CHAPTER 12

Nutraceuticals in Diabetes Management

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THE DISEASE: DIABETES MELLITUS

Overview: Incidence, Prevalence, Demographics, and Statistical Data

Diabetes mellitus (DM), the all-American disease, is currently the seventh major cause of death in the United States, with a staggering healthcare cost of $174 billion dollars annually [Beecher 1999; Houston and Egan 2005; Lovelady 2005; American Diabetes 2008]. Press releases issued by the Centers for Disease Control and Prevention in June 2007 and 2008 stated that the number of people with DM increased to 24 million. This is an increase of more than 3 million in a two-year time interval. According to these data, 8% of our population is afflicted with this disease, and 25% are 60 years of age and older. Concurrently, 57 million are estimated to have pre-diabetes, placing them at a higher risk for DM.

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The statistical impact of DM in the U.S. population is as follows:

- Native Americans and Alaskan Natives, 16.5%
- Blacks, 11.8%
- Hispanics, 11.4%
- Puerto Ricans, 12.6%
- Mexican Americans, 11.9%
- Cubans, 8.2%
- Asian Americans, 7.5%
- Whites, 6.6%

Treatment of diabetes is challenging not because of lack of an available, safe, and effective method; rather, unawareness and denial of this disease add to the treatment challenge. The good news is the incidence of people who were previously unaware or denying they have diabetes has decreased from 30 to 25% over a two-year period. This suggests that efforts to increase awareness are working and people are better prepared to manage the disease and its complications.

DM is a chronic condition that results from an inadequate ability or failure to metabolize carbohydrates, fats, and proteins. The pancreas produces insulin, an important peptide hormone released from the beta cells of the islets of Langerhans in response to high glucose levels. The mechanism by which insulin facilitates availability and utilization of glucose may be pictured as “lock and key” interplay. Insulin serves as the key that opens the doors of the cell and allows entry of available glucose from the bloodstream for cellular fuel (ATP) or energy usage. Insufficient amounts or the absence of insulin in the body, therefore, causes a failure to unlock the cells, resulting in increased glucose in the bloodstream, resulting in hyperglycemia. The inability of the cells to receive and utilize any glucose sources from the bloodstream causes the cells to be exceedingly deprived of energy or glucose sources.

**TYPES OF DIABETES MELLITUS**

**Type I: Insulin-Dependent Diabetes Mellitus**

Type I, or insulin-dependent DM (IDDM), accounts for 10% of our population, and individuals with IDDM are incapable of producing any insulin before the age of 40. It is treated with insulin injections, diet change, and regular exercise.

There have been studies that suggest individuals with this type, not genetically predisposed to this condition, develop the disease as a result of previous exposure to a potent viral infection, causing the total destruction of the pancreas.

**Type II: Non-Insulin-Dependent Diabetes Mellitus**

Type II, or non-insulin-independent DM, accounts for 93% of all cases of diabetes. This group can usually produce some insulin; however, it could be inadequate or ineffective because of insulin resistance. This type is associated with being
overweight, often obese, and usually occurs after one reaches 40 years of age. Obesity decreases insulin sensitivity; conversely, exercise increases it [Langin 2001; Catena et al. 2003; Pittas 2003; Houston and Egan 2005].

MANAGEMENT OF DIABETES MELLITUS: DIET, EXERCISE, AND MEDICATIONS

Treatment for this group is composed of diet modification, exercise, and oral hypoglycemic agents. There have been instances in which type II could be insulin requiring. Recent findings at the 68th Scientific Session by the American Diabetes Association held in San Francisco in June 2008 disclosed that the lack of expected response from oral hypoglycemic agents or the inadvertent failure of oral medications despite the intake of maintenance-prescribed regimens leads to continued chronic loss of beta cells, ultimately resulting in pancreatic failure. Unfortunately, early detection of beta cell dysfunction cannot be foreseen before signs and symptoms appear; therefore, 80% of these cells have already been destroyed.

NUTRACEUTICALS

The current approach to diabetic management is through a combination of dietary choices and supplements. A new trend in the treatment of diabetes is marketed in the form of nutraceuticals. Nutraceuticals are defined as food or food products compounded or manufactured in the form of capsules, tablets, tinctures, etc. This product is often confused with “functional foods.” The latter are consumed foods and not in dosage form. Although nutraceuticals show great promise in the management of diabetes, scientific data and studies are not conclusive enough to establish the optimal effects. Interestingly enough, a report in 2002 observed that diabetics were open to either complementary or alternative medicine, which uses nutraceutical and functional foods [Ames et al. 1993; Egede et al. 2002; Yeh et al. 2002].

