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Plant kingdom Nutraceuticals for diabetes

Rohit Sharma[1], Hetal Amin[2], PK Prajapati[3]

1 *Research Officer, Central Ayurveda Research Institute for Drug Development, CCRAS, Ministry of AYUSH, Government of India, Bidhannagar, Kolkata-700091, India*

2 *Assistant Professor, Department of Basic Principles, Faculty of Ayurveda, Parul University, Vadodara, Gujarat-391760, India*

3 *Professor and HOD, Department of Rasashastra & Bhaishajya Kalpana, All India Institute of Ayurveda, New Delhi, Delhi- 110076, India*

ABSTRACT

Recent years witnessed an upsurge in the use of nutraceuticals, nutritionals and naturals in therapeutics at global level. Conventional treatment options available as synthetic drugs does not meet properly the therapeutic needs for treating diabetes and the herbal remedies provide a better therapeutic hope with lesser side effects. Nutraceuticals are non-specific biological therapies including botanicals, vitamins, anti-oxidants, minerals, amino acids and fatty acids, which are used to promote wellness, prevent malignant processes and control symptoms. Nutraceutical agents have multidimensional therapeutic benefits and have been claimed to have effective disease preventing, curative and health promotive virtues. Present review focuses on the plant kingdom claims as nutraceuticals for diabetes.

Keywords: Ayurveda, Anti-diabetic drugs, Diabetes mellitus, Herbal medicine, Natural products, Nutraceuticals.

INTRODUCTION

Disorderly lifestyle of humans due to the industrial age, mechanistic life, fast track lifestyle, longer work schedules, and various psychological pressures, aloofness from nature and natural products, which have led to an increased incidence of metabolic disorders (diabetes, obesity), cancers, vascular diseases, and psychological disorders. The domain of metabolic disorders including diabetes is in urgent need of safe preventive and therapeutic modalities. Some of the plant based foods that we come across everyday have plenty of nutritional value. We need to ensure that the message is passed on to the public. Thorough scrutiny of Ayurveda classical texts revealed a good number of plants for the cure of diabetes that possess multiple phytoconsituents acting as bodily supplements. Various herbs/herbal parts have been investigated for anti-diabetic potential so far. However, the key hindrance associated with polyherbal formulations is lack of scientific evidences to decode their pharmacological effects and possible mode of action.

Earlier reports revealed that more than 50% of diabetes sufferers rely on complementary and alternative medicine as effective strategy to manage their diabetes. People are now more concerned towards searching the nutraceutical solutions for diabetes.[1] The commonly used antidiabetic Ayurvedic herbal options need to be re-evaluated from this perspective. Considering all these, present attempt has been made to thoroughly screen the available literature and investigate the herbal nutraceutical options to manage diabetes and related complications.

Methodology

Published information from several articles, of which few review articles and cross references thereof were collected. Recent developments in research on neuropsychiatric and neurodegenerative disorders, covering available records and articles in Pubmed, Scopemed, Dhara online and other allied databases covering fields of pharmacology, biomedicine and health were also rationally reviewed and taken into study for the report. The search criteria were restricted to the roles of plants as nutraceuticals in diabetes, by probing the contemporary and Ayurvedic claims in this regard.

Recent upsurge in concept of Nutraceuticals

In current era, people are frustrated with unsafe synthetic pharmacological agents and deeply concerned about how to maintain their health with safer and effective natural products; thus turning their attention

***Corresponding author:**
Dr. Rohit Sharma
Research Officer, Central Ayurveda Research Institute for Drug Development, CCRAS, Ministry of AYUSH, Government of India, Bidhannagar, Kolkata-700091, India
Email: dhanvantari86[at]mail.com

towards dietary supplements, nutrional therapy, phytotherapy and nutraceuticals. Nutraceuticals (Nutrients+Pharmaceuticals) are non-specific biological therapies used to promote wellness, prevent malignant processes and control symptoms. They are categorized as follows based on their chemical constituents (a) Nutrients (vitamins, minerals, Amino acids, etc.) (b) Ayurvedic Herbs or botanicals (c) Dietary supplements (probiotics, prebiotics, antioxidants, enzymes).[2]

Nutraceuticals refer to natural functional/medical foods or bioactive phytochemicals that are health-promoting, disease-preventive, curative, functional foods and beverages containing specific ingredients (vitamins, lipids, proteins, carbohydrates, minerals, or other necessary nutrients) with health benefits. Dietary supplements provide nutraceuticals in a nonfood matrix (tablet or capsule) at a dosage that exceeds the amount present in normal food.[3,4] When such nutraceuticals are used for treatment or prevention of disease, they can be coined as drug.[5]

