WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 7, 542-559. Review Article ISSN 2277– 7105

NUTRACEUTICALS FUNCTIONAL FOOD: A HOLISTIC APPROACH IN MANAGEMENT OF DIABETES

Nabeela Begum[1]*, Kiranmai Mandhava[1] and Venu Madhav Katla[2]

[1]Student, Department of Pharmaceutics

[1]Associate Professor, Department of Pharmaceutical Chemistry

[2]Associate Professor, Department of Pharmaceutics

St. Pauls College Of Pharmacy, Turkayamjal (501510), Nagarjunsagar Road, R.R District, Telangana, India.

Article Received on
03 May 2021,

Revised on 23 May 2021,
Accepted on 13 June 2021

DOI: 10.20959/wjpr20217-20834

***Corresponding Author**
Nabeela Begum
Student, Department of Pharmaceutics St. Pauls College Of Pharmacy, Turkayamjal (501510), Nagarjunsagar Road, R.R District, Telangana, India.

ABSTRACT

This study focussed on the role of Nutraceutical functional food in the management of Diabetes. Diabetes Mellitus is a major chronic metabolic disorder caused by an acquired deficiency in the production of insulin by the pancreas. About 422 million people worldwide have diabetes and 1.6 million deaths attributed to diabetes each year. For the management of Diabetes, Neutraceuticals functional food has been an attractive option over conventional therapies as it is of natural origin imposes fewer side effects, safer in use, and is of nutritional value. Medicinal plant-derived Neutraceutical functional food is defined as "food similar in appearance to conventional food have physiological benefits beyond basic nutritional function". Nutraceuticals comprise herbs, nutrients, dietary supplements, vitamins, and micronutrients. Functional food composed mainly of bioactive components of medicinal plant extracts containing anti-diabetic properties plays a significant role to combat chronic diseases like diabetes. Healthy antioxidants and nutrient-rich food incorporated into the diet of diabetic patients help to overcome diabetic-associated complications such as oxidative stress, obesity, etc. These also have major value in consumer demand and have become the promising approach in the management of Diabetes. This review summarizes Neutraceutical functional food ingredients and herbals extract bioactive phytochemicals with anti-diabetic properties benefiting the quality lifestyle of the diabetic population.

KEYWORDS: Diabetes Mellitus, Nutraceuticals, Functional Food, Diet, Herbal extracts, Bioactive phytochemicals.

INTRODUCTION

The term Nutraceuticals is a combination of nutrition and pharmaceutical. Nutraceuticals are foods or part of foods that play a significant role in maintaining many physiological functions to maintain human health and in preventing and treating many acute and chronic diseases.[1] Foods with biologically active ingredients are considered functional because of their association with physiological health benefits related to the prevention of several chronic diseases such as type 2 diabetes mellitus.[2] Recent years witnessed an upsurge in the use of nutraceuticals in therapeutics at the global level. Conventional treatment options available as synthetic drugs do not meet properly the therapeutic needs for treating diabetes and the herbal drugs provide better therapeutic hope with lesser side effects. WHO defined diabetes mellitus as a chronic disease caused by inherited and/or acquired deficiency in the production of insulin by the pancreas, or by the ineffectiveness of the insulin produced and is characterized by hyperglycemia or hypoglycemia.[3-5] Diabetes Mellitus is of two types i.e. type 1(insulin-dependent) and type 2(insulin-independent) this type is more prevalent in adults than type 1 diabetes.[6] Type 2 Diabetes is a chronic metabolic disorder of multiple etiology characterized by hyperglycemia with disturbances in the metabolism of insulates, a fat, protein that results from defects in secretion and action of insulin, or both. It is associated with severe long-term complications, such as retinopathy, nephropathy, neuropathy, myocardial infarction, cerebral embolism, and blood vessel damages.[7] Minor changes in lifestyle and dietary habits can reduce the chance of getting this condition. The dietary pattern emphasizes consumption of foods high in unsaturated fatty acids encourage daily consumption of fruits, vegetables, low-fat dairy products, and whole grains, low consumption of fish, poultry, tree nuts, legumes, very little consumption of red meat.[8-9-10] These functional foods containing polyphenols, terpenoids, flavonoids, alkaloids, sterols, pigments, and unsaturated fatty acids play an important role in maintaining wellness and contribute to preventing cancer, depression, type 2 diabetes mellitus, obesity, asthma, and cognitive decline.[11-12] Specific to type 2 diabetes mellitus, consumption of such foods involved an enhanced anti-oxidant, anti-inflammatory, and anti-cholesterol properties, enhanced insulin sensitivity, and reduced insulin resistance, considered integral parts in the prevention, management, and treatment of type 2 diabetes mellitus.[13]

