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Anti-Diabetic Potentials of Bitter Melon

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As of 2016, the World Health Organization estimated that around 422 million adults have a form of diabetes mellitus (WHO 2016). In the United States, approximately 30.2 million people had diabetes in 2015, and 7.2 million were undiagnosed (CDC 2017). Due to the rising prevalence of Type 2 diabetes especially, it is crucial that treatment methods for this disease are explored across every health discipline.

Bitter melon is one of the vegetables known to have glucose-lowering (or hypoglycemic activity, and it has been used in various parts of the world to treat diabetes. However, bitter melon is not a familiar food source to many Americans. This article will review the hypoglycemic potential of bitter melon for Virginia Cooperative Extension agents and a general audience.

Diabetes

The WHO (2016) defines diabetes as "a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces."

The human body gets energy from the food we eat. In the digestive tract, carbohydrates (sugars and starches) in the food break down into glucose. The stomach and small intestines absorb the glucose and then release it into the bloodstream. Insulin is a major hormone that regulates blood glucose homeostasis. People with normal insulin sensitivity produce normal levels of insulin to process glucose.

After a meal, insulin is released from the pancreas into the bloodstream. It binds to insulin receptors on the surface of the cells and facilitates the uptake of circulating glucose by cells so that blood glucose levels will remain relatively stable. Tissues such as the liver and muscles use glucose as energy or store glucose in the form of glycogen.

People with diabetes may produce either no insulin (Type 1 diabetes) or little insulin and cannot use insulin effectively (Type 2 diabetes). In many cases, the person may actually produce more insulin than needed because the body's cells are resistant to the effects of insulin. This condition is called insulin resistance (Diabetes).

Among the different types of diabetes mellitus, Type 2 diabetes is the most common type in terms of diagnosed cases. Usually appearing in adulthood, Type 2 diabetes is characterized by abnormal insulin production and insulin resistance. These drawbacks prevent glucose being taken into cells to be used for energy. As a result, individuals with Type 2 diabetes frequently suffer symptoms of high blood glucose levels, such as fatigue, blurred vision, excessive thirst, or tingling sensations in the hands and feet (CDC 2015).

Easy, fast, and accurate screening and diagnosis of diabetes are available, including a hemoglobin A1c (HbA1c) test, a fasting blood glucose test, and an oral glucose tolerance test (table 1; (ADA). Vigilant blood glucose testing along with anti-diabetic medication and an appropriate diet can control many of the immediate symptoms of Type 2 diabetes; however, frequent high blood glucose levels can eventually cause Type 2 diabetes patients to develop serious long-term complications. Additionally, factors such as high blood pressure and high cholesterol can allow these complications to emerge at a faster rate. Common complications of Type 2 diabetes include cardiovascular diseases, kidney damage, nerve damage, and eye damage (ADA).

Metformin, sulfonylureas, and insulin (in monotherapy or in combination therapy) are used as conventional treatments of Type 2 diabetes. These drugs help reduce high blood glucose in the bloodstream and increase

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insulin secretion from the pancreas along different stages of the glucose metabolic cycle; they work in synergy with insulin's hypoglycemic effects (Cherney 2016). However, these pharmaceutical drugs often have side effects that could negatively affect the consumer (Jiang et al. 2016). Therefore, alternative treatments that do not rely on drugs, such as targeted dietary intervention, can offer more diverse Type 2 diabetes treatment options.

Table 1. Diagnosing diabetes (CDC 2015)

Diagnosis	HbA1c[1]	FBG[2]	OGTT[3]
Diabetes	≥ 6.5%	≥ 126 mg/dL	≥ 200 mg/dL
Prediabetes	5.7 – < 6.5%	100 – < 126 mg/dL	140 – < 200 mg/dL
Normal	< 5.7%	< 100 mg/dL	< 140 mg/dL

1. Hemoglobin A1c: The HbA1c test measures average blood glucose level over the past three months.

2. Fasting blood glucose: The FBG test measures the blood glucose level after not eating or drinking (except water) for at least eight hours prior to the test, which is usually done first thing in the morning.

3. Oral glucose tolerance test: The OGTT shows how the body processes glucose by measuring blood glucose levels both before and two hours after drinking a special sweet drink.

