on the muscle cells to force them to remove sugar from the bloodstream, where it is converted to energy.

10. Lemon

Lemon (Citruslimonis) is a species of small evergreen tree of family Rutaceae. The tree's ellipsoidal yellow fruit is used for culinary and non-culinary purposes throughout the world, primarily for its juice

Chemical Constituents
The juice of the lemon is about 5% to 6% citric acid, which gives a sour taste. Lemons are a rich source of vitamins C. Lemons contain numerous phytochemicals,including polyphenols, terpenes, and tannins.

Diabetic Action
Lemon juice is another acid that can help lower postprandial blood glucose. A key ingredient found in lemon peels is polyphenols, which plays a major role in minimizing insulin resistance. An increase in insulin resistance leads to less responsiveness from the insulin hormone, resulting in uncontrolled levels of blood sugar. However, polyphenols has the ability to suppress the accumulation of fat in the abdominal area. In addition, the presence of naringin and hesperidin, bioflavonoids, function as dietary antioxidants, which have been shown in mice studies to prevent the progression of hyperglycemia. They do this by increasing hepatic glycolysis and glycogen concentration, while lowering hepatic gluconeogenesis.

11. Holy Basil

Ocimum tenuiflorum, also known as Ocimum sanctum, holy basil, or tulasi or tulsi (also sometimes spelled thulasi), is an aromatic plant in the family Lamiaceae which is native to the Indian subcontinent and widespread as a cultivated plant throughout the Southeast Asian tropics. It is an erect, many-branched subshrub, 30–60 cm (12–24 in) tall with hairy stems and simple phyllotaxic green or purple leaves that are strongly scented.

Chemical Constituents
Some of the main chemical constituents of tulsi are: oleanolic acid, ursolic acid, rosmarinic acid, eugenol, carvacrol, linalool, β-caryophyllene (about8%), β-elemene (11.0%) and germacrene D (about 2%).

Diabetic Action
Ocimum sanctum probably exerted its hypoglycemic effect by increasing the glucose uptake into cell. This increased glucose level in the cell, which then via the hexose monophosphate shunt led to increased production of NADPH + H+ and thus consequently more of reduced glutathione (GSH). Lipid

peroxides in the presence of GSH are converted to alcohol derivatives and not MDA and hence in presence of increased availability of GSH (due to tulsi) MDA levels decreased to a greater extent in test group after 30 days. Ocimum sativum elevated the glutathione and antioxidant enzyme levels (SOD) and decrease lipid peroxidation.

12. Cucumber

Cucumber (Cucumis sativus) is a widely cultivated plant in the gourd family, Cucurbitaceae. It is a creeping vine that bears cucumiform fruits that are used as vegetables. The cucumber is originally from South Asia, but now grows on most continents.

Chemical Constituent

The fruit of the cucumber 95-98% water, a very small amount of protein, fats and carbohydrates. In the remaining 3% is carotene, vitamin PP, vitamin C and B vitamins and trace elements of potassium.

Diabetic Action

The possible mechanism of cucumber extracts bring about their antidiabetic action may be by potentiating the insulin effect of plasma by stimulating insulin release from the remnant pancreatic β-cells or its release from the bound form. It also include the stimulation of peripheral glucose utilization or enhancing glycolytic and glycogenic processes with concomitant decrease in glycogenolysis and gluconeogenesis. The antihyperglycemic activity of cucumber, may also be due to the presence of hypoglycemic saponins, tannins, triterpines, alkaloids, flavonoids.

Conclusion

Hyperglycemia, an inevitable consequence of T2DM, is the source of most of the deleterious effects usually associated with this disease. High blood glucose concentrations promote auto-oxidation of glucose to form free radicals. The generation of free radicals beyond the scavenging abilities of endogenous antioxidant defenses results in macro- and microvascular dysfunction and polyneuropathy.

Antioxidants such as N-acetylcysteine, vitamin C, and α-lipoic acid are effective in reducing diabetic complications, indicating that it may be beneficial either by ingestion of natural antioxidants or through dietary supplementation. As Diabetes mellitus is a common disease facing the people, some of the natural antioxidant to be included in the diet as mentioned in this article. Proper diet and exercise can limit the complications of diabetes mellitus.

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