It is reported that about 422 million people worldwide suffering from diabetes, the majority living in low-and middle-income countries, and 1.6 million deaths are attributed related to diabetes each year. Both the number of cases and the prevalence of diabetes have been steadily increasing over the past few decades.[14] Diabetes is a growing challenge in India with an estimated 8.7% diabetic population in the age group of 20 and 70 years. The worldwide prevalence of diabetes for all age groups was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030.[15] The greatest increase in prevalence is, however, expected to occur in Asia and Africa, Where most patients were likely to be found by 2030.[16] Recently, Nutraceuticals have received attention due to their potential nutritional value, safety, and therapeutic effectiveness. Therefore, the recent analysis by BCC research stated that the global market of nutraceutical is expanding at an annual growth rate(CAGR) of 7.5% would reach from $198.7 billion in 2016to US $285.0 billion by 2021[17] Despite significant research and developmental effort in this area, many technological, marketing and regulatory challenges still need to be addressed for functional food to succeed in the marketplace.[18]

Nutraceuticals

The concept was first originated in JAPAN. The term Nutraceutical was first coined by DeFelice in 1989 and is defined as "any substance that may be considered a food or part of a food and provides medical or health benefits, including the prevention and treatment of disease". Such products may range from isolated, dietary supplements, nutrients, and diets to genetically engineered 'designer' foods, herbal products, and processed foods(cereals, soups, and beverages).[19] Human inquisitiveness and search for a specific constituent of natural origin that benefits human health can be accomplished with the incorporation of Nutraceuticals.

Categories of nutraceuticals

A nutraceutical can be grouped into the following three broad categories.

Nutrients: Substances with enhanced nutritional functions, such as vitamins, amino acids minerals, and fatty acids.

Herbals: Herbs or medicinal plant products as concentrates and extracts.

Dietary supplements: Reagents derived from other sources (e.g. pyruvate, Chondroitin Sulphate, steroid hormone precursors) serving specific functions, such as sports nutrition, weight-loss supplements, and meal replacement.

Nutraceuticals are usually consumed in pharmaceutical Preparation are such as pills, capsules, tablets, powder, etc. Pharmaceuticals are usually synthesized from pure chemicals and the efficacy was clinically proved to prevent some diseases and is usually associated with undesirable side effects, In contrast, Neutraceuticals are routinely used in the treatment of certain symptoms and are expected to be safer with fewer side effects than conventional Pharmaceuticals. Hence, Nutraceuticals have received recognition for their potential beneficial health effects when consumed as part of the diet, various nutrients are indicated in figure 1.

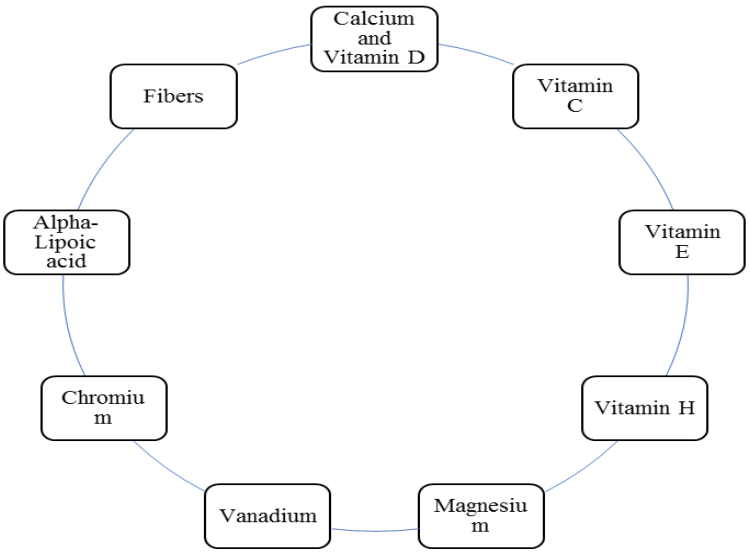

Figure 1: Various vitamins and micronutrients used as nutraceuticals in the treatment of diabetes.[20]

Antioxidants vitamins: An adequate supply of antioxidants in diet may prevent diabetes complications such as renal and neural dysfunction by protecting against oxidative stress indicated by animal studies.

Calcium and Vitamin D

Role of diet on Diabetes risk identified with high calcium intake. Calcium/vitamin D helps to preserve insulin sensitivity and thus prevent diabetes by suppression of the parathyroid hormone (PTH) secretion that compromise adipose insulin sensitivity by increasing free calcium.[21]

Vitamin C

Ascorbic acid is a chain-breaking antioxidant that directly scavenges ROS and propagates the chain reaction results in a reduction of protein glycation. Hence prevent diabetes.[22]

Vitamin E

Vitamin E is an essential fat-soluble vitamin and functions primarily as an antioxidant**.** Diabetes is associated with a low level of vitamin E and hence Doses of vitamin E up to 400 Mg is generally believed to be safe and helps to combat oxidative stress.[23]

Vitamin H

Vitamin H is biotin and part of vitamin B complexes. Help the body to metabolize fats and proteins. Biotin levels influence blood sugar levels and tend to be lower in people with type 2 diabetes.[24]

