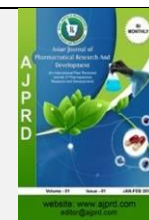


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Review Article

Current status and key Role of Nutraceuticals in diabetes: A comprehensive review

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ABSTRACT

Hyperglycemia is a hallmark of diabetes mellitus, a long-term metabolic disease brought on by deficiencies in insulin activity, production, or both. Diabetes is becoming more commonplace worldwide, which has led to a lot of research into different treatment approaches. Among these, nutraceuticals have garnered significant attention due to their potential benefits in managing diabetes. Nutraceuticals are health-promoting food-derived products that present a possible alternative to traditional diabetic therapies. The role of different nutraceuticals, such as vitamins, minerals, antioxidants, and plant-based substances, in the treatment of diabetes mellitus is examined in this review. Important nutraceuticals with anti-diabetic qualities include omega-3 fatty acids, chromium, alpha-lipoic acid, and polyphenols from plants including bitter melon, green tea, and cinnamon. Along with clinical data demonstrating their effectiveness, the processes by which these substances affect insulin sensitivity, glycemic management, and diabetic complications are examined. Although nutraceuticals offer a strong supplement to diabetes treatment, further study is required to completely understand their mechanisms, ideal dosages, and long-term safety. The potential of nutraceuticals as a component of an integrated approach to diabetes management is highlighted in this review, which also emphasizes the necessity of individualized treatment plans based on patient profiles.

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INTRODUCTION

Diabetes mellitus is a complex metabolic disorder that is linked to the development of insulin resistance, impaired insulin signaling and β -cell dysfunction, abnormal glucose and lipid metabolism, sub-clinical inflammation, and increased oxidative stress. It was estimated to affect 2.8% of the world's population in 2000, and it is predicted to affect 4.4% in 2030 due to population aging and an increase in obesity.[1–3] Diet is the primary modifiable risk factor among the many that contribute to the development and progression of type 2 diabetes mellitus. A growing quantity of epidemiological studies

Numerous pharmacological and non-pharmacological interventions have been developed to improve glycemic control and prevent diabetes complications based on the current understanding of the pathophysiology of insulin resistance and type 2 diabetes mellitus. Recently, the use of functional foods and their bioactive components have been considered as a novel approach in the prevention and management of diabetes and its complications.[10] A meal that has a medical-health benefit, such as illness prevention or therapy, is called a nutraceutical. Additionally, natural functional/medical foods or bioactive phytochemicals with health-promoting properties are referred to as nutraceuticals.

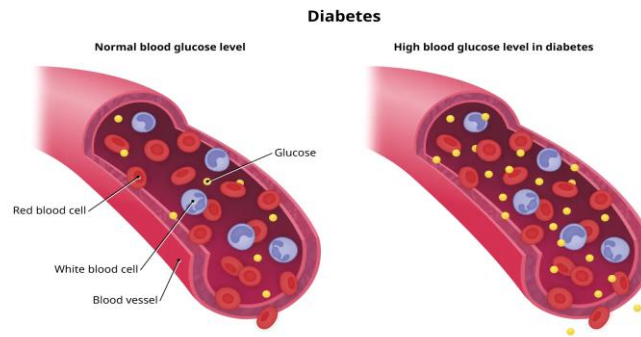


Figure 1: Difference between diabetes mellitus with normal blood sugar level.

Antioxidant of Vitamins

Studies on animals have demonstrated that by protecting against oxidative stress, a sufficient intake of dietary antioxidants may prevent or postpone diabetes consequences, such as renal and neurological impairment.

Vitamin C

Ascorbic acid, or vitamin C, is a chain-breaking antioxidant that directly scavenges reactive oxygen species (ROS) and stops chain reactions from spreading, which would otherwise result in a decrease in protein glycation.¹⁸ Vitamin C also lowers lipid peroxides in erythrocytes and sorbitol buildup brought on by diabetes in animals.

prevalence of diabetes. Further research suggests that individuals with diabetes may also need more antioxidants because of the increased generation of free radicals brought on by hyperglycemia.

