



Role Of Nutraceuticals in The Treatment of Diabetes: A Review

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Abstract: Globally, the use of nutraceuticals, herbal remedies, and natural goods in treatments has increased in recent years. The demands of therapeutic needs for treating diverse pathological conditions are not met by conventional treatment choices that are accessible as synthetic medications. In terms of diabetes and herbal medications, nutraceuticals provide a more promising treatment option with fewer side effects. Nutraceuticals are described as non-specific biological treatments that employ all natural goods to maintain and promote wellbeing, stop cancerous processes, and manage symptoms. It has been asserted that nutritional supplements offer powerful disease-prevention, disease-cure, and health-promoting properties. Diabetes is a complex, chronic disease characterised by a state of hyperglycaemia brought on by a lack of insulin secretion, insulin action, or both. Diabetic has been shown to be targeted by a number of nutraceuticals used in clinical practise, favourably modulating a number of biochemical and clinical endpoints. Many traditional medical systems employ hypoglycaemic medications to prevent, regulate, and cure diabetes mellitus. These medications are derived from plants like *Momordica charantia* (Karela), *Nigella sativa* (Kalonji), and *Cinnamomum cassia* (Cinnamon). These plant extracts have demonstrated a clinically significant benefit in preserving healthy lipid profiles and blood sugar levels. This study aims to highlight and comment on some of the most widely used nutraceuticals for diabetes prevention.

Index Terms - Nutraceuticals, Diabetes, Natural crude drugs, Hypoglycemic, hyperglycemia Vitamins

I. INTRODUCTION

Diabetes Mellitus is a complex, chronic illness associated with a state of high blood glucose level/hyperglycaemia, occurring from a deficiency in insulin secretion, insulin action or both (1) A serious health problem that has reached frightening proportions is diabetes. Today, type 2 diabetes affects more than 500 million individuals globally. Globally, the number of people with diabetes is expected to double by 2030, from 171 million in 2000 to 366 million, with India seeing the largest growth (2). According to predictions, up to 79.4 million Indians might have diabetes by 2030. According to WHO, poorer nations will shoulder the majority of the cost. The long-term pathogenic problems caused by these metabolic abnormalities include micro- and macrovascular consequences, neuropathy, retinopathy, nephropathy, and other ailments that reduce quality of life and raise death rates (3-5).

Types of Diabetes Mellitus

There are three types of Diabetes:

1. Types 1 Diabetes
2. Type 2 Diabetes
3. Gestational Diabetes

Type I diabetes (Insulin dependent) is caused due to insulin insufficiency because of lack of functional beta cells. Patients experiencing this are totally dependent on external source of insulin. But in Type 2 diabetes (Insulin independent) patients are unable to respond to insulin and can be treated with dietary changes, exercise and medication. It is the most common form of diabetes constituting 90% of the diabetic population (6).

Symptoms for both Diabetic conditions may include:

- I. High levels of sugar in the blood
- II. Unusual thirst
- III. Frequent urination
- IV. Extreme hunger and Loss of weight
- V. Blurred vision
- VI. Nausea and Vomiting
- VII Extreme Exhaustion and Weakness
- VIII Irritability and Mood Swings, etc.

If a woman does not already have diabetes, she may acquire gestational diabetes during pregnancy. Women who have gestational diabetes subsequently acquire type 2 diabetes in around 50% of cases, without symptoms and this affects somewhere between two and ten percent of pregnancies each year in USA (6).

1. Diabetes brought on by conditions affecting the pancreas, including pancreatitis, trauma, infection, pancreatic cancer, and pancreatectomy.
2. Drug and chemical-induced diabetes from drugs that disrupt insulin secretion or insulin action.
3. Due to endocrine disorders that cause excess secretion of hormones that antagonize insulin like Cushing's syndrome.
4. Other genetic syndromes sometime associated with this such as Prader-Willi syndrome, down's syndrome, Friedreich's ataxia.
5. Uncommon specific forms of immune-mediated diabetes for example immunological disorders other than those that cause type 1 diabetes.
6. Infection-related diabetes caused by viral infection associated with beta cell destruction (7)

Nutraceuticals: Stephen De Felice, founder and chairman of the Foundation for Innovation in Medicine, Cranford, NJ, invented the phrase "nutraceutical" in 1989 by combining the words "nutrition" and "pharmaceutical."

A food or component of food that offers medical or health advantages, such as the prevention and/or treatment of an illness, is referred to as a nutraceutical, in De Felice's definition. (8) The Greek physician and inventor HIPPOCRATES once remarked, "Let food be your medicine." "Focus on prevention" is the guiding principle.

European medicine law has defined nutraceuticals as a medicine because of these reasons:

1. It can be used for the prevention, treatment, or cure of a disease condition.
 2. It can be administered with a view to restoring, correcting, or modifying physiological functions in human beings (9)
- Nutraceuticals may range from isolated nutrients, herbal products, dietary supplements, and diets to genetically engineered designer foods and processed products like cereals, soups, oats and beverages (10)
- Nutraceuticals used as anti-arthritis, in cold and cough, sleeping disorders, digestion and prevention of certain cancers, osteoporosis, blood pressure, cholesterol control, pain killers, depression, diabetes, cardiovascular disease, and other chronic and degenerative diseases like Parkinson's and Alzheimer's diseases(11)

Health benefits of nutraceuticals

1. Less/No the side effect.
2. May increase the health beneficial effect.
3. May have naturally dietary supplement, without any unpleasant side effect.
4. May increase the health value, our diet and improve medical condition of human.
5. Easily available and economically affordable.

