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Nutraceuticals in the management of diabetes mellitus: A review

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Abstract

Hypoglycemia results from insufficient insulin levels. A variety of nutraceuticals are incorporated into clinical practice to treat diabetes. In the medical framework, hypoglycemic drugs are utilized for treating, managing, and preventing diabetes. These drugs are often derived from different plants. Extracts from these plants provide clinically meaningful benefits for diabetes management. The popularity of nutraceuticals has recently surged on a global scale. Traditional treatment methods involving synthetic drugs frequently fail to adequately fulfill the therapeutic demands required for diabetes care, while herbal remedies can offer superior therapeutic outcomes with reduced side effects. Nutraceuticals encompass a wide range of biological therapies, including botanicals, vitamins, and antioxidants, used in the treatment and prevention of diabetes. This research intends to shed light on and discuss some of the most well-known nutraceuticals used as anti-diabetic treatments.

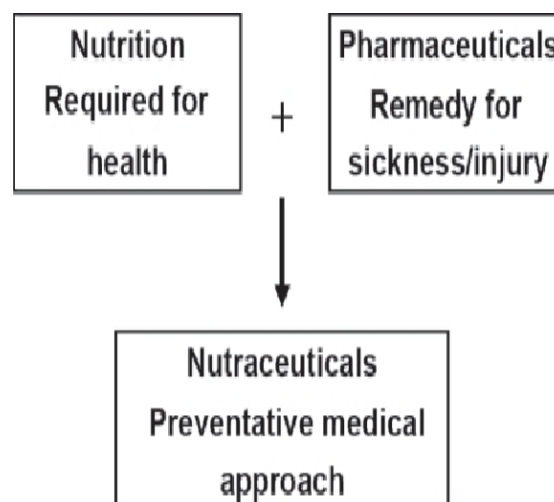
Keywords : Nutraceutical, Diabetes mellitus, Insulin, Herbal drugs

Introduction

Human behavior is unbalanced due to the industrial age, the mechanical lifestyle, the fast pace of life and long working days, a variety of mental health problems and Deprivation of natural resources has led to an increase in the prevalence of metabolic diseases, including diabetes and obesity, malignancy, heart problems and psychological disorders.[1] Among the serious health problems, diabetes mellitus (DM) has gained popularity worldwide. Diabetes mellitus is a metabolic disease characterized by the occurrence of insufficient insulin signaling, abnormal sugar levels and resistance to subclinical inflammatory processes and lipid metabolism, as well as high levels of stress. As reported in the tenth edition of the Atlas of the International Diabetes Federation (IDF), which lists 537 million people. Worldwide, about 10% of people aged 20 to 79 have diabetes. It is expected that up to 79.4 million people in India may be

affected by diabetes mellitus [2] People are increasingly interested in dietary supplements, nutritional treatments, herbal medicine and nutraceutical products due to their frustration with harmful synthetic drugs and the deep concern of how to maintain their well-being with healthier and more natural products .[3] A food that has medicinal and health benefits, such as the treatment and prevention of diseases, is called a nutraceutical. Natural functional foods or bioactive phytochemicals that promote health, fight disease, or act as medicines are also called nutrients.[4] Depending on their purpose, these food products often contain the right amount of vitamins, lipids, proteins, carbohydrates, minerals or other essential components.[5] All over the world, traditional medicinal plants are used to treat various manifestations of diabetes. Because of their effectiveness, lack of adverse side effects, and affordability, herbal medications are often administered.[6] Research on these substances derived from conventional medicinal plants has thus become more crucial.[7]