World-wide consumption of nutraceuticals is higher in Europe and Japan. To date, more Americans use nutraceuticals (herbals/botanicals) than in the past. The American Diabetes Association (ADA) recommends the use of nutraceuticals and food additives to control blood glucose levels, hoping to deter the onset of the disease and its complications among pre-diabetics and diabetics. The U.S market for diabetogenic natural products is estimated at $50 million, with a yearly increase in demand of 20–30% [Hasler 1998]. In light of the baby-boomer generation entering the age of 50 and above, it is foreseeable that nutraceutical supplements could be in higher demand. This warrants a closer look by the FDA to further their quest into the safety of these products, improving regulations, and lifting current restrictions.

Nutraceutical Vitamins, Minerals, and Enzymes

- ALA and its reduced derivative, dihydrolipoic acid, improve insulin sensitivity, glucose tolerance in type II DM, and diabetic neuropathy. However, in clinical trials,
it did not show any significant alteration in the fasting glucose and insulin concentration. This poses a question as to its reliability as a therapeutic agent that would provide significant improvement of glycemic control in DM [Joseph et al. 1999].

- Biotin increases glucokinase activity, thereby improving glucose tolerance and insulin sensitivity. The recommended dose is 16 mg/day in type II DM.

- Carnitine improves glucose metabolism and disposal. The recommended dose is 1–2 g twice daily.

- Chromium is an essential micronutrient acting as a cofactor in numerous insulin regulatory steps. It reduces fasting glucose, postprandial glucose, hemoglobin A1C, C-peptides, fasting insulin, and insulin resistance. Conversely, it increases cellular insulin binding, the number and activation of insulin receptors, and insulin growth factor-I receptor. The recommended dose is 8 mcg/kg/day.

- CoQ10 reduces fasting glucose, postprandial glucose, and hemoglobin A1C. The recommended dose is 100 mg twice daily.

- Copper increases insulin sensitivity and improves glucose levels. However, excessive intake of copper may induce or produce insulin resistance.

- Flavonoids enhance insulin secretion, improve insulin sensitivity, reduce serum glucose, and inhibit sorbitol accumulation in the lens of the eye and nerves.

- Folate and vitamin B12 (cyanocobalamin) have no significant effects on glucose metabolism; however, both are noted to improve symptoms of diabetic peripheral neuropathy.

- Gamma linoleic acid improves glucose tolerance, improves insulin resistance, and protects, as well as improves, diabetic neuropathy. The recommended dose is 500–1,000 mg/day.

- Glutathione is the most potent intracellular antioxidant. Decreasing the levels of glutathione results in insulin resistance, glucose intolerance, and increased oxidative stress.

- Inositol or myoinositol is required for normal nerve function. Consumption improves diabetic neuropathy.

- Magnesium improves insulin sensitivity and secretion. The recommended dose for those with normal kidney function is 500 mg twice a day with 50–100 mg of vitamin B6.

- Manganese is an important cofactor in many glycolytic enzymes; it improves insulin synthesis and insulin sensitivity and serves as “insulin.” An intact pancreatic beta cell is required for manganese to be effective. The optimal dose is 5–10 mg/day.

- Monounsaturated fats improve glycemic control. The recommended dose is extra virgin olive oil, four tablespoons per day, or whole olives, 12–16 per day.

- N-acetyl cysteine improves insulin secretion, reduces insulin resistance, lowers serum glucose, and prevents diabetic cataracts. The recommended dose is 2 g daily.

- Niacinamide improves insulin action and sulfonylurea action. Long-term evidence indicates that niacinamide alone improves glucose tolerance in safe doses at less than 3 g daily.

- Omega 3 fatty acids improve insulin sensitivity and insulin secretion and reduce serum glucose. The recommended dose is 900 mg of EPA and 600 mg of DHA with a total daily dose of EPA plus DHA lower than 3 g.

- Potassium improves insulin secretion, insulin sensitivity, and glucose tolerance when administered orally or intravenously.
- Pycnogenol has been found to lower plasma glucose and hemoglobin A1C, improve glutathione levels, and reduce oxidative stress. The recommended dose is 100 mg/day.
- Selenium is an important antioxidant; it serves as an “insulin-mimetic,” reduces fasting glucose, and protects against diabetic retinopathy. The recommended dose is 200 mcg/day.
- Taurine improves glucose tolerance and insulin sensitivity, reduces glycosylation of proteins and hemoglobin, and improves symptoms of diabetic neuropathy. The recommended dose is 1.5–3 g twice daily.
- Thiamine and B₆ administration improves symptomatic peripheral neuropathy within four weeks, reduces pain in 88.9%, reduces numbness in 82.5%, and reduces paresthesias. The recommended dose is 50–100 mg twice a day [Abbas and Swai 1997; Tamai 1999].
- Vanadate is a protein-tyrosine phosphatase inhibitor that reduces glucose, increases glucose transport and uptake, improves insulin sensitivity, prolongs insulin action, and increases intracellular magnesium. The recommended dose is 40–80 mcg/L.
- Vitamin B₂ (pyridoxine) serves as a coenzyme in carbohydrate metabolism. It prevents diabetic neuropathy, improves symptoms, and inhibits glycosylation.
- Vitamin C (ascorbic acid) reduces glycosylation of proteins and reduces sorbitol accumulation but was found not to have any direct effect on glucose.
- A vitamin E derivative has shown to improve insulin action, reduce resistance, improve glucose control, and reduce glycosylation of proteins. Optimal doses are unclear, but 200–400 IU of a mixture of tocopherols and tocotrienols are recommended.
- Zinc improves insulin binding and insulin sensitivity; increases insulin synthesis, secretion, and utilization; protects beta cells; reduces glucose; and improves diabetic retinopathy. The recommended dose is 30–50 mg daily.