Table 1: Nutraceuticals Available in market

S.No.	Product Brand Name	Plant constituents/Extract	Functions
1	Fenulife	Fenugreek galactomannan	Controls Blood sugar
2	Teamax	Green tea extract	Potent Antioxidant
3	Cholestaid	Saponin	Reduce Cholesterol
4	Soylife	Soybean phytoestrogen	Maintains Bone health
5	Betatene	Carotenoids	Immune Function
6	Clarinol	CLA	Weight loss ingredient
7	Glucocare	Bitter melon	Control Blood sugar

Classification of Nutraceuticals:

1. Functional foods- It provides nutrition's, it also contains antioxidants compounds that prevent diabetes (12)
2. Carotenoids- They are pigmented compounds like alpha-carotene, beta carotene and beta cryptoxanthin. These compounds have antioxidant and anti-inflammatory properties, used to improve vision, prevent certain cancer and improve the immune system (13)
3. Collagen hydrolysate – It is essential human protein secreted from skin. It has several medicinal properties (14)
4. Dietary fibers- They are non-starchy poorly digestible vegetable carbohydrates found in vegetables fruits, wheat bran and oats (15). It improves digestion and reduce Crohn's disease and ulcerative colitis (16)
5. Fatty acids- These covers all vegetable oil like olive oil (17)
6. Phytochemicals- They are active compounds that work on balance inside the body and nervous activity, so they decrease the cancer. One of the most important of these compounds is lutein and lycopene (18)
7. Herbs – They are plants that do not have side effects and having antioxidant properties, for example garlic extract, ginger used for treatment of cholesterol, wound healing and antiulcer (19)
8. Probiotics- Microbes are considered to have many used in the medicinal field and human health. They are found in milk products and they have antioxidant properties. They work to regulate the growth of gut microbiota (20)
9. Dietary supplements –Tablets are dietary supplements that are taken from different sources (21)

Table 2: Nutraceutical used in various diseases

S.No.	Diseases	Nutraceuticals Used
1	Eye health	Lutein and Zeaxanthin
2	Mental health	Phosphatidylserine, Docosahexaenoic, soy, Isoflavones
3	Sleep Enhancement	Melatonin
4	Cancer prevention	Tea, lycopene, flaxseed
5	Bone health	Melatonin, L-carnitine
6	Skin health	Tea, soy, isoflavones, glycosamines, melatonin

Recent upsurge in Nutraceuticals: People are increasingly interested in dietary supplements, nutritional treatment, phytotherapy, and nutraceuticals as a result of their frustration with risky synthetic pharmaceutical medicines and profound worry about how to preserve their health with safer and more effective natural and herbal items (22). The biological treatments known as nutraceuticals (nutrients plus pharmaceuticals) 4 are used to promote health, prevent disease, and treat illnesses.

They are divided into the following categories depending on their chemical composition:

- (a) Foodstuffs (vitamins, minerals, Amino acids, etc.).
- (b) Botanicals (Herbs or botanical products as concentrate and extracts).
- (c) Nutritional supplements (probiotics, prebiotics, antioxidants, enzymes). (23)

Functional foods and beverages containing specific ingredients like vitamins, lipids, proteins, carbohydrates, minerals, or other essential nutrients with health benefits. Dietary supplements provide nutraceuticals in a tablet or capsule form at a dosage that exceeds the amount present in normal food (24-25). When such nutraceuticals are used for prevention or treatment of disease, they can be coined as drug (26). Rich sources of phenolic compounds, terpenoids, sulphur compounds, pigments, and other naturally occurring antioxidants may be found in vegetables, fruits, whole grains, herbs, seeds, and nuts. These substances are used to treat a variety of illness problems (27).

Herbs with Anti-diabetic properties:

1. *Momordica charantia* (Bitter gourd)

Common name: Karela

Family: Cucurbitaceae

Parts used: Fruit, seed, bark, root, leaves, oil

Momordica charantia is found in Asian and African subcontinents. The plant grows up to 5 m with simple, alternate leaves 4–12 cm across. Fruit is regularly used as vegetable in diet. *M. charantia* is a popular as antidiabetic fruit and related actions in native populations of Asia, South America, India, and East Africa. It contains constituents with antidiabetic properties such as charantin, vicine, and polypeptide-p, and antioxidants (28).

Mechanism of hypoglycemic effect: The fruit juice significantly increased the number of β -cells, decreases blood sugar levels by inhibiting fructose-1, 6-phosphatase and glucose-6-phosphatase, and on the other hand, increases glucose oxidation through the shunt pathway by activating G6PDH, which is its important enzyme (29).

2. *Syzygium cumini* (Blackberry)

Common name: Jamun

Family: Myrtaceae

Parts used: Seeds, leaves, fruit, bark

Syzygium cumini is an 8–15 m tall, tree with smooth, glossy arranged opposite to each other and smell like turpentine 3. It also goes by the name *Eugenia jambola*. It produces tasty purplish-black oval berries and fragrant white flowers in branching clusters and one seed in each berry. Typically, the flavour is acidic, somewhat sweet, and slightly astringent (30). *S. cumini* is abundantly produced in the Indian subcontinent and in South Asian nations like Indonesia, Bangladesh, Pakistan, Burma, Nepal, and Sri Lanka (31).