Concept of nutraceutical



Nutraceuticals

- The term 'nutraceuticals' was first introduced by Stephen De Felice in 1989, the founder and president of the Foundation for Innovation in Medicine based in Cranford, New Jersey. He created this term by merging 'food' and 'pharmaceutical'.
- According to De Felice's definition, a nutraceutical is any food or food component that offers health or medicinal benefits, including the capacity to prevent or manage diseases. [8]
- The ancient Greek physician and inventor HIPPOCRATES famously suggested, 'Let food be your medicine.' This concept emphasizes a preventative approach to health. In the context of European medical law,
- nutraceuticals are considered medicine based on two main points:
 - 1) they can treat, cure, or alleviate medical issues
 - 2) they can be used in humans to restore, repair, alter their physiological functions.[9]

Categories of nutraceuticals and their role in diabetes

Nutraceuticals are non-specific biological therapies used for this promote well-being, prevent malignant processes and control symptoms.

They can be grouped into the following three broad categories [10]

Nutrients: Substances with defined nutritional functions, such as Vitamins, minerals, amino acids and fat.

Medicinal plants: Plants or botanical products in the form of concentrates and extracts.

Dietary supplements: reagents derived from other sources (eg filling of pyruvate, chondroitin sulfate, steroid hormone precursors specific functions such as sports nutrition, weight loss supplements and meal replacements[11]

Fatty acids : These cover all vegetable oils such as olive oil.[12]

Probiotics : Microbes are thought to have many applications in medicine and human health. They are present in dairy products and have antioxidant properties. Its function is to control the development of the intestinal microbiota.[13]

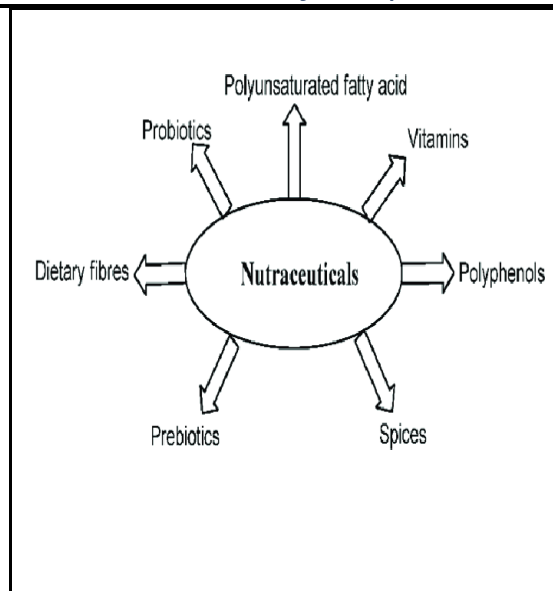


Figure 1:Need for diabetes preventive nutraceutical

Antidiabetic claims of plants

Diabetes mellitus, which affects lipid metabolism and carbohydrates and adversely affects a person's physical and mental health, it is a global threat and a metabolic disease that is growing exponentially in India.[14,17] As our understanding of the diversity of this order increase, so our need for more effective treatment. Traditional herbal medicines are used as a Safe substitute for traditional hypoglycemic drugs, because synthetic treatments, such as insulin in diabetes mellitus induced by diabetes mellitus or non-insulin-dependent diabetes, have a limited role to play and carry a high risk of developing resistance to the medication you would need. an increase in dosage or a change in medication. Due to its abundance of essential plant nutrients [18]

Medicinal herbs with anti-diabetic properties

1. Garlic (*Allium sativum*)



Figure 2: Garlic

The family of plants Liliaceae, which includes Amaryllidaceae, includes the aromatic onion product known as garlic. Its sulfur components give it nutritional and therapeutic properties.[19] Anti-hyperglycemic, antioxidant, hyperlipidemic anti-inflammatory, anti-obesity, anti-atherosclerotic and Anticoagulants are just some of the medicinal effects of garlic. Garlic has an antidiabetic effect

by increasing insulin sensitivity and secretion. In addition, improves glucose absorption by regulation enzymes related to glycolysis and glycogenesis.[20]

2. Aloe vera



Figure 3: Aloe vera

Aloe vera is a plant from the Asphodelaceae family. Xanthorrhoeaceae.[21]