Bitter Melon and Its Anti-Diabetic Components

Bitter melon (*Momordica charantia*; fig. 1; (Zhang, Lin, and Xie 2016) is a potential food source that researchers have investigated for controlling Type 2 diabetes conditions. It is normally cultivated in Southeast Asia and Central America for culinary and medicinal purposes. Bitter melon has been reported to possess a wide variety of health benefits, including antioxidant, antiviral, and anti-ulcer properties (Behera, Behera, and Bharathi 2010).

In the case of bitter melon's anti-diabetic properties, the fruit and seeds are believed to possess various phytochemicals with hypoglycemic activities, including charantin, vicine, momordicin, protein polypeptide-p, and triterpene glycosides (saponins; (Habicht et al. 2014, Krawinkel and Keding 2006). Charantin and polypeptide-p act like insulin during carbohydrate metabolism (Krawinkel and Keding 2006). The other major components of vicine, momordicin, and saponin-rich fraction promote insulin secretion in the pancreas (Habicht et al. 2014, Keller et al. 2011). Together, these substances (as well as various phytochemical components) in bitter melon can promote blood glucose control by increasing glucose intake within fat and skeletal muscle cells and reduce glucose absorption from the small intestine into the bloodstream (Jiang et al. 2016).

In addition to consuming bitter melon fruit directly, some commercial brands offer dietary supplements containing dried bitter melon or bitter melon extract. Many of the animal and human studies involved with bitter melon have used either dried fruit or extract as the preferred method for delivering the mentioned anti-diabetic components.

Research Findings

Over the last decade, multiple studies revolving around the health benefits of bitter melon against Type 2 diabetes have been conducted. However, a limited number of these studies involved large-scale clinical trials with Type 2 diabetes patients.

Numerous in vivo and animal studies have demonstrated the hypoglycemic activities of various forms of bitter melon. Bitter melon pulp juice lowered fasting blood glucose levels and improved glucose tolerance in rats with chemical-induced diabetes (Mahmoud et al. 2017). Bitter melon fruit powder

Figure 1. The four pictures show (A) bitter melon leaf and flowers, (B) seed, (C) fresh fruit, (D) mature fruit, respectively.

also lowered fasting blood glucose levels in rats with high-fat diet-induced diabetes (Bai, Zhu, and Dong 2016, Yang et al. 2015). In addition, these two studies observed that bitter melon fruit powder relieved the inflammatory condition and improved insulin sensitivity.

There are studies being conducted to elucidate the potential mechanisms of bitter melon's hypoglycemic activities.

Bitter melon may slow down carbohydrate metabolism by inhibiting enzymes involved in glucose conversion in the digestive track. The amino acid and fatty acid composition isolated from the bitter melon seeds inhibited the activities of carbohydrate-metabolizing enzymes (including alpha-amylase and alpha-glucosidase) in vitro (Ahmad et al. 2012). A rat study also showed that bitter melon extract lowered after-meal glucose levels by inhibiting alpha-glucosidase enzyme activity (Uebanso et al. 2007). Researchers working with diabetic mice found that a daily administration of bitter melon extract (20-100 mg/kg body weight) improved blood glucose and insulin levels while yielding enhanced glucose tolerance tests (Miura et al. 2001). A study conducted with diabetic mice tested the combination of bitter melon extract and exercise and found that the blood glucose of the bitter melon with exercise group was lower than that of the bitter melon only group or the exercise only group (Miura et al. 2004). One study conducted in rats with high-fat diet-induced obesity and insulin resistance found that dried bitter melon powder effectively brought plasma glucose, serum triglycerides, and insulin levels back to the normal range (Huang et al. 2008).

Bitter melon may decrease glucose absorption from the intestine to the blood stream. The saponin fraction of bitter melon limited the absorption of glucose through the gut wall in rats (Oishi et al. 2007). A study that used rodent intestinal cell models showed a significant decrease in glucose absorption following exposure to bitter melon extracts, suggesting that bitter melon extract may decrease glucose absorption from the intestine to the bloodstream (Mahomoodally, Fakim, and Subratty 2004).

Bitter melon may increase glucose uptake from the bloodstream into the tissue. When rodent skeletal muscle cells were treated with varying concentrations of bitter melon juice (5-200 μg/mL), a significant negative correlation was interpreted between the dosage concentration and total glucose uptake into the skeletal muscle (Ahmed et al. 2004). In diabetic mice, bitter melon extract helped facilitation of glucose uptake into the muscle and improved insulin sensitivity (Miura et al. 2001).