Magnesium

Magnesium deficiency may worsen the blood sugar control in type 2 diabetes interrupts insulin secretion by the pancreas and increases insulin resistance in the body tissues. A magnesium-rich diet decreases the risk of diabetes.[25]

Vanadium

Research indicates that this mineral acts similarly to insulin in transporting glucose into the cells, and is therefore valuable for diabetes mellitus. Vanadium supplementation decrease fasting blood glucose levels, Haemoglobin A1c levels, and cholesterol levels 50. Dose-ranging from 45-150 mg/day is beneficial in improving fasting glucose levels.[26]

Chromium

It is the most known of anti-diabetic ingredients, a trace mineral, which potentiates the actions of insulin. Studies reported that chromium supplementation may improve diabetes control.[27]

Alpha-Lipoic acid

It is the most promising natural treatment of diabetes and researchers concluded that three weeks of treatment using 600mg per day of alpha-lipoic acid reduces the symptoms of diabetic neuropathy a complication of diabetes.[28]

Dietary fiber supplements

Dietary fiber characterizes a heterogeneous group of natural food sources such as commercial supplements and processed grains. It includes polysaccharides oligosaccharides and associated plant substances. Several forms of dietary fibers are used as complementary or alternative agents in the management of metabolic disorders. Soluble dietary fiber

consumption is associated with lower postprandial glucose levels withstand insulin sensitivity in diabetic and healthy subjects. Insoluble dietary fiber exerts a negligible effect on postprandial glycemia. Increased consumption of cereal dietary fiber significantly reduces the risk of diabetes that includes 2 servings per day increment in whole grain consumption may reduce with increase diabetes by 21%.[29]

Example of food with higher content of specific nutraceutical substances

sulfur compounds – Onions, garlic

Isoflavones (e.g., genistein, daidzein) –Soybeans, legumes.

Quercetin – Onion, red grapes, citrus fruit, broccoli, Italian yellow squash

Capsaicinoids- Pepper fruit

EPA and DHA - Fish oils

Lycopene – Tomatoes and tomato products

Isothyocyanates- Cruciferous, vegetables

β-Glucan- Oat bran

CLA – Beef and dairy

Resveratrol – Grapes (skin), red wine

B-Carotene – Citrus fruit, carrots, squash, pumpkin

Carnosol- Rosemary

Catechins - Teas, berries

Adenosine – Garlic, onion

Indoles – Cabbage, broccoli, cauliflower, kale, brussels sprouts

Curcumin -Tumeric

Ellagic acid – Grapes, strawberries, raspberries, walnuts

Anthocyanins- Red wine

3-n-butyl phthalide – Celery

Cellulose – Most plants (a component of cell walls)

Zeaxanthin, Lutein- Kale, collards, spinach, corn, eggs, citrus

Psyllium – Psyllium husk

Monounsaturated fatty acids – Tree nuts, olive oil

Inulin, Fructooligosaccharides (FOS) – Whole grains, onions, garlic

Lactobacilli, Bifidobacteria- Yogurt and another dairy

Catechins – Tea, cocoa, apples, grapes

Lignans - Flax, rye

Functional food

Food Information Council (IFIC) defines functional foods as "foods or dietary components that may provide a health benefit beyond basic nutrition". When the bioactive compound is included in a food formulation with a specific purpose, the new product could be considered a functional food. There are three important aspects of functional food- 1. The functional effect is different from that of normal nutrition, 2. The functional effect must be demonstrated satisfactorily, 3. The benefit can consist of an improvement of physiological function or reducing the risk of developing a disease.[30]

Functional foods are of two types 1. Conventional functional food which Natural whole food ingredient rich in important nutrients (vitamin, mineral, antioxidant, heart-healthy fat) ex: fruit vegetables seeds nuts whole grains, etc., 2. Modified functional food Which is fortified with additional ingredients (vitamin, mineral, fiber, or probiotic to increase food health benefit). ex: fortified juices, fortified dairy products, fortified milk alternative, fortified grains, etc.

The functional food industry has a growing interest in developing functional food upon consumer demand for food products.

Table 1: Availability of nutraceuticals in different food formats.

Nutraceuticals ingredients	Food formats
Dietary Lipids(Eicosapentaenoic acid, docosahexaenoic acid, alpha-linoleic acid)	Fish, algae, krill, genetically modified seeds
Phenolic compounds and polyphenols(Phenolic acids, resveratrol, curcuminoids, catechins, flavanols, and flavones,)	Tea, grapeseed, olives, pomegranates, wine, cocoa, vegtables.
Carotenoids(beta carotene, lycopene, lutein, astaxanthin)	Carrot, tomatoes, marigolds, green leafy vegetables, microalgae.
Bioactive peptides	Milk, meat, fish, plants.
Minerals(Ca, Fe, Mg, Zn)	Usually available as salts Soluble vitamins

Table 1 illustrate Nutraceutical ingredients from different food sources available in the form of different functional food types such as super food, health food, enhance food, enriched food, fortified foods and beverages[18]