Figure 2: Ascorbic acid found in citrus fruits

In individuals with type 2 diabetes and low vitamin C levels, vitamin C (800 mg/day) somewhat restores vitamin C levels, but it has little effect on endothelial dysfunction or insulin resistance.

Vitamin E

The primary role of vitamin E, an essential fat-soluble vitamin, is antioxidant. Research indicates that individuals with diabetes may have lower levels of antioxidants, and low vitamin E levels have been linked to a higher

Figure 3: Vitamin E core structure found in many plants and fruits.

It is generally accepted that doses of vitamin E up to 400 IU are safe. Blood coagulation may be affected by doses greater than 800 IU, however no changes have been observed in supplement trials that tracked patients' prothrombin times.

Carbohydrates

The energy substrate with the biggest effect on glycaemia levels is carbohydrates. The post-prandial reaction is primarily caused by the total amount of carbohydrates, but other factors including the kind of carbohydrate, fiber content, cooking method, maturity level, etc. may also be involved. Additionally, pre-prandial glycaemia, the distribution of macronutrients (proteins and fats) during the meal, and the hypoglycemic medication used (insulin or oral pills) can all affect post-prandial glycaemia.

Figure 4: Different carbohydrates examples

The majority of scientific bodies concur that the diet should include carbohydrates from fruits, grains, pasta, legumes, vegetables, and tubers, and they advocate for the individualization of carbohydrate contribution. Despite the lack of long-term research, eating legume starches appears to have a beneficial effect on glycaemia due to the long-lasting influence on post-prandial glycaemia without abrupt spikes; it may also avoid late hypoglycemia and post-prandial hyperglycemia.

Fats

High-fat diets have been shown in numerous studies to worsen glucose tolerance and increase the risk of obesity, dyslipidemia, and atherosclerotic heart disease. Reducing consumption of saturated fat has also been shown to improve or reverse these same metabolic problems. People with diabetes should follow the same current guidelines regarding fat intake as the general population: limit cholesterol intake to 300 mg/d or fewer and saturated fats to 10% or less of total calorie intake.

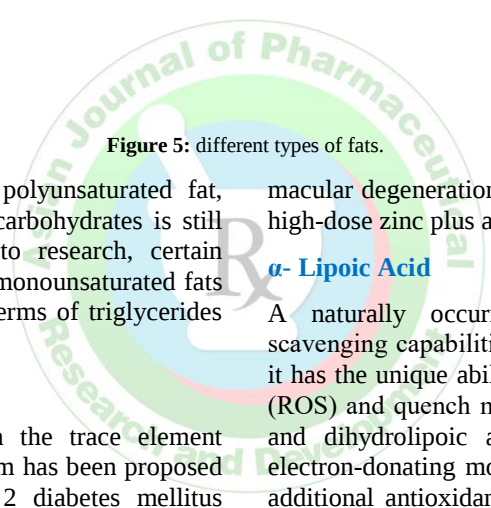


Figure 5: different types of fats.

The best substitute for saturated fat, polyunsaturated fat, monounsaturated fat, or calories from carbohydrates is still up for scientific dispute. According to research, certain people with diabetes may benefit from monounsaturated fats such as canola, olive, and peanut oils in terms of triglycerides and glycemic management.

Chromium

People with diabetes may be low in the trace element chromium. Supplementing with chromium has been proposed as a way to help people with type 2 diabetes mellitus improve their glucose tolerance and insulin sensitivity. A meta-analysis of randomized controlled trials examining the impact of chromium supplementation on insulin response and glucose in both healthy individuals and those with diabetes revealed a slight but substantial increase in glycaemic control in the latter group, but not in the former. According to the official position of the American Diabetes Association, there is conflicting information about the advantages of chromium supplementation for diabetics.