Vegetables, fruits, whole grains, herbs, nuts and seeds contain an abundance of phenolic compounds, terpenoids, sulfur compounds, pigments, and other natural antioxidants which act as compounds for the treatment of various disease conditions.[6]

Nutraceuticals as therapeutic agents

Studies have highlighted the role of nutraceuticals in several diseases including diabetes. Majority of nutraceutical agents have multidimensional therapeutic benefits and have been claimed to have physiological benefits[7] or provide protection against various diseases as the following products: Cardiovascular agents, Anti-obese agents, Anti-diabetic agents, Anti-cancer agents, Immune boosters, Substances that manage chronic inflammatory disorders and Formulations to cure degenerative diseases.[6]

Antidiabetic claims of Herbs

Diabetes mellitus is a worldwide menace and exponentially growing metabolic disease in India,[8] affecting the lipid and carbohydrate metabolism,[9,10] and affecting the person physically as well as mentally.[11] The knowledge on the heterogeneity of this order is advanced, the need for more appropriate therapy increases. Traditional herbal medicines are used as a safe alternative for conventional hypoglycaemic agents, because synthetic drugs in NIDDM or insulin in 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. By virtue of richness in essential phytonutrients, Ayurvedic herbs may help as “potentiators” for these drugs and play a supportive role to maintain the quality of the diabetic life.

There is vast potential of selected medicinal plants from Ayurveda and Indian folkrole medicine. Several works have been attempted by CSIR, ICMR, DBT, and academia on role of herbal nutraceuticals, nutritionals and naturals in metabolic disorders like diabetes.[12-13] Recently, one such formulation (DM‑FN02) has been taken up for further drug development.[14]

Moringa oleifera (drumstick) has 25 times more iron than spinach, 17 times more calcium than milk, 15 times more potassium than bananas, 9 times more protein than yogurt, and 10 times more vitamins than carrot.” Besides, its richness in these micronutrients, the therapeutic potential of *M. oleifera* leaves in hyperglycemia and dyslipidemia is also reported in several experimental and clinical studies.[15-20]

Aloe vera extract possess compounds such as polysaccharides, anthraquinones and lectins, which have been reported for anti-diabetic activity.[21] The powdered seeds of A. arabica and roots of Caralluma edulis were administered in doses of 2, 3 and 4 g/kg body‑weight to normal rabbits induced hypoglycaemic effect by initiating release of insulin of pancreatic β cells.[22,23] Table 1 enlists various herbal nutraceuticals having anti-diabetic potential.[24,25]

Table 1: Herbal nutraceuticals with anti-diabetic potential

Plant	Family	Plant part
Artocarpus integrifolia Linn	Moraceae	Root barks
Abelmoschus esculentus Linn	Malvaceae	Fruits
Acacia arabica	Leguminosae	Seeds
Acacia modesta Wall	Fabaceae	Leaves
Adhatoda zeylanica Nees	Acanthaceae	Leaves and fruits
Aegle marmelos	Rutaceae	Root bark, fruits and leaves
Allium cepa	Liliaceae	Bulbs
Aloe vera Linn	Lilliaceae	Leaves
Alpinia calcarata Rosc	Zingiberaceae	Rhizomes
Alpinia galanga Willd	Zingiberaceae	Rhizomes
Alternanthera sessilis Linn	Amarantaceae	Whole plant
Amaranthus esculents	Amaranthaceae	Whole plant, oil
Ampelodesma mauritanica Durand	Poaceae	Roots
Andrographis paniculata Nees	Acanthaceae	Roots
Annona squamosa	Annonaceae	Leaves
Artemisia pallens	Compositeae	Aerial parts
Biophytum sensitivum Linn	Oxalidaceae	Leaves
Boerhaavia diffusa Linn	Nyctagenaceae	Aerial parts
Bridelia Retusa Spreng	Euphorbiaceae	Stem barks
Caesalpinia bonducella Roxb	Caesalpiniaceae	Seeds