Perhaps no other disease is closely linked to nutrition as diabetes and nutrition are also one of the most powerful tools in the management of diabetes. Functional foods present within the mediterranean diet containing polyphenols, terpenoids, flavonoids, alkaloids, sterols, pigments, and unsaturated fatty acids play an important role in maintaining wellness and contribute to preventing cancer, depression, diabetes, obesity, asthma, and cognitive decline.[31-32] Regular consumption of functional food with antioxidant, anti-inflammatory, anti-cholesterol, enhanced insulin sensitivity, and red reduce insulin resistance is considered an intan integral part of the prevention and management of diabetes.[33]

Natural herbal extracts

Phytoconstituentswith anti-diabetic activity

Many phytoconstituents have been isolated from medicinal plants including the compounds belongs to the class of alkaloids, glycosides, terpenoids, flavonoids and are constituted as vital elements to combat diabetes mellitus.

Alkaloids: different alkaloids have been isolated from the medicinal plant and exert a wide range of anti-diabetic activity.

Berberine, an isoquinoline alkaloid obtained from the roots and stem bark of Berberis L. (Berberidaceae). Berberine acts as antihyperglycemic agent by inhibiting the activity of disaccharidases in Caco-2 cells due its ability to inhibit alpha-glucosidase and decrease glucose transport through the intestinal epithelium.[34]

Leurosine, vindoline, vindolinine and catharanthine isolated from Catharanthus roseus (L.) G. Don (Apocynaceae) reduces blood glucose in normal and alloxan diabetic rabbits.[35]

Cryptolepine is an indoloquinolone alkaloid isolated from Cryptolepis sanguinolenta (Apocynaceae) have antihyperglycaemic effect leads to a significant decline in blood glucose concentration, associated with evidence of an enhancement in insulin-mediated glucose disposal.[36]

Piperinefound in the family of Peppers (Piperaceae) potentially useful to prevent diabetic vascular complications by attenuating vascular inflammation.[37]

Glycoside: Phenolic glycosides and hederagenin glycosides were isolated from the stem bark of Kalopanax pictus Nakai (Araliaceae). The antidiabetic evaluation of these Isolated

compounds in streptozotocin-induced diabetic rats showed that Kalopanax (saponin A) has potent antidiabetic activity in contrast to mild activity to hederagenin.[38]

Neomyrtillin extracted from the leaves of V. myrtillus (Ericaceae) which is used widely as a treatment for diabetes before the availability of insulin and the compond is found to be effectiva in reducing glycosuria and postprandial hyperglycemia in most adult-onset diabetic patients.[39] flavonoids glucoside viz, vitexin, isovitexin, and isorhamnetin 3-O-D-rutinoside isolated from the leaves of Microcos paniculata L. (Tiliaceae), were investigated for their -glucosidase inhibitory effects revealed satisfactory inhibitory effects.[40]

Flavonoids: Flavonoids can be widely classified into different categories like Anthocyanins, catechins, flavonols, flavones, flavanones, etc. Some flavonoids have hypoglycemic properties.

Anthocyanins, a group of polyphenols extracted from berries prevent type 2 diabetes and obesity. Anthocyanins from different sources have been shown to affect glucose absorption and insulin level, secretion, action, and lipid Metabolism.[41]

Polyphenols such as catechin, epicatechin, epigallocatechin, epicatechin gallate and Isoflavones from soya beans also decrease S- Glut-1 mediated intestinal transport of glucose.[42] Epigallocatechins gallate constituent in green tea (Camellia sinensis) Modulate vascular inflammation in diabetic patients.

Apigenin, chrysin, kaempferol, luteolin, myricetin and quercetin belong to the group of Flavones and flavonols, these compounds are widely regarded as strong antioxidants and anti-inflammatory plays an important role in diabetic vascular complications. Quercetin is an important flavonoid and their administration to streptozocin induced diabetic rats results in marked reduction of plasma glucose level in a glucose tolerance tests, reduced plasma cholesterol and triglycerides significantly and increased their hepatic glucokinase activity probably by enhancing the release of insulin from pancreatic islets of the diabetic rats.[43]

Terpenoids and Steroids: Triterpenes are precursors to steroids in both plants and animals. Triterpenoid and steroidal glycosides are collectively referred to as saponins. These are bioactive compounds known to possess potent hypoglycemic activity.