Magnesium

Prospective epidemiology links magnesium-rich diets to decreased risk for diabetes, with an inverse correlation between magnesium intake and fasting insulin levels, suggesting an improvement in insulin sensitivity. This view is supported by limited clinical data, as well as by animal studies demonstrating that magnesium helps preserving adipocyte insulin sensitivity.³⁶ The retina is particularly vulnerable to oxidative damage because of its abundance of polyunsaturated fatty acids, predominantly found in photoreceptor outer membranes, which are readily oxidized.³⁷ Nutritional supplementation for age-related

macular degeneration (AMD) and were supplemented with a high-dose zinc plus antioxidants formulation.

α -Lipoic Acid

A naturally occurring antioxidant with strong ROS-scavenging capabilities is α -lipoic acid. In its oxidized state, it has the unique ability to scavenge reactive oxygen species (ROS) and quench multiple radicals. Together, α -lipoic acid and dihydrolipoic acid function as a redox couple (an electron-donating molecule and its oxidized form) and have additional antioxidant qualities, such as chelating transition metals and regenerating other antioxidants like glutathione, vitamin C, and vitamin E. It has been demonstrated that α -lipoic acid protects the retina from ischemia-reperfusion injuries both in vivo and in vitro. One of the main causes of vision loss is thought to be ischemic damage to the retina, which happens in diabetic retinopathy. In individuals with type 2 diabetes, α -lipoic acid improves insulin sensitivity by about 18–20%.

Protein

According to available data, the daily protein requirements of individuals with diabetes are comparable to those of the general population, at roughly 0.86 g/kg. Excessive protein consumption should be avoided since it may contribute to the pathophysiology of diabetic nephropathy, even if it plays a part in promoting insulin secretion. Eating vegetable protein instead of animal protein may help lower blood cholesterol and manage nephropathy, according to some research. Liquid protein supplements, protein powders, and liquid protein shots are among the several kinds of protein supplements. Protein supplements come from a variety of sources.

L-carnitine

A naturally occurring vitamin-like substance, L-carnitine (β -hydroxy- γ -trimethyl aminobutyrate) is widely present in mammalian plasma and tissues, primarily found in skeletal and cardiac muscles. L-carnitine is produced by biosynthesis from lysine and methionine as well as dietary sources like meat and dairy items. Research on supplements has shown that L-carnitine has insulin-sensitive and lipid-lowering qualities. Numerous vital intracellular and metabolic processes, including fatty acid transport across the inner mitochondrial membrane into the matrix for β -oxidation, detoxification of potentially toxic metabolites, control of the mitochondrial acyl-Co A/CoA ratio, and stabilization of cell membranes, are carried out by L-carnitine. L-carnitine helps eliminate short- and medium-chain fatty acids that build up in mitochondria due to either normal or abnormal metabolism. Furthermore, the oxidative metabolism of glucose in tissues is impacted by L-carnitine.

Anti-diabetic claims of herbs

Diabetes mellitus is a global threat and a metabolic disease that is rapidly spreading in India. It affects the metabolism of fats and carbohydrates and has an impact on a person's physical and emotional well-being. As our understanding of this order's heterogeneity grows, so does the demand for more effective treatment. Because synthetic drugs in non-insulin dependent diabetes mellitus (NIDDM) or insulin in Insulin dependent diabetes mellitus (IDDM) have a limited role to play, and have high risk of drug tolerance, thereby causing a raise in dosage or a change of drug. Ayurvedic herbs may act as "Potentiators" for these medications due to their abundance of vital phytonutrients, and they may also aid to preserve the quality of life for those with diabetes. Certain therapeutic herbs from Ayurveda and Indian traditional medicine have enormous potential. The role of herbal nutraceuticals, nutritionals, and naturals in metabolic illnesses like diabetes has been the subject of several studies by CSIR, ICMR, DBT, and academics.