The hypoglycaemic effects of *S. cumini* may be brought about via enhanced insulin secretion or decreased insulin breakdown. Studies on the phytochemistry and pharmacology of ethanol extract show that it includes traces of phenol, steroids, saponins and flavonoids. The activation of pancreatic cells and subsequent production of insulin seem to be mediated by saponin (32). According to reports, *S. cumini* has a hypolipidemic impact by lowering blood triglycerides, free fatty acids and cholesterol (33). This action was said to be brought on by the extract's flavonoids, saponins, and glycosides, which in turn reduced the activity of the liver's 3-HMG Co-A reductase (34). Additionally, *S. cumini* seed extract includes ellagic acid, which have the property to lower blood pressure (35)

3. *Trigonella foenum-graecum* (fenugreek)

Common name: Methi

Family: Fabaceae

Parts used: Leaves, seeds

Trigonella foenum-graecum is cultivated throughout India as well as in some other parts of world as a semiarid crop (36). Its green leaves and seeds are used as vegetable and spice in India. *T. foenum-graecum* is popular for its flavours and pungent aromatic properties and it is used commonly in food. Mechanism of hypoglycemic effects: several experimental studies suggested that *T. foenum-graecum* as an effective antidiabetic agent (37,38,39). Human studies confirmed for its glucose and lipid-lowering potential (40). Several research have shown that its leaf and seed extracts, mucilage and powder can lower blood glucose and cholesterol levels in people and experimental diabetic animals (41). Due to the presence of saponins, high fibre content, 4-hydroxyisoleucine, and the alkaloid trigonelline, it has medicinal promise (42), the hypoglycemic impact of *T. foenum-graecum* may have extra pancreatic consequences (43).

4. *Cinnamomum zeylanicum* (cinnamon)

Common name: Dalchini

Family name: Lauraceae

Parts used: Leaves, bark

Cinnamomum zeylanicum used as spice, medicine, it is obtained from the inner bark of the tree and used in several Ayurvedic preparations. Oil extracted from *C. zeylanicum* leaf and bark contains active components including cinnamaldehyde, cinnamyl acetate, cinnamyl alcohol and eugenol and other volatile substances. Mechanism of hypoglycaemic effects: Therapeutic studies have proved it as a hypoglycaemic agent as it inhibits the activity of aldose reductase, the key enzyme of polyol pathway. Inhibition of this enzyme prevents the conversion of glucose to sorbitol, thus preventing several diabetic complications like cataract, neuropathy, and retinopathy (44).

5. *Nigella sativa* (Black cumin)

Common name – Kalonji

Family – Ranunculaceae

Part used – seeds

N. sativa is an annual flowering plant, used in infertility, fever, cough, bronchitis, asthma and many more. The chemical constituents are nigellicine, nigellidine, thymol, linoleic, oleic, etc (45). The bioactive constituent for diabetes is thymoquinone (1.8% - 48%). Its seeds are been used for centuries as a natural remedy such as anti-hyperglycaemic, antioxidants, anti-hypertensive, anti-hyperlipidaemia, and anti-microbial. Mechanism of hypoglycaemic effects: As per the studies it helps in insulin secretion by restoring the activity of enzymes involved in glucose metabolism such as glucose-6-phosphatase and fructose-1, 6- phosphatase and fructose-1, 6- bisphosphatase of gluconeogenesis. It also acts like SGLT-2 inhibitors and thiazolidinediones (46).

6. *Allium sativum* (Garlic)

Common name – Garlic

Family – Amaryllidaceae

Parts used – leaves, flower, cloves

Allium sativum has been a traditional herb used in heart disease, arthritis, toothache, constipation and various infections (47). Its main bioactive constituent is Allicin (0.2-0.53%). Mechanism of hypoglycemic effect: Allicin helps as a hypoglycemic compound by activating PI3K/AKT pathway which helps in secretion of insulin and reduces the production of advanced glycation end products (48).

7. *Gymnema sylvestre*

Common name: Gurmar

Family name: Asclepiadaceae

Parts used: Rhizomes, leaves, volatile oils

Gymnema sylvestre is an herb native to the tropical forests of India and Sri Lanka. It is a large climber, with roots at nodes and it is potential anti-diabetic plant used in Ayurvedic preparations since ancient times. Mechanism of hypoglycaemic effects: Aqueous extract of *G. sylvestre* caused reversible increase in intracellular calcium and insulin secretion in mouse and human β -cells with type 2 diabetes (49 and 50). It has been reported that *G. sylvestre* can prevent adrenal hormones from stimulating the liver to produce glucose in mice, thus reducing blood sugar level (51) by the potential components like triterpene saponins, known as gymnemic acids (I–XVIII) and gymnemosaponins (I–V).