Aloe vera extract contains polysaccharides, anthraquinones, and lectins that have anti-diabetic qualities.[22] The gel formed from the pulp of the consumed leaves may have hypoglycemic properties to stimulate the cells.[23, 24]

Aloe vera has numerous known health benefits, such as immune system modulators, anti-inflammatory, anti-hypoglycemic, anti-hyperlipidemic, and antioxidant properties.[25] Among the potential mechanisms causing the drop in blood sugar are the enhancement of glycemic control, the inhibition of glucose absorption (-glucosidase), the positive modulation of insulin signaling pathways, and the postponement of stomach emptying.[26]

3. Ginger (*Zingiber officinale*)



Figure 4 : Ginger

Zingiber officinale is the name of a flowering plant in the Zingiberaceae family.[27] This plant's three primary constituents—gingerol, shogaol, and zingerone—respond to different biological processes.[28, 29] Ginger contains a number of chemicals that have been shown to have potent anti-inflammatory, antioxidant, and anti-free radical properties.[30] In addition to stimulating glucose uptake in Gluc4 transport, glucose transport and beta cell protection,[29] insulin release/insulinotropic activity, inhibition of α -amylase and α -glucosidase synthesis, and inhibition of enzymes related to gluconeogenesis and glycogenolysis, it can also regulate insulin signaling pathways (AMPK, Akt) associated with insulin sensitivity

[31] It guards against diabetic complications such as neuropathy, retinopathy, and damage to the liver and kidneys.[21]

4. Turmeric (*Curcuma longa*)

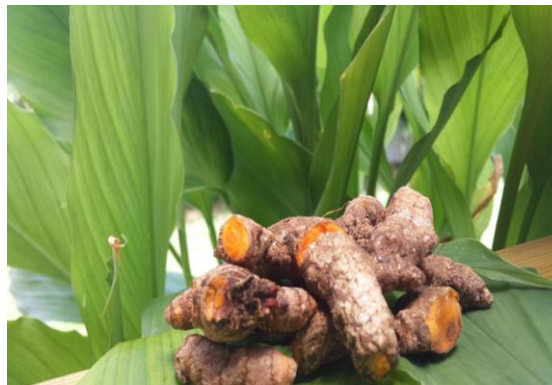


Figure 5: Turmeric

Turmeric, also known as *curcuma longa*, offers health benefits including anti-stress, anti-depressant, anti-bacterial and skin-protective properties.[32] The most important medicinal benefits of turmeric come from its curcuminoids, which include curcumin, desmethoxycurcumin, demethoxycurcumin and bisdemethoxycurcumin. These compounds also have anti-inflammatory, antioxidant, anti-apoptotic, anti-obesity, anti-atherosclerotic and anti-carcinogenic properties.[21] Diabetic wounds, arthritis, joint pain, anorexia, cough, gastrointestinal problems, and heart disease are all treated with turmeric.[33] The antidiabetic properties of turmeric influence insulin secretion and insulinotropic activity. They also control several insulin signaling pathways (AMPK, Akt), which in turn stimulate insulin release.[34] Turmeric reduces insulin resistance and prevents the reabsorption of glucose, -glucosidase and -amylase.[35]

5. Saffron



Figure 6 :Saffron

Saffron is derived from the dried stigma of the *Crocus sativus* L. plant and is primarily used for flavoring and coloring in cooking. The key secondary metabolites include crocin, picrocrocin, and safranal[36]. Research indicates that saffron could aid in the management of diabetes and reduce oxidative stress[37]. The therapeutic actions of saffron are believed to involve various mechanisms such as enhancing glucose uptake, preventing glucose absorption in the intestines, inhibiting insulinase activity in the liver and kidneys, reducing glucose production, limiting glucose uptake in the

kidneys, improving insulin sensitivity, and stimulating beta cells[38]. These findings imply that saffron may offer a novel approach to diabetes treatment.[37]

