

The Therapeutic Potential of Nutraceutical in Diabetes Management: A Comprehensive Review

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Abstract

Diabetes is a long-term and complex condition characterized by high blood sugar levels resulting from inadequate insulin production, ineffective insulin function, or a combination of both. Various nutraceuticals used in clinical settings have shown beneficial impacts on a range of biochemical and clinical markers related to diabetes. In many traditional medical systems, hypoglycemic agents derived from plants are used to treat, manage, and prevent diabetes mellitus. These plant extracts have demonstrated significant clinical benefits in maintaining normal blood glucose and lipid levels. The global use of natural products, herbal remedies, and nutraceuticals in therapeutic applications has been on the rise. Conventional treatment options, including synthetic drugs, often fall short of meeting therapeutic needs across a spectrum of pathological conditions. Nutraceuticals offer a promising therapeutic option for diabetes, potentially causing fewer side effects than synthetic medications. Defined as non-specific biological therapies derived exclusively from organic products, nutraceuticals aim to support health, prevent disease progression, and alleviate symptoms. Nutritional supplements are recognized for their powerful roles in disease prevention, health maintenance, and potentially even disease treatment. This study intends to examine and discuss some of the most utilized nutraceuticals for diabetes prevention.

Keywords: Nutraceuticals, diabetes mellitus, insulin, phytoconstituents, micro-nutrients

INTRODUCTION

The industrial era, with its mechanized lifestyles, rapid pace, long working hours, numerous mental pressures, and a growing disconnect from nature, has led to an increase in lifestyle imbalances. These changes have led to an increase in metabolic disorders, such as diabetes and obesity, as well as cancers, cardiovascular conditions, and mental health challenges. Diabetes has become a major global concern, currently affecting approximately 537 million adults worldwide, with estimates suggesting

this number could rise to 783 million by 2045 (IDF, 2023). Although Type 1 diabetes (T1DM) is insulin-dependent and typically diagnosed in childhood, type 2 diabetes (T2DM) is the most prevalent form and is closely associated with lifestyle factors, such as poor diet, physical inactivity, and obesity. Diabetes management traditionally involves lifestyle interventions (diet, exercise), oral hypoglycemic agents (e.g., metformin, sulfonylureas), and insulin therapy (Figure 1) However, the long-term use of medications can lead to adverse effects, such as gastrointestinal disturbances, hypoglycemia, and weight gain [1–3].

NUTRITIONAL

In 1989, Stephen De Felice, the founder and

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chairman of the foundation for Innovation in Medicine in Cranford, New Jersey, coined the term “nutraceutical” by merging the words “nutrition” and “pharmaceutical.” He described a nutraceutical as a food, or a substance derived from food that provides health benefits. Therapeutic or health advantages, including disease prevention and treatment capabilities [4–6].

The Greek physician Hippocrates is famously quoted as saying, “Let food be your medicine.” This philosophy emphasizes the importance of prevention in health.

According to European medical law, the classification of nutraceuticals as a medicinal.....



Figure 1. Nutraceuticals for diabetes.

PRODUCT IS BASED ON THE FOLLOWING CRITERIA

1. They may be used for the treatment, cure, or alleviation of a medical condition.
2. They can be administered to individuals to restore, repair, or modify their physiological functions.

Nutraceuticals encompass a range of products, including isolated nutrients, herbal preparations, dietary supplements, and specific diets. They also include processed foods, such as cereals, soups, oats, beverages, and specially formulated foods created through genetic engineering [7–9].

Nutraceuticals are used for a variety of health conditions, including relief from arthritis, colds, coughs, sleep disturbances, digestive issues, and prevention of certain cancers (Figure 2). They also help manage osteoporosis, control hypertension, lower cholesterol, relieve pain, alleviate depressive symptoms, and support the treatment of diabetes, heart disease, and other chronic or progressive conditions, such as Parkinson’s and Alzheimer’s disease [10–12].

HEALTH BENEFITS OF NUTRACEUTICALS

1. They have minimal or no side effects.
2. They can enhance health benefits.
3. They may serve as natural dietary supplements, without adverse effects.
4. They can improve nutritional value, support a balanced diet, and enhance human health.
5. They are readily accessible and cost-effective.



Figure 2. Nutraceuticals.

CLASSIFICATION OF NUTRACEUTICALS

1. Functional foods – these provide essential nutrients and contain antioxidant compounds that help prevent diabetes.
2. Carotenoids are pigmented compounds, such as alpha-carotene, beta-carotene, and beta-cryptoxanthin. These substances possess antioxidant and anti-inflammatory effects and are used to enhance vision, prevent specific cancers, and boost the Immune system.
3. Collagen hydrolysate is an important protein produced by the skin, known for its various therapeutic benefits.
4. Dietary fibers are plant-based carbohydrates that are not fully digested and can be found in foods, such as fruits, vegetables, wheat bran, and oats.
5. Fatty acids include all types of vegetable oils, such as olive oil.
6. Phytochemicals are bioactive compounds that influence the body's internal balance and nerve function, helping to reduce the risk of cancer. Lutein and lycopene are among the most notable examples.
7. Herbs are plants known for their lack of side effects and antioxidant properties, such as garlic extract and ginger, which are used to reduce cholesterol levels and aid in the healing of wounds and ulcers.
8. Probiotics are beneficial microbes with various medical and health applications. Found in dairy products, they have antioxidant properties and help regulate the growth of gut microbiota.
9. Dietary supplements, often consumed in tablet form, are available in various types.