Charantin a steroidal saponin, obtained from Momordica charantia L. (Cucurbitaceae) seeds is having insulin-like activity, responsible for its hypoglycemic effect.[44]

Corosolic acid used from the VitexleucoxylonL.f. (Lamiaceae) was found to be effective in treating inflammatory conditions and diabetes. Iridoid glucoside is a monoterpene isolated from the leaves of V. negundo L. and evaluates its effects on the arrangement in plasma and tissue glycoprotein components in streptozotocin-induced diabetic rats indicate the levels of blood glucose, plasma, and tissue glycoproteins were significantly increased whereas plasma insulin levels were significantly decreased in diabetic rats.[45]

Ginsenosides, a steroidal saponin bioactive constituents isolated from ginseng (Panax spp.) (Araliaceae). Some ginsenosides have demonstrated hypoglycemic properties studies performed by Chung et al. showed that ginseng has distinct anti-diabetic properties.[46]

Ruscogenin Belongs to the group of steroid saponins isolated from rhizomes of Ruscusaculeatus also found in RafixOphiopogon japonicas, an important herb for the treatment of diabetes, inflammatory disease, and cardiovascular.[47]

Polysaccharide: Various plants like Aloe vera (L.) Burm. f. (Xanthorrhoeacare), Ocimum sanctum L. (Lamiaceae), and Alpinia galanga (L.) Willd. (Zingiberaceae) have been found to contain polysaccharides. Polysaccharide acts differently by several mechanisms such as those by increasing the serum insulin levels, reduces the blood glucose levels, and improves glucose tolerance. Many polysaccharides have been proven beneficial for the treatment of hypoglycemia those are glycans which contain anemarans, Atractans, Polysaccharidede glucomannan, lithospermans, and oryzarans etc.[48]

Miscellaneous: Resveratrol represents a group of polyphenolic compounds called stilbenes and is present in some plants (grapes, peanuts, and berries) and red wine. Resveratrol is having antioxidant and anti-inflammatory properties beneficial in treating Diabetic foot syndrome which results from impaired tissue regeneration, vasculopathy, neuropathy, and inflammation due to insulin resistance. dietary polyphenols (resveratrol) May considerably yeild effects on glucose homeostasis. It has been shown in vitro and in vivo studies that pure resveratrol can considerbly improve glycemic profiles, normalize insulin secretion rate and insulin.[49]

Curcumin is a key curcuminoid found in turmeric (Curcuma longa Linn.) and has shown antidiabetic, cholesterol-lowering, and anti-inflammatory properties. Evaluated in vitro for the alpha-glucosidase inhibitory activity. The results of the study have shown that that the curcuminoid compound bis dimethoxy curcumin showed a remarkable inhibitory effect.[50]

Table 2: Herbal nutraceutical of popular indian herbs with antidiabetic potential.

Plant	Family	Plant part	Bioactive compounds
Blackberry (*Eugenia jambolana)*	*Myrtaceae*	leaves, bark, root, stem, seeds.	Flavonoids, alkaloids, sterols, tannins, Carbohydrate, polyphenols, ellagic acid, salicylic acid, fiber
Peepal (*ficusreligiosa)*	*Moraceae*	Leaves, bark, fruits, roots, seed.	Flavonoids, glyco sites, alkaloids, steroids, saponins, vitamin C, and enzymatic constituents are catalase, peroxides, etc.
Fenugreek (*Trigonellafoenum*grace*)*	*Fabaceae*	Leaves and seeds.	Saponins, steroids, methanol extract, gingerol, Eugenol, cedrane, vanillin,zingerone.
Onion (*Allium cepa)*	*Amaryllidaceae*	Whole.	Alkaloids, flavonoids, cardiac glycosides, terpenes, steroids, and resins.
Bittermelon (*Momordicacharantia)*	*Cucurbitaceae*	Pulp, sea, and leaves.	Triterpene, protein, steroid, alkaloid, inorganic, lipids and phenolic compounds, saponins, charantin, resins.
Holy basil (*Ocimum sanctum)*	*Lamiaceae*	Leaves	Volatile oil, crisilineol, circimaritin, isothymusin, rosmeric acid, apigenin, campesterol
Gum arabica (*Acacia nilotica)*	*Fabaceae*	Bark, pods, leaves	Tannins, Gallic acid, alkaloids, saponins
Aloe vera (*mill)*	*Asphodelaceae*	Leaves extract	Anthraquinone, glyco sites, vitamin ACE, lipids, sterols, gibberlins, psuedoprototinosaponin A111 and prototinosaponin A111
Gooseberry *(Ribesuvacrispa)*	*Grossulariaceae*	Whole	Tannins, phenols, alkaloids, flavonoids,