8. *Ocimum sanctum*

Common name: Tulsi

Family: Lamiaceae

Parts used: Whole plant and leaf oil

O. sanctum is stated to grow worldwide, native to South Asia and it is an erect, much branched subshrub, 30–60 cm tall with hairy stems and simple opposite green or purple leaves. Chemical and nutritional composition proves *O. sanctum* a plant with varied potency. Eugenol, the bioactive constituents, additionally to eugenol leaf oil also contains euginal, urosolic acid, carvacrol, linalool, limatrol, and caryophyllene in abundant amounts (52). Mechanism of hypoglycemic effects: The antidiabetic property of tulsi was appreciated in Ayurveda. In STZ-induced diabetic rats, supplementation with the plant's ethanolic extract led to a considerable decrease in blood glucose, glycosylated haemoglobin, and urea as well as a concurrent rise in glycogen, haemoglobin, and protein levels (53). The physiological mechanisms of insulin secretion have been reported to be stimulated by the leaf extracts (54).

Table 3: Various herbs used in Diabetes

S.No.	Plant Common Name	Biological source	Phytoconstituent	Health Benefits
1	Karela	<i>Momordica charantia</i>	Charantin, Vicine, Polypeptide-p, antioxidant	Anti-diabetic Properties
2	Jamun	<i>Syzygium cumini</i>	Flavonoids, saponins, glycoside	Anti-diabetic properties, Reduce BP
3	Methi	<i>Trigonella foenum graecum</i>	Saponin, 4-Hydroxy isoleucine and Trigonelline, Alkaloid	Hypoglycemic agent
4	Dal Chini	<i>Cinnamomum zeylanicum</i>	Cinnamaldehyde	Anti-diabetic
5	Kalonji	<i>Nigella sativa</i>	Thymoquinone	Hypoglycemic agent
6	Garlic	<i>Allium Sativum</i>	Allicin	Anti-diabetic
7	Gurmar	<i>Gymnema sylvestre</i>	Triterpene Saponins (gymnemic acid and gymnemo saponins)	Hypoglycemic agent

Supplementing with macronutrients as antidiabetics: Micronutrients are vitamins, minerals, and other substances that our bodies require in minute concentrations to carry out certain tasks. They can support healthy metabolism and the conversion of sugars and other carbohydrates in your diet into energy. Micronutrients (Ca, Mg, Cr, etc.), Alpha Lipoic Acid (ALA), Coenzyme Q10, Carnitine, Inositol, Vitamins (B12, C, D, E, H), Vanadium, and others are some of the major documented nutraceuticals affecting diabetes (55).

1. Alpha-Lipoic Acid (ALA): It is a disulfide compound, produced in small amounts in cells, and serves as a coenzyme in the alpha-ketoglutarate dehydrogenase and pyruvate dehydrogenase mitochondrial enzyme complexes. ALA a potent antioxidant property, its intravenous infusion has been shown to improve insulin-mediated glucose clearance. It had been utilised to alleviate neuropathy brought on by diabetes (56). Additionally, it has been claimed that ALA protects against diabetic cardiomyopathy (57). ALA enhance insulin sensitivity and lipid metabolism, together with 13 omega 3 fatty acids and vitamin E (58). Parenterally administered ALA in 15 doses of 600 mg for 7 days had a good impact on BMI, HbA1C, and cholesterol levels. This had a demonstrable positive impact on erectile dysfunction and metabolic problem in diabetes (59). It has been discovered that ALA is useful in treating diabetic distal sensory-motor neuropathy (60).

2. Magnesium: Nerve transmission, RNA and DNA synthesis, glucose regulation, and magnesium-containing enzymes are all essential for these processes (61). Magnesium deficiency has been linked to a reduction in insulin-mediated glucose absorption. Diabetics have been found to have low blood magnesium levels and higher magnesium excretion (62). The usefulness of magnesium supplementation in preventing insulin resistance (63).

3. Chromium: People with diabetes may not have enough of the trace element chromium (64). Supplemental chromium may improve glucose tolerance and increase insulin sensitivity in persons with type 2 diabetes mellitus. The latter had a moderate but significant improvement in glycaemic control, but not the former, according to a meta-analysis of randomised controlled trials looking at the effects of chromium supplementation on glucose and insulin responsiveness in healthy persons and those with diabetes (65). The American Diabetes Association's official position is that there is contradictory evidence concerning the advantages of chromium supplementation for diabetes (66).

4. Vanadium: Research on vanadium suggests that it delivers glucose to the cells in a manner comparable to that of insulin, making it useful for both type 1 and type 2 diabetes mellitus. Vanadium supplementation also decreased fasting blood glucose, cholesterol, and haemoglobin A1c levels 50. (67-69). It may be beneficial to take doses of between 45 and 150 mg daily to raise fasting blood sugar levels. According to toxicological testing, these dose levels are secure and typically well tolerated by patients. Some persons report moderate stomach distress when taking higher dosages (up to 400 mg/day) or in the first week of treatment (70)

5. Vitamin C: It in the form of ascorbic acid is a chain-breaking antioxidant that directly neutralises reactive oxygen species (ROS) and prevents the progression of chain reactions that would otherwise lower protein glycation (71). Additionally, diabetes-related lipid peroxides and sorbitol accumulation in animal erythrocytes are reduced by vitamin C. 800 mg of vitamin C daily is given to patients with type 2 diabetes who have low vitamin C levels, but neither endothelial dysfunction nor insulin resistance are addressed (72).