However, during human clinical trials, researchers obtained mixed results concerning bitter melon's effects on Type 2 diabetes. Daily bitter melon extract supplement (200 mg per day) was shown to have synergistic effects on the diabetic drugs metformin or glibenclamide with 15 patients with Type 2 diabetic (Tongia, Tongia, and Dave 2004).

A larger clinical trial containing 112 diabetic patients with fasting glucose levels of 126-240 mg/dl evaluated the safety and efficacy of bitter melon powder with glibenclamide. Two randomized groups were given either 2 or 4 g/day of bitter melon powder while a third group received glibenclamide. Both groups who received bitter melon powder showed decreased HbA1c and fasting blood glucose levels as well as reduced cardiovascular risks at a greater degree than the glibenclamide group (Rahman et al. 2015).

A meta-analysis (completed by the Cochrane Collaboration) reviewed data collected from four randomized controlled trials with up to three months' duration in 479 participants and concluded that bitter melon did not have a significant impact on Type 2 diabetic patients' blood glucose control (Ooi, Yassin, and Hamid 2012).

A Health Claim for Bitter Melon in the U.S.

Due to limited research documenting the response of Type 2 diabetes patients to bitter melon, a reliable dietary intake of this plant cannot be suggested. While the suspected phytochemicals have exhibited hypoglycemic behavior in the in vivo and animal studies, clinical trials involving Type 2 diabetes patients may have introduced a multitude of factors that have affected their findings. The effectiveness of charantin, polypeptide-p, and vicine, and momordicin in bitter melon could vary across age, baseline blood glucose levels, and duration of dietary intervention (Habicht et al. 2014).

Unfortunately, many of these human studies also varied how much bitter melon each subject received,

and because of this uncertainty, bitter melon's alleged utility as an alternative treatment for Type 2 diabetes cannot be confidently acknowledged. Further clinical trials conducted with more specific parameters may provide a better understanding about the potential and limitations of bitter melon consumption.

Without a hard consensus on this subject, bitter melon is recommended as a diabetes management regimen only with regular medical supervision.

Potential Adverse Effects of Bitter Melon

Reports of side effects have arisen in both animal and human studies working with bitter melon. One prevalent adverse effect of bitter melon extract among animals is a decrease in fertility rate and sperm cell development (or spermatogenesis) (Stepka, Wilson, and Madge 1974, Dixit, Khanna, and Bhargava 1978). During clinical trials, gastrointestinal symptoms such as abdominal discomfort and diarrhea were reported (Dans et al. 2007) along with headaches (Raman and Lau 1996), which could indicate that a large quantity of bitter melon leads to hypoglycemic conditions.

Once again, current available research does not provide an accurate dosage range that gives the desired control over hyperglycemia without causing unwanted symptoms. Recent review articles for the bitter melon clinical trials have concluded that individuals with glucose-6-phosphate-dehydrogenase deficiency (favism) should avoid consuming bitter melon (Leung et al. 2009). Bitter melon alkaloids such as vicine are suspected to be triggers for this disorder, which can lead to red blood cell death (Dutta and Banyal 1981, Barbieri et al. 1980).

How To Use Bitter Melon

Fresh bitter melon; dried bitter melon fruit, seeds, flowers, and leaves; pickled bitter melon; canned bitter melon; bitter melon juice; and bitter melon tea bags are available at most Asian grocery stores. For food preparation, seeds are removed from the fresh fruit, which is then blanched, parboiled, or soaked in saltwater before cooking to reduce its bitter taste. Bitter melon fruits are usually cooked with other vegetables, stuffed, fried, stir-fried, or added to soups. Bitter melon flowers, leaves, and young shoots are also used as flavoring agents in various Asian dishes, and the dried fruits, seeds, flowers, leaves, and stems can be used to brew tea.

For preparation instructions and recipes, see "How to Prepare Bitter Melon" (www.thespruce.com/how-to-prepare-bitter-melon-p2-695360) and "The Best Bitter Melon Recipes" (www.thespruce.com/the-best-bitter-melon-recipes-4071414).

Summary

The stress of high blood sugar levels on the body can later cause people with Type 2 diabetes to develop serious nerve, kidney, heart, and eye complications. Cell culture models and animal models support that bitter melon can control blood sugar like a hypoglycemic agent. Although additional clinical trials should be completed before fully accepting bitter melon as a method of alternative treatment for Type 2 diabetes, bitter melon may be helpful for the treatment and prevention of Type 2 diabetes and for reducing the use of oral anti-diabetic drugs.

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