			gallic acid, corilagin, geraniin, elllagic acid.
Olives *(Oleaeuropaea)*	*Oleaceae*	Leaves, fruits, roots	Alkaloids, terpenes, ethanol, tyrosol, oleosides, secoridoids
Cumin *(Syzygiumcumini)*	*Umbellifers*	Seeds	Flavonoid, anthraquinones, phyto sterol, saponins, steroids, tannins, triterpenoids
Cinnamon *(Cinnamomum cassia)*	*Lauraceae*	Stems, seeds	Methyl hydroxychalcone, tannins, flavonoids, glycositdes, terpenenoids, coumarins, anthraquinones
Ginger *(Zigiberofficinale)*	*Zingiberaceae*	Whole	Flavonoids, saponins, tannins, terpenoids, phenols
Garlic *(Allium sativun)*	*Amaryllidaceae*	Whole	Alkaloids, saponins, steroids, carbohydrates, tannins, flavonoids, terpenoids, phenolics
Curru leaves *(Murrayakoenigii)*	*Rutaceae*	Leaves	Carbohydrates, alkaloids, phytosterols, alcohol, flavonoids, saponins, tannins, glycosidase, carbohydrates
Coriander *(Coriandrumsativum)*	*Umbellifers*	Leaves, roots and seeds	Flavonoids, steroids, amino acids, saponins and tannins
Pippermint *(Menthapiperita)*	*Lamiaceae*	Leaves	Flavonoids, phenols, terpenes
Cardamom *(Elettariacardamomum)*	*Zingiberaceae*	Leaves, fruit, seeds	Epicatechin, flavanoids, tannins, saponins, quinone, glycoside, terpenenoids, phenol, steroids, alkaloids, anthocyanin
Black pepper *(Piper nigrum)*	*Piperaceae*	Seeds	Alkaloids, flavonoids, steroids, lignans, phenolic, terpenes
Guava *(Psidiumguajava)*	*Myrtaceae*	Leads, Flowers, bark, roots, twig, fruit skin	Oxalic acid, malic acid, amylase, phenylpropylacetate, butanyl acetate, tannins, resins, tannic acid, flavanoids, calcium oxalate, phenolic acid
Mulberry *(Morindacitrifolia)*	Moraceae	Leaves, fruit	Rutin, isoquercitrin, astragalin, caffeic acid, ethanol, kaempferol,

			methanol
Radish *(Raphanussativus)*	*Brassicaceae*	Roots and leaves	Acetone, acetic acid, anthocyanin, phenols, anthocyanin, potassium chloride, sodium acetate, trifluoroacetic acid
Sesame seed *(Sesamumindicum)*	*Pedaliaceae*	Seeds, leaves	Flavonoids, protein, triterpenes, ethanol, polyphenols
Celery seeds *(TrachyspermumAmmi)*	*Apiaceae*	Seeds, leaves	Alkaloids, flavonoids, steroids, tannins, saponins, glycosides, proteins, quinones, coumarins
Senna *(Senna didymobotyra)*	*Legumes*	Leave	Flavonoids, steroids, phenols, tannins, alkaloids, terpenoids, glycosidase, saponins
Fennel *(Foeniculum)*	*Umbellifers*	Leaves, flowers	Tannins, saponins, flavonoids, alkaloids, terpenoids
Licorice root *(Glycyrrhizaglabra)*	*Legumes*	Leaves, roots, stem, fruit	Flavanoid, steroids, amino acid, saponins, terpenoids, tannic acid, flavonoid, coumarins, still bend

Table 2 illustrates the list of popular Indian herbs with Nutraceutical bioactive component with anti-diabetic activity helpful in the management of Diabetes.[51-52]

CONCLUSION

It was clear that many natural products have anti-hyperglycemic, hypoglycemic, anti-inflammatory, anti-oxidative, anti-hyperlipidaemic, and insulin-sensitizing activities. Most of the natural medicinal plant-derived nutraceutical functional food used in clinical practice is known to modulate pathogenesis underlying diabetes mellitus providing a promising approach to prevent and manage Diabetes. The potency of herbal drugs and functional food are significant and have negligible side effects than synthetic anti-diabetic treatment. Consumptions of low carbohydrate functional food rich in antioxidants in the diet of diabetic patients help to combat oxidative stress minimizing Diabetic complications. Despite extensive research, the search for effective treatment remains explosive. Simultaneous administration of herbal Nutraceutical functional food may be the most suitable solution for the holistic treatment of diabetes.

FUNDING

Nill

AUTHORS CONTRIBUTION

All the authors have contributed equally

CONFLICT OF INTEREST

The authors declare no conflict of interest

REFERENCES

1. SaurabhNimesh, VrishDhwajAshwlayan.Nutraceuticals in the management of diabetesmellitus.Pharm Pharmacol Int J, 2018; 6(2): 114-120.
2. Ahmad Alkhatib, Catherine Tsang, Ali Tiss, TheeshanBahorun, Hossein Arefanian, RoulaBarake.Functional Foods and Lifestyle Approaches forDiabetes Prevention and Management. MDPI J.Nutrients, 2017; 9, 1310: 1-8.
3. World Health Organization. Definition, diagnosis, and classification of diabetes mellitus and its complications: report of a WHO consultation. Part 1. Diagnosis and classification of diabetes mellitus, 1999.
4. American Diabetic Association. Classification Diagnosis Diabetes, 2015; 38, 1: S8-16.
5. Li WL, Zheng HC, Bukuru J, De Kimpe N. Natural medicines used in the traditional Chinese medical system for therapy of diabetes mellitus. J Ethnopharmacol, 2004; 92: 1-21.
6. Nagalakshmi K, Sujatha S. Nanoencapsulation augments release efficiency and glucose tolerance of 14-deoxy, 11,12-didehydro andrographolide loaded polycaprolactone nanoparticles in streptozotocin-nicotinamide induced type 2 diabetes. Int J Appl Pharm, 2017; 9: 51-3.
7. Simonetta Ballali1 & Federico Lancia.Functional food and diabetes: A natural way in diabetes prevention?. International Journal of Food Sciences and Nutrition, 2011: 1-11.
8. American Diabetes Association. Standards of medical care in diabetes-2010. DiabetesCare, 2010; 33(1): S11–61.
9. American Diabetes Association: Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications (PositionStatement) Diabetes Care, 2003; 26(1): S51–61.