6. Vitamin E: It is a necessary fat-soluble vitamin, primarily functions as an antioxidant. Low vitamin E levels have been associated with diabetes, and some research suggests that persons with diabetes also have reduced antioxidant levels. According to another study, the increased free radical production caused by hyperglycaemia may also mean that diabetic individuals need more antioxidants. Vitamin E dosages of up to 400 IU are typically regarded as safe. Although prothrombin time monitoring in supplement trials has not revealed any changes in subject prothrombin times, over-800 IU dosages may impact blood coagulation. (73).

7. Coenzyme Q10: The importance of this vitamin cannot be overstated, in part because many drugs used to treat diabetes and/or its consequences decrease Coenzyme Q10. At least in patients with hypertension, coenzyme Q10 is a possible nutritional supplement for addressing insulin resistance. Singh et al. carried out an eight-week randomised, double-blind study in 59 hypertension patients comparing the administration of a water-soluble form of CoQ10 (60 mg twice day) to a vitamin B complex. Their findings suggested a potential improvement in insulin resistance because CoQ10 at this dosage reduced fasting insulin and glucose levels (74).

8. Vitamin B: Treatment for type 2 diabetes typically includes the B vitamins thiamine (B1), pyridoxine (B6), biotin, folic acid (B9), and cobalamin (B12). Given that many people who have neuropathy also have thiamine deficits, thiamine is routinely used to treat diabetic neuropathy. Thiamine requires large dosages since it is poorly absorbed. Thiamine levels have been found to be lower in those with type 2 diabetes. Despite its usual use for treating neuropathy, thiamine has been shown to reduce glucose and lipid levels in diabetic people (75).

9. Vitamin D: Liese *et al.*, found a seasonal shift in the status of the disease's management and a correlation between geographic latitude and the prevalence of both type 1 and type 2 diabetes. This demonstrates a negative correlation between the prevalence of diabetes and sunshine. Vitamin D is believed to decrease insulin resistance and increase insulin production since pancreatic beta cells have vitamin D receptors. Vitamin D deficiency and type 2 diabetes have been connected, perhaps as a result of vitamin D being stored in fat, where it is less readily available. Lower insulin sensitivity is a result of vitamin D insufficiency, vitamin D may reduce the incidence of type 2 diabetes, according to clinical research using calcium and vitamin D supplements (76)

Table 4: Various vitamins and their health benefits

S.No.	Vitamins	Source	Health benefits
1	Vitamin A	Green leafy vegetables, Guava, Ripe yellow fruits, milk, Broccoli	Reduce Blood sugar and Potent Anti-Oxidant, Improve skin health.
2	Vitamin B1 (Thymine)	Fresh fruits, potatoes, sweet potatoes, peas, corn, cashew, nuts, milk	Control Diabetes and essential neurologic.
3	Vitamin B3 (Niacin)	Meat, fish, eggs, milk, cereals, mushroom	Reduce blood sugar.
4	Vitamin B6 (Pyridoxine)	Chicken, beans, avocado, sunflower seeds, sesame seeds	Helps to produce essential proteins and maintain blood sugar level.
5	Vitamin C (Ascorbic acid)	Fresh fruits, broccoli, goat milk, chestnuts, black currant	Anti-oxidant (reduce damage cause by free radicals), Decrease hypertension.
6	Vitamin D	Fish liver oil, egg, beef, Chicken breast	Improve glucose tolerance and insulin resistance, improve bone health.
7	Vitamin E	Potatoes, pumpkin, milk, nuts, seeds, Mango	Improve renal dysfunction, the retinal blood flow.

Marketed Antidiabetic Nutraceuticals:

1. Organic Gymnema (Himalaya)
2. Dia free juice (kapiva)
3. Glucocare (Himalaya)
4. V-GANO DIABETES
5. Nutrilite
6. Fenulife
7. Cinnamon Extract
8. Glucomap

Market Forecast for Nutraceuticals (2022-2032): The size of the world market for nutraceuticals, estimated at USD 454.55 billion in 2021, is anticipated to rise at a 9.0% compound annual growth rate (CAGR) from 2021 to 2030.

Key Companies List Profiled:

1. Herbalife Nutrition Limited is one (California, United States)
2. The Archer Daniels Midland Corporation (Illinois, United States)
3. General Mills (Minnesota, United States)
4. PepsiCo, Inc. (New York, United States)
5. BASF SE (Mannheim, Germany)
6. Abbott (Illinois, United States)
7. Amway (Michigan, United States)
8. Glanbia Plc. (Ireland)
9. Danone S.A. (Paris, France)
10. Nestle S.A. (Vevey, Switzerland).

Conclusion: When consumed within the appropriate Recommended Dietary Intakes, nutraceuticals have been shown to have positive effects on health and can help people stay healthy in general. Although nutraceuticals show great potential in promoting human health and preventing illness, regulatory toxicologists, health professionals, and nutritionists should strategically collaborate to establish proper regulation to deliver the greatest possible health and therapeutic value to humanity. To standardize the nutraceutical business, regulatory bodies must be put in place. Reviewing this subject is especially vital because the nutraceutical business is expanding far faster than the food and pharmaceutical industries. Herbal nutraceuticals are an effective tool for preserving health and combating acute and chronic illnesses caused by poor nutrition, consequently promoting good health, long life, and quality of life.