6. Cinnamon



Figure 7: Cinnamon

Cinnamon is an evergreen bushy tree belonging to the Lauraceae family,[39] renowned for its antioxidant, antifungal, and anti-inflammatory qualities. Its use in medicine can be traced back to around 2800 BC.[40] It is known to be beneficial for treating diabetes, heart conditions, high lipid levels, and hypertension.[41] The *C. Zeylanicum* species is especially adept at reducing cholesterol and blood sugar [42] levels. The polyphenols within cinnamon are capable of enhancing insulin sensitivity, which is associated with lower blood pressure levels[41]. These molecules also possess various benefits, including antioxidant and anti-obesity effects.[43] The hypoglycemic properties of cinnamon may work through several pathways, such as promoting insulin production and receptor activity, managing enzymes that control carbohydrate metabolism, supporting glucose absorption and glycogen synthesis, and boosting the expression of glucose transporter type 4 (GLUT-4) and peroxisome proliferator-activated receptors (PPARs).[44] A study by Anderson et al. indicated that consuming 500 mg of cinnamon water extract daily for two months resulted in diminished blood glucose, fasting insulin, total cholesterol, and LDL-C levels while enhancing insulin sensitivity in those with elevated blood [45]. In a similar vein, Qin et al. observed that cinnamon effectively brought down both blood glucose and lipid levels, aiding in the prevention of obesity, particularly in the abdominal region[46]. A different clinical trial involving cinnamon (120 and 360 mg/day) together with gliclazide over a three-month period significantly lowered fasting blood glucose and HbA1c levels.[47] However, inconsistencies have been reported in some clinical trials, with a meta-analysis of randomized controlled trials[48] indicating that cinnamon did not significantly affect fasting blood glucose, HbA1c, or lipid profiles in diabetes patients. Consequently, additional investigations are necessary to assess the therapeutic potential of cinnamon.[49]

7. Sesame oil



Figure 8: Sesame oil

Sesame oil contains lignans, minerals, vitamins, phytosterols, unsaturated fatty acids, and tocopherols. Research indicates that sesame oil has anti-hyperglycemic, anti-hyperlipidemic, anti-hypertensive, antioxidant, anti-cancer effects, and immune-regulating properties[50]. Diabetic rats receiving sesame butter (1.25 g/kg) and sesame oil (0.5 g/kg) over a six-week period exhibited lower glucose levels and increased high-density lipoprotein compared to the control group. Supplementing with sesame butter enhanced total antioxidant capacity and reduced malondialdehyde levels in diabetic rats[51]. Another study found that a daily intake of 35g of sesame oil considerably lowered blood pressure, heart rate, and arterial stiffness.[52] Daily consumption of sesame oil (35 g) produced an anti-glycemic effect in hypertensive patients with diabetes over 60 days.[53]

8. Green tea (*Camellia sinensis*)



Figure 9: Green tea

Research on green tea (*Camellia sinensis*) indicates that hypertensive patients who took 379 mg of green tea extract daily for three months experienced a significant reduction in systolic and diastolic blood pressure compared to those on placebo [54]. Evidence suggests that drinking green tea, black tea, and coffee has protective effects against type 2 diabetes and cardiovascular diseases both directly and indirectly [55]. Moreover, a regimen of 500 mg of green tea extract taken three times daily for 16 weeks significantly bettered insulin resistance and increased glucagon-like peptide-1 (GLP-1) production in type 2 diabetes patients [56].

