

REVIEW ARTICLE

Importance of Nutraceuticals in the Management of Diabetes Mellitus

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ABSTRACT

In recent years there is a growing interest in nutraceuticals which provide health benefits and are alternative to modern medicine. Nutrients, herbals and dietary supplements are major constituents of nutraceuticals which make them instrumental in maintaining health, act against various disease conditions and thus promote the quality of life. Diabetes mellitus is one of them. This dreadful disease is found in all parts of the world and is becoming a serious threat to mankind health. There are lots of chemical agents available to control and to treat diabetic patients, but total recovery from diabetes has not been reported up to this date. Alternative to these synthetic agents, plants and nutrients provide a potential source of hypoglycaemic drugs and are widely used in several traditional systems of medicine to prevent diabetes. The effects of these plants may delay the development of diabetic complications and correct the metabolic abnormalities using variety of mechanisms. This review attempts to display and remark some of the most popular nutraceuticals being use as antidiabetic.

Key words: Nutraceutical, Diabetes Mellitus, Macronutrient, Micronutrient.

INTRODUCTION

The quality of life in terms of income, spending and lifestyle has improved with economic development. However, it has also thrown up a major challenge in the form of `lifestyle diseases ^[1]. The first victim of this lifestyle change has been food habits. Consumption of junk food has increased manifold, which has led to a number of diseases related to nutritional deficiencies. Nutraceuticals can play an important role in controlling them. No wonder more and more people are turning to nutraceuticals.

A nutraceutical is a food with a medical-health benefit, including the prevention and treatment of disease. The term was coined in the late1980s by Stephen DeFelice, M.D., founder and chairman of the Foundation for Innovation in Medicine¹. Nutraceuticals also refer to natural functional/medical foods or bioactive phytochemicals that have health promoting, disease preventing or medicinal properties. These nutraceuticals normally contain the required amount of vitamins, lipids, proteins, carbohydrates, minerals, or other necessary nutrients, depending on their emphases ^[2, 3].

When food is being cooked or prepared using "scientific intelligence" with or without knowledge of how or why it is being used, the food is called "functional food".

Thus, functional food provides the body with the required amount of vitamins, fats, proteins, carbohydrates, etc. needed for its healthy survival. When functional food aids in the prevention and/or treatment of disease and/or disorder other than anaemia, it is called a nutraceutical . Examples of nutraceuticals include fortified dairy products (e.g. milk) and citrus fruits (e.g. orange juice)

Nutraceuticals and Diabetes

Diabetes mellitus is characterized by abnormally high levels of blood glucose, either due to insufficient insulin production, or due to its ineffectiveness. The most common forms of diabetes are type1 diabetes (5%), an autoimmune disorder, and type2 diabetes (95%), which is associated with obesity. Gestational diabetes occurs in pregnancy ^[5]. As a result of elevated levels of blood glucose, two problems occur: body cells become starved for energy, and, over time, the high glucose levels can damage the nerves,

eyes, kidneys, heart and blood vessels. Globally the total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2003^[6]. Several medicinal plants have found potential use as hypoglycaemic in the Indian system of medicines, including ayurveda^[7].

Nutraceuticals have the capability to control diabetes. Nutraceuticals denote foods having medicinal effect on the health of human beings. According to the American Diabetes Association, if you have the symptoms of developing diabetes then appropriate change in diet will certainly do wonders for you. Research is also supportive of the benefits of diets high in certain types of fiber for promoting improved post-prandial glucose and insulin responses in normal individuals and in individuals with type 2 diabetes, dyslipidemia, and insulin resistance^[8]. The types of dietary fiber that appear to be most significant with respect to insulin resistance include oat fiber and sugar gum, while psyllium has produced mixed results^[9-17]. Coffee is another great nutraceutical. It comprises of chlorogenic acid which act as an antioxidant. After having food, it aids in slowing down the release of glucose in our blood stream. A few more popular nutraceuticals include magnesium, chromium piccolinate, conjugated linoleic acid, bitter melon and our beloved cinnamon. These nutraceuticals effectively enhances glucose tolerance as well as insulin sensitivity^[18].

Traditional plant medicines are used throughout the world for a range of diabetic presentations. Herbal drugs are prescribed widely because of their effectiveness, less side effects and relatively low cost^[19]. Therefore, investigation on such agents from traditional medicinal plants has become more important^[20]. The present review, deals with some selective Indian medicinal plants having pharmacologically established hypoglycaemic potential.

Categories of nutraceuticals and their role in diabetes

Nutraceuticals are non-specific biological therapies used to promote wellness, prevent malignant processes and control symptoms. These can be grouped into the following three broad categories^[21].

1. Substances with established nutritional functions, such as vitamins, minerals, amino acids and fatty acids - **Nutrients**
2. Herbs or botanical products as concentrates and extracts - **Herbals**

3. 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 replacements – **Dietary supplements**.