Camellia sinensis	Theaceae	Leaves
Casearia esculenta	Flacourtiaceae	Roots
Cassia auriculata Linn	Leguminosae	Flowers
Catharanthus roseus	Apocyanacee	Aerial parts
Chamaemelum nobile	Asteraceae	Leaves
Chrysanthellum indicum Linn	Compositae	Aerial parts
Citrullus colocynthis Linn	Cucurbitaceae	Fruits
Cinnamomum zylanicum Nees	Lauraceae	Stem barks
Coccinia indica	Cucurbitaceae	Leaves
Coscinium fenestratum	Menispermaceae	Stem barks
Cucurbita maxima Duch	Cucurbitaceae	Aerial parts
Dioscorea bulbifera Linn	Dioscoreaceae	Bulbs
Diospyros cordifolia Roxb	Ebenaceae	Stems
Dodonae viscose Linn	Sapindaceae	Leaves
Egyptian morus	Moraceae	Root barks
Elaeodendron glaucum Pers	Celastraceae	Stem barks
Enicostemma littorale	Gentiaceae	Whole plant
Eugenia jumbolana Lam	Myrtaceae	Seeds
Ficus bengalensis	Moraceae	Barks
Ficus glomerata	Moraceae	Leaves
Ficus racemose Linn	Moraceae	Fruits
Foeniculum Vulgare Mill	Apiaceae	Volatile oil
Glycrrhiza glabra Linn	Leguminosae	Roots
Gnidia glauca Linn	Thymelaeaceae	Whole plant
Helicteres isora	Sterculiaceae	Roots
Hibiscus rosa	Malvaceae	Whole plant
Lycium shawii Roem	Solonaceae	Aerial parts
Madhuka longifolia	Sapotaceae	Barks
Mangifera indica Linn	Anacardiaceae	Leaves
Melia azadirachta Linn	Meliaceae	Leaves
Michelia champaca Linn	Magnoliaceae	Leaves
Mirabilis jalapa Linn	Nyctagineceae	Roots
Momordica charantia	Cucurbitaceae	Fruits
Momordica cymbalaria	Cucurbitaceae	Fruits
Morinda tinctoria Roxb	Rubiaceae	Fruits
Morus alba	Moraceae	Leaves
Morus indica	Moraceae	Leaves
Mucuna pruriens	Leguminosae	Whole plant
Murraya koenigii	Rutaceae	Leaves
Noolamarckia cadamba Roxb	Rubiaceae	Leaves
Ocimum sanctum Linn	Labiateae	Leaves
Orthosiphon stamineus Benth	Lamiaceae	Leaves
Ougeinia oojeinensis Roxb	Fabaceae	Barks
Piper betle	Piperaceae	Leaves
Psidium guajava	Myrtaceae	Whole plant
Pterocarpus marsupium Roxb	Fabaceae	Wood and barks
Punica granatum	Puniaceae	Whole plants
Rubus ellipticus Smith	Rosaceae	Fruits
Salacia reticulate	Celastaceae	Leaves
Sesbania sesban Linn	Fabaceae	Leaves
Shorea tumbuggaia Roxb	Dipterocarpaceae	Leaves
Sida acuta Burm	Malvaceae	Leaves
Sida cordifolia	Malvaceae	Roots
Sorbus decora	Rosacea	Inner barks
Strychnos potatorum Linn	Loganiaceae	Ripened fruits
Swertia chirayita	Gentiaceae	Barks
Tabernaemontana divaricata Linn	Apocynaceae	Flowers
Terminalia chebula	Combretaceae	Seeds
Tinospora cordifolia	Menispermaceae	Roots
Trigonella foenum ¯graecum	Leguminosae	Seeds
Triumfetta rhomboidea	Liliaceae	Whole plant
Viscum album	Llorenthaceae	Whole plant
Withania somnifera	Solanaceae	Roots

Role of Flavonoids as Nutraceuticals

The major active nutraceutical ingredients in Ayurvedic herbs are flavonoids. As is typical for phenolic compounds, they have antioxidant, antimicrobial, anti-ulcer, hepatoprotective, anti-inflammatory, anti-diabetic, vasorelaxant, anti-atherosclerotic, anti-thrombogenic, cardioprotective and anti-neoplastic activities in addition to their profound effects on the central nervous system. It suggests their potential role to manage intricate patho-physiology of diabetes and related complications.[26]

Micronutrient supplementation for diabetes

Micronutrients are vitamins, minerals and other compounds that our body needs in small amounts in order to accomplish certain functions and they can help to regulate metabolism, to convert sugars and other carbohydrates in your diet into energy.