10. Barnard ND, Socially AR, Turner-McGreevy G, Lanou AJ, Glass J. The effects of a low-fat, plant-based dietary intervention on body weight, metabolism, and insulin sensitivity. Am J Med, 2005; 118: 991-7.
11. Vasto S, Barera A, RizzoC, Di Carlo M, CarusoC, Panotopoulos G. Mediterranean diet, and longevity:An example of nutraceuticals? Curr. Vasc. Pharmacol, 2014; 12: 735–738.
12. GrecaM, Zarrelli A. Nutraceuticals and the Mediterranean diet. Med. Aromat. Plants, 2012; 1: e126.
13. GeorgoulisM, Kontogianni M.D,YiannakourisN. Mediterranean diet, and diabetes: Prevention andtreatment. Nutrients, 2014; 6: 1406-1423.
14. Diabetes overview. Available from: https://www.who.int/health-topics/diabetes#tab=tab_1. Accessed on:14 Feb 2021.
15. Sarah Wild, Mb Bchir, GojkaRoglic, Anders Green, Richard Sicree, Hilary King, Globe Prevalence Of Diabetes.Estimates For The Year 2000 And Projections For 2030, Diabetes Care, 2004; 27(5): 1047-1053.
16. AsishBaldi, Naveen Choudhary, SumitKumar.Nutraceuticals as therapeutic agents for holistic treatment of diabetes.Int J Green Pharm, 2013; 7: 278-87.
17. Nutraceutical:Global Markets. Available from. https://www.bccresearch.cNutrah/food–and–beverage/nutraceuticals–markets–report–fod013f.html. Accessed on: 14 Feb 2021.
18. Mary Ann Augustin and Luz. Challenges and solutions to the incorporation of neutraceuticals in foods. Rev. Food Sci. Technol, 2015; 6(0): 463-77.
19. Robert E.C, Wildman and Mike Kelley.Handbook of nutraceuticals and functional foods.Robert E.C,Wildman, editors.chapter 1:Nutraceuticals and Functional foods. Newyork: CRC press, 1964; 2: 1-22.
20. G. Joana Gil-Chávez, José A. ViVill, J. Fernando Ayala-Zavala, J. BasilioHeredia, DavidSepulveda, Elhadi M. Yahia, Gustavo A. González-Aguilar.Technologies for Extraction and Production of Bioactive Compounds to be Used as Nutraceuticals and Food Ingredients: An Overview. Comprehensive reviews in food science and food safety, 2013; 12: 5-23.
21. Mitri J, Dawson‐Hughes B, Hu FB, Pittas AG. Effects of vitamin D and calcium supplementation on pancreatic β cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: The calcium and vitamin D for diabetes mellitus (CaDDM) randomized controlled trial. Am J ClinNutr, 2011; 94: 486-94.

22. Riccioni G, Bucciarelli T, Mancini B, et al. Antioxidant vitamin supplementation in cardiovascular diseases. Ann Clin Lab Sci, 2007; 37(1): 89-95.
23. Sarubin A. The Health Professional's Guide to Popular Dietary Supplements. Chicago, IL: The American Dietetic Association, 2000; 692.
24. Will JC, Byers T. Does diabetes mellitus increase the requirement for biotin? Nutr Rev, 1996; 54: 193‑202.
25. Badyal A, Sodhi KS, Pandey R. Emerging clinical significance of magnesium In type 2 diabetes mellitus. Curr Trends BiotechnolChem Res, 2011; 1: 53‑9.
26. SaurabhNimesh, VrishDhwajAshwlayan. Nutraceuticals in the management of diabetes Mellitus. Pharm PharmacolInt J, 2018; 6(2): 114-120.
27. Freund H, Atamian S, Fischer JE. Chromium deficiency during total parenteral nutrition. JAMA, 1979; 241: 496‑8.
28. Packer L, Kraemer K, Rimbach G. Molecular aspects of alpha-lipoic acid in the prevention of diabetes complications. Nutrition, 2001; 17: 888‑95.
29. International Food Information Council. Web site, http://ific.org/nutrition/functional/index.cfm, 2006.
30. Plaza M, Cifuentes A, Ibáñez E. In the search for new functional food ingredients from algae. Trends Food SciTechnol, 2008; 19(1): 31– 9.
31. Vasto S, BareraA,RizzoC, Di CCarl M, CarusoC,Panotopoulos G. Mediterranean diet, and longevity:An example of nutraceuticals? Curr. Vasc. Pharmacol, 2014; 12: 735-738.
32. GrecaM,Zarrelli A. Nutraceuticals and the Mediterranean diet. Med. Aromat. Plants, 2012; 1: e126.
33. Georgoulis, M. Kontogianni, M.D.Yiannakouris, N. Mediterranean diet, and diabetes: Prevention andtreatment. Nutrients, 2014; 6: 1406–1423.
34. PanG.Y, Huang Z.J, WangG.J, Fawcett J.P, LiuX.D, ZhaoX.C, SunJ.G, Xie Y.Y. The antihyperglycaemic activity of berberine arises from a decrease of glucose absorption. Planta Med, 2003; 69: 632–636.
35. Chattopadhyay, R.R. A comparative evaluation of some blood sugar lowering agents of plant origin. J. Ethnopharmacol, 1999; 67: 367-372.
36. Luo J, Fort D.M, Carlson T.J, NoamesiB.K, nii-Amon-KoteiD, KingS.R, et al. Cryptolepsissanguinolenta: an ethnobotanical approach to drug discovery and the isolation of a potentially useful new antihyperglycaemic agent. Diabet. Med, 1998; 15: 367-374.