Methodological Approach to Nutraceutical Use

- **Assessment:** Examine the patient's eating practices, current medications, and medical history.
- **Selection:** Based on the demands of the individual and proof of product efficacy, select the right nutraceuticals.
- **Dosage:** Based on individual reaction and clinical guidelines, choose the appropriate dosage.
- **Monitoring:** Keep a close eye on your HbA1c, blood sugar levels, and any possible adverse effects.
- **Modification:** Based on the patient's development and any modifications to their condition, modify the nutraceutical regimen.

Clinical Evidence and Studies

- **Review of Literature:** Provide an overview of studies and clinical trials that demonstrate the effectiveness of particular nutraceuticals in the treatment of diabetes.
- **Case Studies:** Give examples of how nutraceuticals have been successfully included into the treatment of diabetes.
- **Integrative Approach**
- **Diet and Lifestyle:** Use nutraceuticals in conjunction with dietary adjustments, physical activity, and other lifestyle changes.

- **Conventional Therapy:** Nutraceuticals should be used in addition to, not instead of, traditional diabetes drugs.

Safety and Regulations

- **Quality Control:** Verify that nutraceuticals are free of impurities and come from reliable producers.
- **Regulatory Compliance:** Follow the rules for the use of nutraceuticals and dietary supplements in medical practice.

Patient Education and Counselling

- **Inform:** Explain to patients the advantages and possible dangers of nutraceuticals.
- **Engage:** Motivate patients to take an active role in their treatment plan and make knowledgeable health-related decisions.

Results of Using Nutraceuticals in the Management of Diabetes Mellitus

1. Improved Glycaemic Control

- **Blood Glucose Levels:** Studies have shown that several nutraceuticals can significantly reduce fasting and postprandial blood glucose levels.
- **HbA1c Reduction:** Long-term use of a number of nutraceuticals has been associated with lower HbA1c readings, indicating better overall glycemic control.

2. Enhanced Insulin Sensitivity

- **Mechanisms:** By strengthening insulin signaling pathways and lowering insulin resistance, nutraceuticals such as polyphenols, omega-3 fatty acids, and chromium have been shown to improve insulin sensitivity.
- **Clinical Evidence:** Studies have shown that patients using these nutraceuticals have increased insulin sensitivity, which improves the cells' ability to absorb and use glucose.

3. Reduction in Oxidative Stress and Inflammation

- **Antioxidant Effects:** Nutraceuticals with potent antioxidant qualities, like vitamins C and E, alpha-lipoic acid, and certain polyphenols, lower oxidative stress markers in diabetic patients.
- **Anti-inflammatory Benefits:** Consuming curcumin, omega-3 fatty acids, and other anti-inflammatory nutraceuticals on a regular basis helps reduce systemic inflammation, which is a major cause of insulin resistance and problems from diabetes.

4. Improvement in Lipid Profile

- **Lipid Levels:** It has been demonstrated that plant sterols and omega-3 fatty acids improve lipid profiles by raising HDL cholesterol and decreasing triglycerides, LDL cholesterol, and total cholesterol.
- **Cardiovascular Benefits:** Patients with diabetes are more likely to develop cardiovascular problems, which can be prevented with improved lipid profiles.

5. Weight Management

- **Appetite Regulation:** Fiber supplements, such as glucomannan and psyllium, can help manage type 2 diabetes by reducing appetite, increasing fullness, and controlling weight.
- **Metabolic Effects:** Some nutraceuticals can help with weight loss and maintenance by increasing metabolism and promoting fat oxidation.

6. Improved Gut Health

- **Probiotics and prebiotics:** These can improve the composition of the gut microbiota, which can improve glucose metabolism, lower inflammation, and improve metabolic health.
- **Clinical Results:** Probiotic users have reported improved glucose control and less gastrointestinal problems, which are frequently linked to diabetes.

7. Reduced Risk of Diabetic Complications

- **Microvascular problems:** Antioxidant and anti-inflammatory nutraceuticals lower the incidence of microvascular problems like diabetes retinopathy, nephropathy, and neuropathy.
- **Macrovascular Complications:** A lower risk of macrovascular complications, such as coronary artery disease and stroke, is associated with improved lipid profiles and decreased inflammation.