Various vitamins and micronutrients having significant role in treatment of diabetes are supplemented by Ayurvedic herbs. Some key reported nutraceuticals acting on diabetes are: Micronutrients (Ca, Zn, Mg, Cr etc.), Alpha Lipoic acid (ALA), Coenzyme Q 10, Amino acids (Glu, Cys), Carnitine, Inositol, Calcium, Vitamins (B12, C, D, E, H), Vanadium, etc.[25]

Plants such as *Tinospora cordifolia,*[27] *Embilica officinalis, Aloe vera*, *Momordica charantia, Eugenia jambolana* etc provide essential mineral supplements for diabetes such as chromium, manganese, magnesium, and zinc. Ascorbic acid in herbs viz. *Amla* and *Aloe vera* is a reducing agent and can reduce in cells by reaction with glutathione, which can be catalyzed by protein disulfide isomerase and glutaredoxins and thereby neutralize reactive oxygen species such as hydrogen peroxide which is known to mediate the glycation-dependent degradation of several proteins and is widely involved in the damage of various β-cells and decreasing the β-cell mass in type-2 diabetes.[28,29] Chromium when administered with biotin resulted in 9.7% reduction in 2-hour glucose level, and 0.54% reduction in HbA1C.[30] Chromium potentiates the action of insulin by increasing insulin receptor-mediated signaling.[31] Chromium increases the number of insulin receptors present in a target tissue and increases the binding of insulin to its receptors and regulates key reactions involving phosphorylation/dephosphorylation, which turn on and off insulin action. Chromium via the enzyme insulin receptor tyrosine kinase catalyses the phosphorylation in the presence of insulin. Additionally, chromium inhibits tyrosine phosphates, which is responsible for terminating the insulin receptor response. Thus, by both increasing activation and inhibiting termination of insulin receptor-mediated responses, chromium can significantly influence glucose utilization by peripheral tissues and regulate glucose levels. Magnesium is a co-factor in glucose oxidation, and modulates glucose transport across cell membranes. It may increase insulin secretion and/or improve insulin sensitivity/peripheral glucose uptake whereas glucomannan (hydrosoluble fiber) delaying glucose absorption.[32] Manganese, zinc,[28,33] and iron are co-factors for superoxide dismutase (SODs) that catalyse the breakdown of the superoxide anion into oxygen and hydrogen peroxide which further reduce to give water and protect β-cells from the toxic effects of reactive oxygen species.

ALA is potent anti‑oxidant and has been shown to significantly reduce the symptoms of diabetic neuropathy. In experimental and clinical studies, ALA markedly reduced diabetic pathologies including: Cataract formation, vascular damage and polyneuropathy.[34,35] Nutraceutical agents for improving insulin sensitivity and glycaemic control include α‑lipoic acid, vitamins C and E and magnesium. Omega-3 PUFAs (EPA, DHA, linolenic acid), L‑arginine and vitamin C could be used for cardiovascular complications.[25]

Calcium and vitamin D supplementation may help to preserve insulin sensitivity and thus help prevent diabetes by suppressing secretion of parathyroid hormone (PTH) because PTH can compromise the insulin sensitivity of adipocytes (and possibly other tissues) by increasing intracellular free calcium.[36,37]

Carnitine helps to break down fatty acids in the body and binds acyl residues, thus, could have role to prevent diabetic ketoacidosis.[38,39] Coenzyme Q10 oxygenates the blood, and could be used in some cases of diabetic retinopathy.[40]

Prior to the discovery of insulin, vanadium was used to control blood sugar levels. Few clinical studies on diabetics had confirmed the effectiveness of vanadyl sulphate at a dose of 100 mg/day in improving insulin sensitivity.[41]

Zinc is an essential component for the normal function of more than 100 enzymes involved in digestion, metabolism, and wound healing. Zinc is very important in the synthesis, storage, secretion of insulin as well as in maintaining conformational integrity of insulin in the hexameric form, and thereby improves impaired metabolism.[42]

Though, the effective treatment for diabetes still remain elusive, present review warrants the concomitant use of herbal supplements along with non-pharmacological approaches (Yoga and adopting suitable dietary and lifestyle guidelines)[43,44] to alleviate the symptoms, prevent complications and improve Quality of life of diabetics.

CONCLUSION

The analysis of documented antidiabetic reports on herbs ascertains their potential preventive, promotive and curative role as anti-hyperglycemic, improving insulin sensitivity, anti-hyperlipidaemic, anti-hypertensive, and metabolism regulator. Hundreds of studies on experimental and clinical levels have evaluated and validated the nutraceutical supplementation role of Ayurvedic herbs in diabetes in safer and effective manner. Keeping in view the tremendous antidiabetic supplements at phytoconsituent level having significant antidiabetic pharmacological activities, these herbs possess, they may be utilized to alleviate the symptoms of diabetes and improve the quality of life.

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