REFERENCES

- [1]. American diabetes association diagnosis and classification of diabetes mellitus, *Diabetes Care* 2009 Jan; 32(Suppl 1): S62–S67.
- [2]. Wild S. Sicree R. Roglic G. 2004. Global prevalence of diabetes. *Diabetes Care*, 27(5):1047-1053.
- [3]. Santaguida PL. Balion C. Hunt D. 2005. Diagnosis, prognosis, and treatment of impaired glucose tolerance and impaired fasting glucose. *Evid Rep Technol Assess*, 128:1–11.
- [4]. Evans JL. Goldfine ID. Maddux BA. 2002. Oxidative stress and stress activated signaling pathways: a unifying hypothesis of type 2 diabetes. *Endocr Rev*, 23(5): 599–622.
- [5]. Spranger J, Kroke A, Möhlig M. 2003. Inflammatory cytokines and the risk to develop type 2 diabetes: results of the prospective population-based European Prospective Investigation into Cancer and Nutrition (EPIC) Potsdam Study. *Diabetes*, 52(3):812–817.
- [6]. Centers for disease control and prevention. <https://www.cdc.gov/diabetes/basics/gestational.html>
- [7]. IDF Diabetes Atlas 2021 ,10th edition, www.diabetesatlas.org
- [8]. Das L. Bhaumik, E. Raychaudhuri, U., and Chakraborty, R. 2012. Role of nutraceuticals in human health. *Journal of Food Science and Technology*, 49:173–183.
- [9]. Pandey M. Verma, R.K. and Saraf S.A. 2010. Nutraceuticals: new era of medicine and health. *Asian Journal of Pharmaceutical and Clinical Research*, 3:11–15.
- [10]. Dureja H. Kaushik, D. and Kumar, V. 2003. Developments in nutraceuticals. *Indian Journal of Pharmacology*, 35:363–372
- [11]. Bagchi Debasis, Harry G Preuss, Swaroop Anand. Nutraceuticals and functional foods in human health and disease prevention , CRC press Taylor and francis Group. <http://www.taylorandfrancis.com>
- [12]. Asif M. 2014, The prevention and control the type-2 diabetes by changing lifestyle and dietary pattern. *J Educ Health Promot*. 3:3977-406. doi:10.4103/2277-9531.127541.4.
- [13]. Bhatt T, Carotenoids PK. 2020. Potent to Prevent Diseases Review. *Nat Prod Bioprospect*, 10(3):109–17. doi:10.1007/s13659-020-00244-2.5.
- [14]. Wang Z. Liu H. Luo W. 2020. Regeneration of skeletal system with genipin crosslinked biomaterials. *J Tissue Eng*. 11:2041731420974861. doi:10.1177/2041731420974861.6.
- [15]. Dhingra D. Michael M. Rajput H. Patil RT. 2011. Dietary fibre in foods: a review. *J Food Sci Technol*. 49(3):255–66. doi:10.1007/s13197-011-0365-5.7.
- [16]. Castro F. and Souza HD. 2019. Dietary Composition and Effects in Inflammatory Bowel Disease. *Nutrients*. 11(6): 1398. doi:10.3390/nu11061398.8.
- [17]. Kuijpers MC. Dijkstra G. 2021. Food and Food Groups in Inflammatory Bowel Disease (IBD): The Design of the Groningen Anti-Inflammatory Diet (GrAID). *13(4): 1067*. doi:10.3390/nu13041067.9.
- [18]. Tan BL. Norhaizan ME. Liew WP. and Rahman S. 2018. Antioxidant and Oxidative Stress: A Mutual Interplay in Age-Related Diseases. *Front Pharmacol*. 9:1162. doi:10.3389/fphar.2018.01162.10.