Considering micronutrient supplementation for diabetes management:

Micronutrients are essential compounds, including vitamins and minerals, that our bodies need in trace amounts for various functions. They contribute to the healthy metabolism and the conversion of dietary sugars and carbohydrates into energy. Notable nutraceuticals impacting diabetes include micronutrients such as Calcium, Magnesium, and Chromium, along with Alpha Lipoic Acid (ALA), Coenzyme Q10, Carnitine, and Vitamins (B12, C, D, E, H), Vanadium, among others.[57]

1. Alpha-Lipoic Acid (ALA)

Alpha-Lipoic Acid is a disulfide compound that is synthesized in minimal amounts in cells and acts as a coenzyme for mitochondrial enzyme complexes such as alpha-ketoglutarate dehydrogenase and pyruvate dehydrogenase. Known for its strong antioxidant properties, ALA, when infused intravenously, has been shown to enhance insulin-mediated glucose clearance. It has been employed to relieve neuropathy resulting from diabetes.[58] Additionally, ALA is claimed to provide protection against diabetic cardiomyopathy.[59] ALA, along with omega-3 fatty acids and vitamin E, plays a role in boosting insulin sensitivity and lipid metabolism[60]. A regimen of parenteral ALA in 15 doses of 600 mg over 7 days positively affected BMI, HbA1C, and cholesterol, leading to significant improvements in erectile dysfunction and metabolic disorders linked with diabetes.[61] Studies indicate that ALA is beneficial in managing diabetic distal sensory-motor neuropathy.[62]

2. Chromium

Those with diabetes could have insufficient levels of the trace mineral chromium [63]. Supplementation of chromium may help improve both glucose tolerance and insulin sensitivity for individuals suffering from type 2 diabetes mellitus. According to a meta-analysis of randomized controlled trials investigating the effects of chromium supplementation on glucose and insulin responses in both healthy subjects and those with diabetes, the latter experienced a moderate yet noteworthy improvement in glycaemic control; however, no significant change was noted in healthy subjects [64]. The American Diabetes Association maintains an official stance that the evidence regarding the benefits of chromium supplementation for diabetes is inconsistent [65].

3. Vitamin C

In its ascorbic acid form, this chain-breaking antioxidant neutralizes reactive oxygen species (ROS), preventing the initiation of chain reactions that could lead to protein glycation.[66] It also lowers the levels of sorbitol and lipid peroxides associated with diabetes in animal red blood cells. For type 2 diabetes patients with insufficient vitamin C levels, a daily supplementation of 800 mg is

recommended, yet this does not treat endothelial dysfunction or insulin resistance.[67]

4. Magnesium

The nervous system, RNA and DNA synthesis, glucose regulation, and magnesium-containing enzymes are all essential for all of these processes [68]. It has been found that diabetics have low blood magnesium levels and high magnesium excretion [69]. Magnesium supplementation has been shown to prevent insulin resistance [70].

5. Vitamin E

As a vital fat-soluble vitamin, it mainly serves as an antioxidant. Insufficient vitamin E levels have been correlated with diabetes, and research indicates that individuals with diabetes may also experience lower antioxidant levels. Additionally, a study proposes that the heightened free radical generation resulting from hyperglycemia could increase the need for antioxidants among diabetic patients. Safety is typically acknowledged for vitamin E dosages up to 400 IU. However, although monitoring in supplement trials has shown no alterations in prothrombin times, doses above 800 IU may influence blood clotting.[71]

Conclusion

Nutraceuticals, commonly known as food supplements obtained from natural sources have been studied for diabetes mellitus for centuries. When consumed within the appropriate Recommended Dietary Intakes, nutraceuticals have been shown to have positive impacts on health, and can help people stay healthy in general. Although nutraceuticals have great potential to promote human health and prevent illness. Diabetes is one of numerous illnesses or diseases that affect the metabolism of carbohydrate, fat, and protein. The condition is accompanied by a reduction in insulin production or resistance to insulin's effects. People with diabetes, both insulin-dependent and non-insulin-dependent, have long been treated with plants. Nutraceuticals are nutritional food supplements. As the nutraceutical industry expands at a much faster rate than the food and pharmaceutical industries, reviewing this subject is particularly important. By preventing and combating acute and chronic illnesses caused by poor nutrition, herbal nutraceuticals promote a healthy lifestyle, a long life, and high quality of life.

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