Discussion

Glycemic Control

- **Polyphenols:** These substances can lower blood glucose levels and increase insulin sensitivity. They are present in foods including grapes, berries, and green tea. They work by altering important signaling pathways related to the metabolism of glucose.
- **Omega-3 Fatty Acids:** These fatty acids, which are present in fish oil, have anti-inflammatory and insulin-sensitive qualities. Additionally, they can lower HbA1c and fasting glucose levels.
- **Fiber:** Soluble Fibers, such as those found in oats and psyllium, improve postprandial glycaemic control by slowing the absorption of glucose.
- **Chromium:** By boosting the quantity and binding capacity of insulin receptors, this trace element improves glucose metabolism and increases insulin action.

Antioxidant and Anti-inflammatory Effects

- **Oxidative Stress Reduction:** Free radicals are neutralized by nutraceuticals with antioxidant qualities, such as vitamins C and E, alpha-lipoic acid, and certain polyphenols. This reduces oxidative stress, which is a major contributor to complications from diabetes.
- **Inflammation Reduction:** Diabetes and insulin resistance are associated with persistent inflammation. By blocking inflammatory cytokines and pathways, nutraceuticals including resveratrol, curcumin, and omega-3 fatty acids improve metabolic health.

Clinical Evidence

Human Trials

- **Polyphenols:** Supplementing with polyphenols has been found in clinical trials to increase insulin sensitivity and lower HbA1c levels. For instance, a study on green tea extract showed that diabetes patients' HbA1c and fasting glucose levels significantly decreased.
- **Omega-3 Fatty Acids:** Supplementation has been linked to better insulin sensitivity and lipid profiles, such as lower triglycerides and higher HDL cholesterol.
- **Fiber:** Soluble Fibers have been shown to improve postprandial blood glucose levels and overall glycaemic management. Psyllium husk intake significantly lowered fasting blood glucose and HbA1c, according to research.
- **Chromium:** Research shows that supplementing with chromium can enhance insulin sensitivity and lower fasting blood glucose levels, especially in people who are chrome deficient.

Meta-Analyses and Systematic Reviews

These thorough assessments have combined results from several research, offering reliable proof of the effectiveness of several nutraceuticals in the treatment of diabetes. For example, studies on omega-3 fatty acids have repeatedly demonstrated their advantages in lowering inflammation and enhancing lipid profiles.

Integrative Approach

Complementary Role

Rather than taking the place of traditional diabetic therapies like medication, nutraceuticals should be used in conjunction with them. By tackling other pathways implicated in diabetic pathogenesis, they can increase the efficacy of conventional treatments.

Personalization

Individual reactions to nutraceuticals differ greatly. To maximize benefits, customized strategies that take into account variables like genetics, baseline health status, and coexisting medical conditions are crucial. Genetic testing and biomarker analysis can direct customized nutraceutical interventions.

Challenges and Considerations

Quality and Standardization

- **Variability:** Nutraceuticals can differ greatly in terms of the concentration and bioavailability of their active ingredients, which can impact their efficacy.
- **Standardization:** To guaranty consistent therapeutic effects, standardized dosages and formulations must be established. Regulatory bodies must enforce strict quality control measures.

Regulation and Safety

- **Regulatory Compliance:** The stringent testing and approval procedures needed for pharmaceuticals are sometimes absent from nutraceuticals. It is essential to

make sure that products fulfil safety and efficacy requirements.

- **Safety Monitoring:** For many nutraceuticals, there is a lack of long-term safety evidence. It is crucial to continuously check for side effects, especially when using various drugs.

Patient Education

Patients must be informed about the advantages and disadvantages of nutraceuticals in order to make an informed choice. To prevent any drug interactions, patients should be encouraged to talk to their healthcare providers about using nutraceuticals.

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