Nutraceutical Herbs and Botanicals

Indian gooseberry, Jambal fruits, Bengal gram, black gram, mango leaves, parsian, string beans, cucumbers, celery, and onions are vegetables and fruits found useful in the treatment of diabetes [Diet Health Club 2008]. Others worth mentioning include the following:

- Bittermelon contains an extract called “plant insulin.” It is also known as bitter gourd or gourdin. Ayurvedic medicine uses the extract, which was found to activate in inactive insulin present in the blood as well as rejuvenate the pancreas, thus being beneficial to patients with diabetes. When it is administered, it is documented to lower sugar levels 15 min after intake. Bitter gourd “Karela” juice is a popular remedy for diabetics in the tropics. Consumption of 50 ml of raw Karela juice daily improves blood glucose tolerance in type II DM [Indiadiets 2008].
- Cinnamon (Cinnamomum aromaticum) cassia is the most common related species sold in most supermarkets in the United States and has been reported to have remarkable pharmacological effects in the treatment of type II DM. The mechanism of action includes the activation of glycogen synthase in glucose uptake, the inhibition of glycogen synthase, the activation of insulin receptor kinase, the inhibition of dephosphorylation of insulin receptor, and its antioxidant effects. A study
of 60 patients with type II DM showed a reduction of fasting glucose by 18–29% at a cinnamon dose of 1, 3, and 6 g/day for 40 days [“Honey and Cinnamon” 2008]. Adversely, cinnamon contains a toxic component, coumarin, that causes hepatic and renal damage as well as blood-thinning effects in high concentrations [Wong 2007; Wikipedia 2008]. A cinnamon and honey mixture has beneficial health effects. Ayurvedic as well as Yunani medicine have been using honey as a vital medicine for centuries. Currently, scientific studies suggest that, although honey is sweet, if taken in the right dosage as a medicine, it does not harm diabetic patients. The mixture causes a cleansing effect in the digestive system, which eliminates parasites, fungi, and bacteria. These microorganisms slow down digestive processes, which leads to toxic buildup. Cleansing will cause weight loss, ultimately removing a DM risk factor. The mixture is known to lower gastric emptying time and rate, which significantly lessens postprandial blood sugar levels [Science Daily 2008]. The recommended use specifically for weight loss is one part cinnamon to two parts raw honey. Use half a teaspoon of cinnamon to one teaspoon of honey at a ratio of 1:2 [“Honey and Cinnamon” 2008].

- Fenugreek seeds contain an alkaloid called trigonelline that has been shown to lower blood glucose and prevent cataracts attributable to diabetes [Indiadiets 2008].
- Garlic (Allium sativum) is best noted to minimally decrease systolic blood pressure [Allium ursinum 2008]. It has beneficial vascular effects and has antibiotic potential [Bergner 1995]. Studies done and reported at the 68th ADA June 2008 convention found a correlation between diabetes and periodontal “gum disease.” Uncontrolled diabetes produces high glucose levels in the saliva, which helps bacteria to thrive. Diabetes reduces the body’s resistance to infection, and the gums are among the tissues most likely affected. Periodontal disease, and loss of more teeth, is often linked to the control of diabetes. In a full-study finding published in the July 2008 issue of Diabetes Care, periodontal disease was found to be an independent predictor in the incidence of type II DM [Indiadiets 2008]. Generally, teeth are covered with plaque and a sticky film of bacteria. After the consumption of a meal, snack, or beverage that contains sugars or starches, bacterial reactions to these substances cause the release of acids that attack tooth enamel. Repeated attacks can cause the enamel to break down, resulting in cavities [About.com 2006; American Diabetes 2008]. Recurrent untreated dental cavities leads to recurrent abscess formation. Subsequently, this leads to chronic periodontitis and ultimately the loss of teeth. Additional studies are required to establish the long-term beneficial effects of garlic application to gingival tissues and oral intake in the systemic control of periodontal disease in diabetes.
- Grapes have a naturally present compound known as resveratrol, which can protect against cellular damage to blood vessels caused by the high production of glucose in diabetes. This is found naturally in grape skins as well as in grape seeds, peanuts, and red wine. Research was performed by scientists at the Peninsula Medical School in the southwest part of England. The findings were published in the science journal Diabetes, Obesity and Metabolism. The elevated levels of glucose that circulate in the blood of diabetic patients cause microvascular and macrovascular complications resulting from damaged mitochondria, an organelle responsible for generating energy. The mitochondrial damage causes leakage of electrons and the formation of highly damaging free radicals. Resveratrol protects against damage by the production of a protective enzyme that prevents leakage of electrons and toxic free radicals [Science Daily 2008]. The custom of drinking wine for centuries enhanced the
scientific research into the health benefits derived from red grapes, which began in Europe in the mid- to late 20th century. Supplemental oligomeric proanthocyanidins (OPCs), “pycnogenols,” have been used in Europe since 1950 and have been found to reduce diabetic retinopathy. Generally, the more intense the color of the grape skin, the more OPCs it contains, which explains why red wine has greater health benefits than white wine. Grape juice also contains OPCs; however, researchers have found that the beneficial effects are not as comparable [Slomski 1994].