HERBAL ANTI-DIABETIC CLAIMS

Diabetes mellitus is a growing global concern, particularly in India, where it is rapidly increasing. This metabolic disorder interferes with lipid and carbohydrate metabolism, adversely affecting both physical and mental well-being. As our knowledge of this disorder expands, the demand for more effective treatments also increases. Traditional herbal remedies are increasingly used as a safe alternative to conventional hypoglycemic drugs, as synthetic treatments, such as insulin for IDDM or NIDDM, have limited effectiveness and carry a high risk of drug resistance, necessitating dosage adjustments or medication changes. Herbal remedies are rich in essential plant-based nutrients, making them a promising option. Ayurvedic herbs can serve as “enhancers” for these medications, supporting efforts to improve the quality of life for individuals with diabetes [13–15].

Aloe Vera

Aloe vera is a plant belonging to the *Asphodelaceae* or *Xanthorrhoeaceae* family. *Aloe vera* extract

contains polysaccharides, anthraquinones, and lectins, which possess anti-diabetic properties [16, 17].

Garlic (*Allium sativum*)

Garlic belongs to the *Liliaceae* family, which is also associated with the *Amaryllidaceae* family. Its distinct sulfur compounds are responsible for its nutritional and medicinal benefits. Garlic exerts an anti-diabetic effect by enhancing insulin sensitivity and secretion. It also promotes glucose uptake by regulating enzymes involved in glycolysis and glycogenesis [18, 19].

Turmeric (*Curcuma longa*)

Turmeric, or *Curcuma longa*, offers various health benefits, including anti-stress, antidepressant, antibacterial, and skin-protective properties. Turmeric is used to treat conditions, such as diabetic wounds, arthritis, joint pain, anorexia, cough, digestive problems, and heart disease. Turmeric's anti-diabetic effects impact insulin secretion and insulinotropic activity. It also regulates various insulin signaling pathways (such as AMPK and Akt), which helps stimulate insulin release [20–22].

Ginger (*Zingiber officinale*)

Zingiber officinale is a flowering plant from the *Zingiberaceae* family. It can regulate insulin signaling pathways (AMPK, Akt) linked to insulin sensitivity, enhance glucose uptake via Glut4 transport, facilitate glucose transport, and protect beta cells. Additionally, it supports insulin release/insulinotropic activity, inhibits the synthesis of alpha-amylase and alpha-glucosidase, and suppresses enzymes involved in gluconeogenesis and glycogenolysis [23–25].

Cinnamon

Cinnamon, a bushy evergreen tree from the *Lauraceae* family, is known for its anti-inflammatory, antifungal, and antioxidant properties. It is effective in treating diabetes, cardiovascular diseases, high cholesterol, and hypertension. The hypoglycemic effects of cinnamon may involve mechanisms, such as the activation and regulation of enzymes related to carbohydrate metabolism (like glycolysis and gluconeogenesis), stimulation of cellular glucose uptake and glycogen synthesis, and increased levels of GLUT-4 and peroxisome proliferator-activated receptors (PPARs) [26–28].

Saffron

Saffron is derived from the dried stigma of *Crocus sativus L.* and is primarily used for its flavor and color in cooking. Saffron contains three primary secondary metabolites: crocin, picrocrocin, and safranal. Saffron may assist in improving diabetes management and reducing oxidative stress. Saffron's effects are believed to be driven by various mechanisms, such as enhancing glucose uptake, reducing intestinal glucose absorption, inhibiting insulinase activity in the kidneys and liver, suppressing glucose production, blocking renal glucose uptake, improving insulin resistance, and stimulating beta cells [29–31].

Fenugreek

Fenugreek may help reduce insulin resistance in fat and liver cells, enhance glucose absorption, boost the activity of liver enzymes like glucokinase and hexokinase, raise blood insulin levels, and improve insulin sensitivity, along with other potential mechanisms. The key compounds responsible for fenugreek's hypoglycemic effects include galactomannan, saponin, and 4-hydroxyleucine [32, 33].

ANTI-DIABETIC PROPERTIES OF VARIOUS MICRO-NUTRIENTS:

Micronutrients, including vitamins, minerals, and other nutrients, are essential for our body in small amounts to perform specific functions. They can help maintain balanced metabolism and regulate the conversion of sugars and other carbohydrates into energy. Several dietary supplements that have been extensively studied for their potential effects on diabetes include alpha lipoic acid (ALA), coenzyme Q10, carnitine, inositol, and various vitamins like B12, C, D, E, and H, along with vanadium and others [34–36].