37. Eshaifol A Omar, Antony Kam, Ali Alqahtani, Kong M Li, Valentina Razmovski-Naumovski, Srinivas Nammi, et Al. Herbal medicines and nutraceuticals for diabetic vascular complications: mechanisms of action and bioactive phytochemicals. Current Pharmaceutical Design, 2010; 16: 3776-3807.
38. H J Park , D H Kim, J W Choi, J H Park, Y N Han. A potent antidiabetic agent from Kalopanaxpictus. Arch. Pharm. Res, 1998; 21: 24-29.
39. Allen F.M., Wilder R.M., Blueberry leaf extract: physiologic and clinical properties about carbohydrate metabolism. JAMA, 1927; 89: 1577-1581.
40. Chen Y.G, Li P, Yan R, Zhang X.Q, Wang Y, Zhang X.T, et al.Alpha-glucosidase inhibitory effect and simultaneous quantification of three major flavonoid glycosides in Microctis folium yan-ganChen, Molecules, 2013; 18: 4221-4232.
41. Jayaprakasam B, Varied S.K,OlsonL.K, Nair M.G. Insulin secretion by bioactive anthocyanins and anthocyanidinspresent in fruits. J. Agric. Food. Chem, 2005; 53: 28-31.
42. TiwariA.K, RaoJ.M.Diabetes mellitus and multiple therapeutic approaches of phytochemicals: present status and prospects. Curr. Sci, 2002; 83: 30-38.
43. Manickam M, RamanathanM, Jahromi M.A, ChansouriaJ.P, Ray A.B. Antihyperglycaemic activity of phenolics from Pterocarpus marsupium. J. Nat. Prod, 1997; 60: 609-610.
44. FortD.M, Ubillas R.P, Mendez C.D, JoladS.D, InmanW.D, CarneyJ.R. Novel antihyperglycemicterpenoidquinones from Pycnanthusangolensis. J. Org. Chem, 2000; 65(20): 6534-6539.
45. SundaramR, Naresh R, ShanthiP, SachdanandamP. Anti-hyperglycemic effect of iridoid glucoside, isolated from the leaves of Vitexnegundo in streptozotocin-induced diabetic rats with special reference to glycoprotein components. Phytomedicine, 2012; 19(3-4): 211-216.
46. Jing-TianXie,MehendaleS, Chun-Su Yuan. Ginseng and Diabetes. Am. J. Chin. Med, 2005; 33(3): 397-404.
47. Huang YL, Kou JP, Ma L, Song XJ, Yu BY. Possible mechanism of the anti-inflammatory activity of ruscogenin: Role of intercellular adhesion molecule-1 and nuclear factor-kappa. B J Pharmacol Sci, 2008; 108(2): 198-205.
48. Swati B. Gaikwad, G. Krishna Mohan, and M. Sandhya Rani. Phytochemicals for Diabetes Management. Pharmaceutical Crops, 2014; 5: 11-28.
49. Yuriy K. Bashmakov, Samir Assaad-Khalil b, Ivan M Petyaev. Resveratrol may be beneficial in the treatment of diabetic foot syndrome. Med Hypotheses, 2011: 1-4.

50. Du Z.Y, Liu R.R, Shao W.Y, Mao X.P, Ma L, Gu LQ. Alpha-Glucosidase inhibition of natural curcuminoids and curcumin analogs. Eur. J. Med. Chem, 2006; 14: 213-218.
51. Dimple, AshwaniKumar, VikasKumar, VidishaTomar. Traditional medicinal systems for treatment of diabetes mellitus: A review. Int J Pharm Sci, 2018; 10(5): 7-17.
52. Giovanni Davi, Francesca Santilli, Carlo Patrono. Nutraceuticals in diabetes and metabolic syndrome. Cardiovascular Therapeutics, 2010; 28: 216-226.