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Review Article

Complementary Medicine Provides Natural Insulin Alternatives

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Abstract

There are many oral hypoglycemic agents currently used to treat diabetes. A side from insulin, none are capable of binding to and activating the insulin receptor. Approximately 45%-50% of the current drugs are derived from natural sources such as plants. A recent study highlights that a protein in bitter melon is capable of binding to and activating the insulin receptor, expanding the use of bitter melon as a traditional medicine and food for diabetes treatment.

Keywords: Bitter Melon; Diabetes; Insulin; Complementary; Alternative Medicine

Abbreviations

mcIRBP, M. charantia insulin receptor-binding protein; T1DM, diabetes mellitus type 1; T2DM, diabetes mellitus type 2; G6PD, glucose-6-phosphatedehyrogenase

Diabetes Mellitus

Diabetes affects over 18 million people in the United States as the number one endocrine disorder and affects over 200 million people worldwide [1]. Diabetes is defined as an elevation in plasma blood glucose above the established normal values based on fasting, random testing and glucose tolerance levels. Erythrocytes circulating in the blood are modified by high levels of glucose and can be tested to determine the average blood glucose levels over a three-month time frame; this is known as the hemoglobin A1c level. The classic presentation of symptoms includes polyuria, polyphagia, polydipsia, fatigue, poor wound healing and blurry vision. Diabetic patients are at significantly increased risk for cardiovascular disease, cerebrovascular accidents, hypertension, renal disease, amputations, depression, autoimmune diseases, pain, periodontal disease, retinopathy, and various neuropathies [2]. The underlying cause of diabetes is basically due to an inability of the pancreas to secrete the hormone insulin (T1DM) or a resistance to insulin by certain cells of the body (T2DM). Glucose levels increase in the blood after meals stimulating beta cells of the pancreas to release insulin. Individual fat and muscle cells, responsible for taking up glucose from the blood as a fuel source will not permit the entry of glucose without first being acted upon by insulin. In diabetics, this causes an unstable rise in blood glucose [3] levels which then damages various tissues and organs within the body [2].

Family medicine physicians treat patients with diabetes on a daily basis as it has become one of the top five causes of death worldwide with its incidence steadily increasing [1]. In addition to the 18 million patients currently diagnosed as diabetic, over 79 million Americans are now considered pre-diabetic. As one complication of metabolic syndrome, pre-T2DM patients reach a fork in the road of good and bad health. Which path they ultimately take can be greatly influenced by the application of various complementary and alternative options.

The Role of Alternative Medicine

In the United States, there is growing interest in complementary and alternative medicine [4]. Many of these therapies have been safely used for thousands of years, yet most physicians are never exposed to, let alone trained on their potential clinical applications. There is a tendency of some physicians to dismiss the efficacy of complementary and alternative medicine or to label its effects as mere placebo. It is estimated that more than one third of diabetic patients currently use some form of complementary and alternative medicine [5]. As family medicine physicians, it is important to have a working knowledge of these alternative therapies and understand which ones have clinical applications.

Healthcare costs in the United Sates have continued to rise and threaten to bankrupt programs like Medicare and Medicaid. America now spends more on healthcare than any other country in the world [6]. Questions arise about the benefits of U.S. healthcare spending. Where does the United States rank in population health as compared to other countries? Is it time for patients and physicians alike to take a step back and re-evaluate our approach to healthcare? Have we allowed the pharmaceutical industry and health insurers to influence the care that our patients receive? Do most patients really need to be on prescription drugs for the rest of their lives? How much emphasis should we place on prevention and lifestyle choices? Alternative, complementary and integrative medicine offer solutions to many of the problems facing American healthcare because these modalities focus on the prevention of disease and provide lower cost alternatives to some prescription medications.

Most of the medicine in the world is derived from plants, many of which have been safely used for thousands of years. A significant amount of modern medications owe credit to the plants from which they were derived. Many practitioners of traditional medicine have known certain plants to be effective for various disorders, the science behind which is only recently beginning to elucidate the biochemical proteins and pathways responsible for these ancient anecdotes. Many plant-based medicines are both cost effective and efficacious [7]. In some undeveloped and developing countries, plant based alternative medicines are all that is available. Here in the U.S. many of these same

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therapies can safely complement our existing arsenal of treatment options and possibly improve the quality of life for patients with diabetes and other illnesses.

Alternative Treatments for Diabetes

There are numerous complementary and alternative treatments for diabetes. This review article will focus primarily on bitter melon since it has benefit as both food and as medicine. The most important concept of complementary and alternative medicine is that healthy lifestyle choices are indispensable to good health. Diet, exercise and stress management have tremendous impact on various diseases affecting Americans today. These three modifiable components merit a substantial investment of time and energy on the part of both patient and physician.

In addition to diet, exercise and the management of stress, alternative treatments for diabetes aim to reduce blood glucose levels and the associated complications of the disease with the fewest side effects possible. Dietary supplementation with bitter melon, fenugreek, ginseng, milk thistle, grape seed extract, bilberry, alpha-lipoic acid, chromium, vitamin C, Vitamin E, Niacin, Vitamin B6, Magnesium, Zinc, Manganese, Biotin, omega three fatty acids, garlic, onions, green tea, fiber and quercetin are just a few of the alternative options available [2].

Bitter Melon

Momordica charantia, (bitter melon) a member of the Cucurbitaceae family has been used for thousands of years as both food and medicine. The fruit resembles a gnarled cucumber and possesses a bitter taste that becomes stronger as the fruit ripens. The fruit and seeds are the primary medicinal components. Bitter melon has traditionally been used to treat as an antidiabetic, anti-inflammatory, antiviral, antineoplastic and as a lipid lowering agent. Recent studies have also shown bitter melon with anti-cancer efficacy [8, 9]. For example, our laboratory has shown that bitter melon extract suppresses adrenocortical cancer cell proliferation through modulation of the apoptotic pathway, steroidogenesis, and insulin-like growth factor type 1 receptor/RAC-α serine/threonine-protein kinase signaling [9]. The major bioactive compounds in bitter melon have shown to include charantin, vaccine, triterpenoids and antioxidants.