Alpha-Lipoic Alpha Acid (ALA)

lipoic acid is a rare disulfide compound that acts as a coenzyme in mitochondrial enzyme complexes, including alpha-ketoglutarate dehydrogenase and pyruvate dehydrogenase. As a potent antioxidant, ALA has been shown to improve insulin-mediated glucose clearance when given intravenously. It has also been used in the treatment of diabetes-related neuropathy. Administering ALA parenterally at 600 mg in 15 doses over 7 days has shown positive effects on BMI, HbA1C, and cholesterol levels. This treatment has demonstrated significant benefits for diabetic metabolic issues and erectile dysfunction. Additionally, ALA has been found to be effective in treating diabetic distal sensory-motor neuropathy [37].

Calcium

Supplementing calcium and vitamin D may support the maintenance of insulin sensitivity, potentially aiding in diabetes management calcium supplementation may help prevent diabetes by inhibiting the secretion of parathyroid hormone (PTH), which can reduce insulin sensitivity in adipocytes (and potentially other tissues) by raising intracellular free calcium levels [38].

Magnesium

Magnesium is essential for various functions that rely on magnesium-dependent enzymes, including nerve transmission, DNA, and RNA production, glucose regulation, and the synthesis of RNA and DNA. A deficiency in magnesium has been linked to reduced insulin-mediated glucose uptake. Studies have shown that individuals with diabetes tend to excrete more magnesium and have lower blood magnesium levels, highlighting the potential benefits of magnesium supplementation in preventing insulin resistance [39].

Zinc

Zinc is essential for over 100 enzymes involved in digestion, metabolism, and wound healing. It plays a key role in maintaining the structural integrity of insulin in its hexameric form and is vital for the synthesis, storage, and secretion of insulin, helping to improve metabolic function [40–42].

Vitamin B

B vitamins, such as thiamine (B1), pyridoxine (B6), biotin, folic acid (B9), and cobalamin (B12), are frequently utilized in the management of type 2 diabetes. Thiamine is often used to treat diabetic neuropathy, as many individuals with neuropathy also suffer from thiamine deficiencies. Since thiamine is poorly absorbed, higher doses are required. Studies have shown that people with type 2 diabetes tend to have lower thiamine levels, and thiamine has been found to help reduce glucose and lipid levels in diabetics, in addition to its role in treating neuropathy [43].

Vitamin C

Vitamin C, in the form of ascorbic acid, acts as a chain-breaking antioxidant by directly neutralizing reactive oxygen species (ROS) and stopping the initiation of chain reactions that could result in protein glycation.

Vitamin D

Liese et al. found that there is a seasonal variation in diabetes control and a correlation between latitude and the incidence of both type 1 and type 2 diabetes, suggesting a negative relationship between sunlight exposure and the risk of developing diabetes. Since pancreatic beta cells contain vitamin D receptors, it is believed that vitamin D helps reduce insulin resistance and enhance insulin production. Vitamin D deficiency has been associated with type 2 diabetes, potentially because the vitamin is stored in fat, reducing its availability. Clinical studies with calcium and vitamin D supplementation indicate that vitamin D deficiency leads to reduced insulin sensitivity and may lower the risk of developing type 2 diabetes.

Vitamin E

Vitamin E is one of the important fat-soluble vitamins that acts mainly as an antioxidant. It has been suggested that diabetes is associated with low vitamin E levels and some studies show that diabetics appear to have low levels of antioxidants.

Additionally, research indicates that people with diabetes may require more antioxidants due to the increased production of free radicals caused by hyperglycemia. A daily dose of up to 400 IU of vitamin E is generally considered safe, although doses exceeding 800 IU could potentially affect blood coagulation. However, studies monitoring prothrombin time in subjects taking supplements have not shown any significant changes.

CONCLUSIONS

Diabetes is a metabolic disorder affecting the metabolism of carbohydrates, fats, and proteins, and it impacts a significant portion of the global population. Whether it is due to a lessened output of insulin or an opposition to the effect of insulin. Both types of diabetes, the one that requires insulin and the one that does not require insulin, have been historically treated with herbal medicine.

Nutraceuticals, which are food supplements, provide nutritional benefits and have demonstrated notable clinical and pharmacological actions. Herbal treatments offer greater efficacy and fewer side effects compared to synthetic anti-diabetic drugs. Many patients now prefer using natural remedies with anti-diabetic properties. Hypoglycemic herbs function by stimulating insulin secretion, enhancing glucose uptake by fat and muscle cells, reducing glucose absorption in the stomach, and decreasing glucose production in the liver. While nutraceuticals are becoming increasingly utilized in clinical settings, further research is required to resolve key clinical and pharmacological challenges.

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