- [19]. Markowiak P. Sli'zewska K. 2017. Effects of Probiotics, Prebiotics, and Synbiotics on Human Health. *Nutrients*. 2017;9(9):1021. doi:10.3390/nu9091021.11.
- [20]. Dietary Supplements Market Size & Trends Report. 2021. Available from: <https://www.grandviewresearch.com/industry-analysis/dietary-supplements-market.12.13>
- [21]. Syed W. Muhammad A. Current trends and future prospect of medicinal plants derived nutraceuticals-a Review https://www.researchgate.net/publication/358571927_Current_trends_and_future_prospect_of_medicinal_plants_derived_nutraceuticals_A_review
- [22]. Rohit S. Hetal A. Prajapati PK. 2016. Plant Kingdom nutraceuticals for diabetes, *Journal of Ayurvedic and Herbal Medicine*, 2(6): 224-228.
- [23]. Hathcock J. 2001. Dietary supplements: How they are used and regulated. *J Nutrition*. 131:1114-1117.
- [24]. Zeisel SH. 1999. Regulation of Nutraceuticals. *Science*. 285:185-6.
- [25]. Brower V. 1998. Nutraceuticals: Poised for a healthy slice of the healthcare market? *Nat Biotechnol*. 16:728-31.
- [26]. Dzanis DA. 1998. Nutraceuticals: Food or drug? The North American Veterinary Conference Publishing Committee, Florida, TNAVC proceedings. 430-431.
- [27]. Prabu SL, Suriyaprakash TN, Kumar CD, Kumar SS. 2012. Nutraceuticals and their medicinal importance. *Int J Health Allied Sci*. 1:47-53.
- [28]. Krawinkel MB and Keding GB. 2006. Bitter melon (*Momordica Charantia*): A dietary approach to hyperglycemia. *Nutr Rev*. 64:331–337.
- [29]. Joseph B and Jini D. 2013. Antidiabetic effects of *Momordica charantia* (bitter melon) and its medicinal potency. *Asian Pacific journal of Tropical Medicine*. 3(2): 93–102.
- [30]. Periyathambi R. 2007. Jamun -The potential untapped. *Horticulture*. 1:30–32.
- [31]. Ayyanar M. and Subash-Babu P. 2012. *Syzygium cumini* (L.) Skeels: A review of its phytochemical constituents and traditional uses. *J Trop Biomed*. 2:240–246.
- [32]. Srivastava B. Sinha AK. Gaur S. 2012. Study of hypoglycaemic and hypolipidemic activity of *Eugenia Jambolana* pulp and seed extract in streptozotocin induced diabetic albino rats. *Asian J Pharm Life Sci*. 2:10–19.
- [33]. Sagrawat H. Mann AS. and Kharya MD. 2006. Pharmacological potential of *Eugenia jambolana*: A review. *Pharmacog Mag*. 2:96–105.
- [34]. Ravi K. Rajasekaran S. and Subramanians S. 2005. Anti-hyperlipidemic effects of *Eugenia jambolana* seed kernel on streptozotocin induced diabetic rats. *Food Chem Toxicol*. 43:1433–1439.
- [35]. Morton JF. 1987. *Fruits of Warm Climates*. Creative Resource Systems, Inc., Winterville, NC, 505.
- [36]. Kavishankar GB. Lakshmidivi N. Mahadeva MS. 2011. Diabetes and medicinal plants—A review. *Int J Pharm Biomed Sci*. 2:65–80.
- [37]. Vats V. Grover JK. and Rathi SS. 2002. Evaluation of anti-hyperglycemic and hypoglycemic effect of *Trigonella foenum-graecum* Linn, *Ocimum sanctum* Linn and *Pterocarpus marsupium* Linn in normal and allox-anized diabetic rats. *J Ethnopharmacol*. 79:95–100.
- [38]. Wang Z. Wang J. and Chan P. 2013. Treating type 2 diabetes mellitus with traditional Chinese and Indian medicinal herbs. *Evid Based Complem Alter Med*. 1–17.
- [39]. Zia T. Hasnain SN. and Hasan SK. 2001. Evaluation of the oral hypoglycemic effect of *Trigonella foenum-graecum* in normal mice. *J Ethnopharmacol*. 75:191–195.
- [40]. Sharma RD. Raghuram TC. and Rao NS. 1990. Effect of fenugreek seeds on blood glucose and serum lipids in type I diabetes. *Eur J Clin Nutr*. 44:301–306.
- [41]. Gupta A. Gupta R. and Lal B. 2001. Effect of *Trigonella foenum-graecum* (fenugreek) seeds on glycaemic control and insulin resistance in type 2 diabetes mellitus: A double blind placebo-controlled study. *J Assoc Phys India*. 49:1057–1061.
- [42]. Petit PR. Sauvaire YD. Hillaire-Buys DM. 1995. Steroid saponins behavior and plasma cholesterol. *Steroids*. 60:674–680.
- [43]. Raghuram TC. Sharma RD. Sivakumar B. and Sahay K. 1994. Effect of fenugreek seeds on intravenous glucose disposition in non-insulin dependent diabetic patients. *Phytotherapy Res*. 8:83–86.
- [44]. Saxena A. and Vikram NK. 2004. Role of selected Indian plants in management of type 2 diabetes: A review. *J Altern Complem Med*. 10:369–378.
- [45]. Lee SC. Xu WX. Lin LY. 2013. Chemical composition and hypoglycemic and pancreas-protective effect of leaf essential oil from indigenous cinnamon (*Cinnamomum osmophloeum* Kanehira) *J Agric Food Chem*. 61: 4905–4913.
- [46]. Gholamnezhad Z. Havakhah S. Boskabady MH. 2016. Preclinical and clinical effects of *Nigella Sativa* and its constituent, thymoquinone: A review. *Journal of Ethnopharmacology*. 190: 372-86
- [47]. Magkos F. Yannakoulia M. Chan J. 2009. Management of the metabolic syndrome and type 2 diabetes through lifestyle modification. *Annual Review of Nutrition*, 29:223–56.
- [48]. Bayan L. Koulivand PH. Gorji A. 2014. Garlic: a review of potential therapeutic effects. *Avicenna J Phytomed*. 4(1):1-14.
- [49]. Sugihara Y. Nojima H. Matsuda H. 2000. Antihyperglycemic effects of gymnemic acid IV, a compound derived from *Gymnema sylvestre* leaves in streptozotocin-diabetic mice. *J Asian Nat Prod Res*. 2:321–327.
- [50]. Whitman M. 2001. Understanding the perceived need for complementary and alternative nutraceuticals: Lifestyle issues. *Clin J Oncol Nurs*. 5:190-4.
- [51]. Liu B. Asare AH. Al-Romaiyan A. 2009. Characterisation of the insulinotropic activity of an aqueous extract of *Gymnema sylvestre* in mouse beta-cells and human islets of Langerhans. *Cell Physiol Biochem*. 23:125–132.
- [52]. Gholap S. and Kar A. 2003. Effects of *Inula racemosa* root and *Gymnema sylvestre* leaf extracts in the regulation of corticosteroid induced diabetes mellitus: Involvement of thyroid hormones. *Pharmazie*. 58:413–415.
- [53]. Pattanayak P. Behera P. Das D. 2010. *Ocimum sanctum* Linn. A reservoir plant for therapeutic applications: An overview. *Pharmacogn Rev*. 4:95–105.
- [54]. Narendhirakannan RT. Subramanian S. and Kandaswamy M. 2006. Biochemical evaluation of antidiabetogenic properties of some commonly used Indian plants on streptozotocin-induced diabetes in experimental rats. *Clin Exp Pharmacol Physiol*. 33:1150–1157.