Nutrients

Apart of choosing herbs as part of natural army against diabetes, vitamins and minerals are also an essential and balancing factor. There is mentioning below the basic vitamins and minerals that our needs especially in case of diabetes. These nutrient classes can be categorized as either macronutrients (needed in relatively large amounts) or micronutrients (needed in smaller quantities). The macronutrients include carbohydrates, fats, protein, and water. The micronutrients are minerals and vitamins.

Macronutrients

Carbohydrates

Dietary carbohydrates from cereals, breads, other grain products, legumes, vegetables, fruits, dairy products and added sugars should provide 50–60% of the individual's energy requirements²². Both the source and the amount of carbohydrate consumed influence blood glucose and insulin responses^{23,24}. When a carbohydrate food is eaten there is a corresponding rise and subsequent decrease in blood glucose level known as the glycaemic response. This response is relevant, for example, to appetite control, sports nutrition and those with diabetes. A number of factors influence the rate and duration of the glycaemic response. It depends on:

The specific food

- The type of the sugar that forms the carbohydrate
- The nature and the form of the starch as some are more digestible than others
- The cooking and processing methods used
- Other nutrients in the food such as fat or protein

Weight reduction is usually necessary and is the primary dietary aim for people with non-insulin dependent diabetes. Consuming a wide range of carbohydrate foods is an acceptable part of the diet of all diabetics, and the inclusion of low glycaemic index foods is beneficial as they help regulate blood glucose levels. Most recommendations for the dietary management of diabetes allow a modest amount of ordinary sugar

as the inclusion of sugar with a meal has little impact on either blood glucose or insulin concentrations in people with diabetes [25].

Protein

Current evidence indicates people with diabetes have similar protein requirements to those of the general population — about 0.86 g/kg per day [22]. Although protein plays a role in stimulating insulin secretion [26, 27] excessive intakes should be avoided as it may contribute to the pathogenesis of diabetic nephropathy [28]. Some evidence suggests eating vegetable protein rather than animal protein is better for reducing serum cholesterol [29] and managing nephropathy [30, 31]. There are a number of different types of protein supplements include liquid protein supplements, protein powders and liquid protein shots. There are a number of sources for protein supplements. Some of these sources include: Whey, Casein, Soy, Rice, and Egg [32].

Fat

Numerous studies indicate high-fat diets can impair glucose tolerance and promote obesity, dyslipidemia and atherosclerotic heart disease. Research also shows these same metabolic abnormalities are reversed or improved by reducing saturated fat intake. Current recommendations on fat intake for the general population apply equally to people with diabetes: reduce saturated fats to 10% or less of total energy intake and cholesterol intake to 300 mg/d or less [33]. Scientific debate continues over which alternative is preferable to saturated fat polyunsaturated fat, monounsaturated fat or carbohydrate calories [34, 35]. Research suggests monounsaturated fat such as canola, olive and peanut oils may have beneficial effects on triglycerides and glycemic control in some individuals with diabetes³⁶, but care must be taken to avoid weight gain. Omega-3 fatty acids, found in fish such as salmon and mackerel, may reduce serum triglycerides without impairing glycemic control [37].

Micronutrients

Minerals

Chromium (Cr+3) is an essential trace element required for normal glucose metabolism³⁸⁻⁴¹. It appears to act by enhancing insulin's actions, with increases in the number of insulin receptors, increased binding of insulin to the insulin receptor and increases in activation of the insulin receptor reported⁴²⁻⁴⁵. Because chromium is a nutrient, supplements are likely to be beneficial only in

those people with chromium deficiencies. Chromium levels in the body tend to decline with age, which may be one factor affecting older people's risk of developing Type II diabetes. Dosage levels between 100-500 mcg/day have been shown to reduce blood glucose, insulin and cholesterol [46].

Vanadium

Research indicates that this mineral acts similarly to insulin in transporting glucose into the cells, and is therefore valuable for both Type I and Type II diabetics. Vanadium supplementation also decreased fasting blood glucose levels [47-49], Hemoglobin A1c levels [47, 48] and cholesterol levels 50. Dosages ranging from 45-150 mg/day can be useful for improving fasting glucose levels (how much sugar is in the blood when one wakes up in the morning). Toxicity studies show these dosage levels to be safe and well tolerated by most people. Some individuals experience mild gastrointestinal distress, either during the first week of use or at higher dosage levels (up to 400 mg/day) [46].

Magnesium:

The mineral magnesium functions as an essential cofactor for over 300 enzymes in the body. It is essential for all energy dependent transport systems, glycolysis, oxidative energy metabolism and biosynthetic reactions [51, 52]. While this mineral is not directly implicated in the mechanisms of diabetes, it helps to protect patients from complications of the disease. For people with diabetes or heart disease, the recommended daily intake level of magnesium is 1000 mg/day. However, because the actions of calcium and magnesium are so strongly connected, one needs an intake ratio of 2:1 or more—for each 1000 mg of calcium, one should also get 500-1000 mg of magnesium [46].