According to a recent study by Lo et al. [10] bitter melon contains a protein that binds and activates the insulin receptor at an adjacent binding site to insulin mimicking the action of insulin and allowing glucose entry into fat and muscle cells from the blood stream. While there are many oral hypoglycemic agents, none are currently known to be capable of binding and activating the insulin receptor. Until recently, *M. charantia* insulin receptor-binding protein (mcIRBP) has been isolated from bitter melon as the active protein capable of acting in lieu of insulin [10]. In T1DM mice incapable of producing insulin, mcIRBP decreased blood glucose levels by 10.8% compared to insulin 34.7%. While the effects of bitter melon are not as potent as insulin, bitter melon is capable of lowering blood glucose in individuals incapable of producing insulin and could decrease the amount of insulin needed by T1DM and provide an oral alternative to insulin in some T2DM. Perhaps most exciting, is the fact that mcIRBP binds to a different receptor than insulin, allowing a direct route to the insulin receptor in patients with insulin resistance.

Multiple studies have documented the antidiabetic, hypoglycemic and pancreatic beta cell stimulating effects of bitter melon *in vitro* and in animal studies [11]. Unfortunately, very few quality human trials have been completed documenting the abilities of the plant. While the antidiabetic effects have been the most studied, bitter melon also possesses lipid-lowering, antibacterial, antiviral and significant anticancer effects [12]. Bitter melon also stimulates the immune system and may provide an alternative therapy for human immunodeficiency virus [13]. In addition to diabetes, bitter melon possesses promising and exciting antineoplastic properties that are effective against multiple cancers [14] both as a treatment and as a preventative through modulating multiple signaling pathways. Bitter melon can also be used to treat bacterial infections from E. coli, S. aureus, Salmonella, Pseudomonas and Streptobaccilus [15].

Bitter melon, a nutrient dense superfood and excellent source of fiber, contains over 225 compounds [16] including the minerals potassium, sodium, calcium, zinc, magnesium, iron, manganese, and copper. It is rich in vitamin A, vitamin E, folic acid, cyanocobalamin (B12), ascorbic acid (Vitamin C) and contains trace amounts of niacin (B3), pyridoxine (B6), cholecalciferol (vitamin D) and phylloquinone (vitamin K) [17]. The mild bitter flavor is attributed to the high level of antioxidants it contains including phenols, flavonoids, isoflavones, glucosinolates, anthroquinones and terpenes [18]. The hypoglycemic effects are attributed to multiple compounds including triterpenes, steroids, proteids, alkaloids, phenolic compounds and lipids [19].

Bitter melon improves diabetic hemoglobin A1c levels, reduces postprandial blood glucose levels [20], reduces waist circumference [21] and reduces symptoms of metabolic syndrome [22]. Bitter melon increases the number of functioning pancreatic beta cells [23] and decreases insulin resistance [24]. Bitter melon also decreases the intestinal absorption of glucose [25] and inhibits multiple hepatic enzymes responsible for glucose storage and production.

Bitter melon is also known to contain a compound called vincine [1]. Vincine is found in fava beans and causes fauvism in patients deficient in glucose-6-phosphatedehyrogenase (G6PD deficiency) [21]. To date, there have been no reports of bitter melon inducing fauvism. Individuals with G6PD deficiency should avoid or use caution with this fruit until additional studies can be performed to address this possibility.

A recent study has discovered that bitter melon may also have a role in the regulation of menstrual cycle regulation and the treatment of menopausal symptoms by stimulating estrogen receptor genes and the production of estradiol. Bitter melon extract promotes uterine tissue regeneration, inhibits uterine apoptosis and protects against oxidative damage to the uterus [26]. However, pregnant women should avoid bitter melon as it has been traditionally used as an abortifacient and may cause abortions in pregnant women [27]. Seeds and seed extracts can be toxic to children and have demonstrated an anti-spermatogenic effect on male mice [28]. Therefore, men who are trying to have children should not take bitter melon or use with caution.

Conclusion

Diabetes is now the most common endocrine related disorder and diabetic patients are at increased risk for vascular disease, renal failure,

neuropathy, retinal damage and other comorbidities. Managing these patients is expensive, time consuming and challenging for family physicians. Teaching and encouraging patients to make healthy changes to their diet and increase their level of activity takes a substantial investment of time and energy on the part of the provider. We live in a country where fast food, sugar and processed foods are abundant and cheap. It can be very challenging if not impossible for many patients to break the dietary and sedentary habits that have taken years to develop. As patients make the transition from the state of health to that of chronic disease, family physicians must strive to prevent and reverse the ill effects that years of unhealthy eating and underactivity have provoked. In addition to conventional medications, complementary and alternative medicine provides physicians with natural treatment options. Patients who present with early signs and symptoms of diabetes are encouraged to implement lifestyle modifications to prevent disease progression. Some are placed on oral hypoglycemic agents to prolong the time period before requiring insulin to control blood glucose levels.

There are over two hundred compounds within bitter melon that have known medicinal values [16]. These compounds likely utilize a harmonious and synergistic mechanism of action that affords bitter melon its vast array of beneficial medicinal qualities.

Bitter melon is one example of many existing alternative treatment options available to family physicians who are interested in providing complementary and alternative medicine for their patients. Many of these therapies yield lower cost, fewer side effects and offer additional options for patients with diabetes and other chronic illnesses [4].

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