- [55]. Hannan JM. Marenah L. Ali L. 2006. Ocimum sanctum leaf extracts stimulate insulin secretion from perfused pancreas, isolated islets and clonal pancreatic beta-cells. *J Endocrinol.* 189:127–136.
- [56]. Baldi A. Choudhary N. Kumar S. 2013. Nutraceuticals as therapeutic agents for holistic treatment of diabetes. *Int J Green Pharm.* 7:278-87.
- [57]. Evans JL. and Goldfine ID. 2000. Alpha-lipoic acid: A multifunctional antioxidant that improves insulin sensitivity in patients with type 2 diabetes. *Diab Technol Ther.* 2:401–413.
- [58]. Hegazy SK. Tolba OA. Mostafa TM. 2013. Alpha-lipoic acid improves subclinical left ventricular dysfunction in asymptomatic patients with type 1 diabetes. *Rev Diab Stud.* 10:58–67
- [59]. Udupa A. Nahar P. Shah S. 2013. A comparative study of effects of omega-3 Fatty acids, alpha lipoic Acid and vitamin e in type 2 diabetes mellitus. *Ann Med Health Sci Res.* 3:442–446.
- [60]. Mitkov MD. Aleksandrova IY. Orbetzova MM. 2013. Effect of transdermal testosterone or alphaslipoic acid on erectile dysfunction and quality of life in patients with type 2 diabetes mellitus. *Folia Med (Plovdiv).* 55:55–63
- [61]. Ibrahimspasic K. 2013. Alpha lipoic acid and glycaemic control in diabetic neuropathies at type 2 diabetes treatment. *Med Arh* 67:7–9.
- [62]. Swaminathan R. 2003. Magnesium metabolism and its disorders. *Clin Biochem Rev.* 13:47–66.
- [63]. Afridi HI. Kazi TG. Kazi N. 2006. Potassium, calcium, magnesium, and sodium levels in biological samples of hypertensive and nonhypertensive diabetes mellitus patients. *Biol Trace Elem Res.* 13:206–224.
- [64]. Mooren FC. Kruger K. Volker K. 2011. Oral magnesium supplementation reduces insulin resistance in non-diabetic subjects—A double-blind, placebo-controlled, randomized trial. *Diab Obes Metab.* 13:281–284
- [65]. Lau FC. Bagchi M. Sen CK. 2008. Nutrigenomic basis of beneficial effects of chromium (III) on obesity and diabetes. *Mol Cell Biochem.* 317(1-2):1–10.
- [66]. Althuis MD. Jordan NE. Ludington EA. 2002. Glucose and insulin responses to dietary chromium supplements: A meta-analysis. *Am J Clin Nutr.* 76(1):148–155.
- [67]. Dureja H. Kaushik D. Kumar V. 2003. Developments in nutraceuticals. *Indian J Pharmacol.* 35:363-72.
- [68]. Halberstam M. Cohen N. Shlimovich P. 1996. Oral vanadyl sulfate improves insulin sensitivity in NIDDM but not obese nondiabetic subjects. *Diabetes.* 45(5):659–666.
- [69]. Cohen N. Halberstam M. Schilmovich P. 1995. Oral vanadyl sulfate improves hepatic and peripheral insulin sensitivity in patients with noninsulin dependent diabetes mellitus. *J Clin Invest.* 95(6):2501–2509.
- [70]. Boden G. Chen X. Ruiz J. 1996. Effects of vanadyl sulfate on carbohydrate and lipid metabolism in patients with non-insulin dependent diabetes mellitus. *Metabolism.* 45(9):1130–1135.
- [71]. Wyn S. Managing Editor. With Diabetes Surging Some Look for Alternative Treatment. 20 October 2006.
- [72]. Riccioni G. Bucciarelli T. Mancini B. 2007. Antioxidant vitamin supplementation in cardiovascular diseases. *Ann Clin Lab Sci.* 37(1):89–95.
- [73]. Chen H. Karne RJ. Hall G. 2006. High-dose oral vitamin C partially replenishes vitamin C levels in patients with type 2 diabetes and low vitamin C levels but does not improve endothelial dysfunction or insulin resistance. *Am J Physiol Heart Circ Physiol.* 290(1):H137–H145.
- [74]. Ni Z. Smogorzewski M. Massry SG. 1994. Effects of parathyroid hormone on cytosolic calcium of rat adipocytes. *Endocrinology.* 135(5):1837–1844.
- [75]. Prunell JG. Brunzell JD. 1997. The central role of dietary fat, not carbohydrate, in the insulin resistance syndrome. *Curr Opin Lipidol.* 8(1):17–22.
- [76]. <https://www.uspharmacist.com/article/the-role-of-supplements-in-diabetes-management>