Vitamins

Vitamin E

Vitamin E is an essential fat soluble vitamin and functions primarily as an antioxidant [41]. Low levels of vitamin E have been associated with increased incidence of diabetes⁵³ and some research suggests people with diabetes have decreased levels of antioxidants⁵⁴⁻⁵⁶. Additional evidence indicates that people with diabetes may also have greater antioxidant requirements, due to increased free radical production secondary to hyperglycemia⁵⁷⁻⁵⁹. Doses of vitamin E up to 400 IU are generally believed to be safe. Doses over 800 IU may alter blood clotting although

supplement trials that have monitored prothrombin times in subjects have noted no increases^[41].

Vitamin C

Research has shown that Vitamin C supplementation may be beneficial to type II diabetes patients. In one study patients took no Vitamin C for the first week, then 1g/day for 4 weeks, followed by 3g/day for a further 4 weeks. The results showed that the mega dose of Vitamin C helped to control blood sugar levels and increased the patient's anti-oxidant status^[60]. There is preliminary evidence that substantial supplements of vitamin C (about 1000 mg daily) may help to prevent or reduce the development of cataracts and nerve disorders that commonly occur in people with diabetes. Such does may also inhibit protein glycosylation, which is believed to be important in the development of the long-term complications associated with diabetes^[61].

Biotin

Biotin, a member of the B vitamin complex, is necessary for both metabolism and growth in humans, particularly in the production of fatty acids, antibodies, and digestive enzymes and in tissue metabolism^[62]. Importantly, for patients with diabetes, biotin stimulates liver glucokinase activity, increases insulin production, and enhances glucose uptake in muscle cells^[63-65]. Food sources of biotin include organ meats, soy, egg yolks, whole grains, and yeast. There is growing evidence of suboptimum biotin intake in the U.S. population^[66]. A recommended dosage level for diabetics is 9 mg/day.

Other Supplements

Omega 3 fatty acids

Fatty acids are an integral "building block" of our cell walls. In order for glucose to get into our cells and provide energy, that wall must be fluid and flexible. However, the body cannot make omega-3 fatty acids, so must get them from dietary sources. The best sources are fatty fish (such as salmon, mackerel, sardines, herring, and tuna), flaxseed, evening primrose, borage, walnuts and wheat germ. Omega-3 essential fatty acids (omega 3 EFAs), improve insulin resistance in animal models^[67]. Their effect in humans has been equivocal. Available human research has shown a range of outcomes regarding insulin metabolism ranging from some improvement to no change to deterioration of glycemic control in one study. A recommended intake level of flaxseed oil is 1-2

tablespoons/day (or 1/4 cup freshly ground flaxseed).

Alpha-Lipoic Acid

This substance is a potent anti-oxidant, soluble in both fats and water, which means it, can act in virtually all areas of the cell to neutralize free radicals. Alpha-Lipoic acid has been shown to improve insulin resistance in a variety of animal models^[68, 69]. Copious anecdotal evidence exists regarding the efficacy of alpha-lipoic acid in restoring insulin sensitivity in type 2 diabetes. Alpha lipoic acid has been demonstrated to inhibit mammalian pyruvate dehydrogenase kinase, thereby providing a possible mechanism for a glucose (and lactate) lowering effect in diabetic subjects^[70]. Dosage levels of 600-1800 mg/day have been shown to improve the transport of glucose into cells by as much as 63%.

Coenzyme Q10

The importance of this nutrient cannot be overstated, primarily because many of the drugs that are needed for management of diabetes and/or its complications deplete CoQ10. Coenzyme Q10 (CoQ10) is a promising nutritional intervention for insulin resistance, at least among subjects with hypertension. Singh et al conducted an eight week randomized, double-blind trial comparing the use of a water soluble form of CoQ10 (60 mg twice daily) to a vitamin B complex in 59 hypertensive patients. Their results indicated CoQ10 at this dose lowered glucose and fasting insulin levels, suggesting possible improved insulin resistance^[71].

Herbal Dietary supplements

A great attention has nowadays been given to discover the link between dietary nutrients and disease prevention. Large numbers of herbs which had been in use since unknown time have been shown to play a crucial role in the prevention of disease. In addition to the macro and micro nutrients such as proteins, fats, carbohydrates, vitamins or minerals necessary for normal metabolism, a plant based diet contains numerous non-nutritive phyto constituents which may also play an important role in health enhancement. A brief overview of the role of various herbs in disease prevention, with a focus on bioactive components from flaxseeds, garlic, citrus, fruits, soybean, and ginkgo biloba has been given in this part of the nutraceuticals^[7].

CONCLUSION

Nutraceuticals are food supplements and have nutritional value. All the nutrients discussed in

this review have exhibited significant clinical & pharmacological activity. There is increasing demand by patients to use the natural products with antidiabetic activity. The natural products especially herbs are the rich source of nutraceuticals which commonly have a significant and negligible side effects than the synthetic antidiabetic drugs. The efficacy of hypoglycemic herbs is achieved by increasing insulin secretion, enhancing glucose uptake by adipose and muscle tissues, inhibiting glucose absorption from intestine and inhibiting glucose production from hepatocytes. A place for nutraceuticals in clinical practice is emerging, but important pharmaceutical and clinical issues need to be addressed by further research.

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