- Green tea and epigallocatechin-3-gallate (EGCG) are substances that reduce fasting and postprandial glucose, fructosamine, and hemoglobin A1C and improve insulin resistance. They increase protection from beta cell destruction by inhibiting inducible NO gene expression and nuclear factor inhibition. The recommended dose is 500 mg twice daily.

- Malunggay or kamuntingay (Philippines), Moringa or horse radish tree (English), or Sajina (India) is a wonderful world-known herb that recently entered the consumer and nutritional markets in the United States. The herb grows wildly in abundance in warm areas or tropical climates. Mounting scientific evidence collected by modern scientists on the herb’s beneficial effects just proves what millions of people thousands of years ago have always known. Its benefits include being an excellent source of nutrition, a natural non-sugar-based energy booster that lowers blood pressure and promotes relaxation and calmness. It also possesses detoxifying effects that lower blood sugar levels. The multitude of medicinal benefits it offers earned it the name “nature’s medicine cabinet” [Kumar 2008; Malunggay 2008]. West African physicians have used this herb for the treatment of diabetes for centuries. This “miracle vegetable” received numerous accolades from various scientific journals and the WHO. According to Market Manila, “Malungay is consumed in huge quantities every day across the archipelago” [Market Manila 2005]. Malunggay can possibly be the future centerfold of the nutraceuticals. Earnest work is contemplated to provide this herb plant in a pill, tablet, or any other dosage form.

CONCLUSIONS

A documented new syndrome, “syndrome X,” also known as metabolic syndrome, represents a constellation of problems that are both cardiovascular in nature and have a predominant degree of insulin resistance. The United States is currently faced with a pandemic of obesity and an epidemic of metabolic syndrome. Increasing rates of obesity amongst children and adults inadvertently lead to glucose intolerance, insulin resistance, DM, and other complications.

Although drug therapy may be required for the treatment of diabetes and metabolic syndrome, appropriate lifestyle changes such as weight loss, exercise, healthy diet, and nutraceutical supplements are the cornerstone for the clinical management and prevention of both conditions.

These advocated modalities are supported by many scientifically proven studies that relate to improvement in the quality of life and an increased lifespan. Treatment and management of diabetes in the past 50 years have changed it from a disease known to produce early disability and demise to one that is complicated to manage but with
an excellent prognosis. The transformation is a result of a better understanding of the pathophysiology, an awareness of the disease, and the early detection of diabetes before onset of complications [Beecher 1999; Buse 2008; Diabetes Dispatch 2008].

The country’s imminent dilemma of increasing healthcare costs is a threat to our continued efforts to progress and improve outcomes in the management of these conditions. Dissatisfied consumers met with exorbitant drug costs, lack of improvement in conventional therapies, poor therapeutic alternatives for chronic diseases such as diabetes, inadequate rapport between medical providers and patients in managed care, desired personalized medicines, an enlarging population trying to prevent the effects of aging, and new insights into the concept of preventive medicine have initiated the emergence of the use of nutraceuticals as an alternative venue to promote wellness and the prevention of ailments. Data show that more than 40% of Americans are using alternative medical therapies, nutraceuticals, herbs, and botanicals [DeFelice 2008]. The surmounting concern in reference to the historical use of nutraceuticals by itself is not enough to ensure safety even if historical use is characterized by consumption or by use in folk medicine all over the world [Degan et al 2005]. Despite these stumbling blocks, the future and continued use of nutraceuticals look bright as a supplement in addition to conventional medically proven drugs in the control and management of this chronic disease, DM.

FOR MORE INFORMATION AND RESEARCH


REFERENCES


