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Use of Opuntia Cactus as a Hypoglycemic Agent in Managing Type 2 Diabetes Mellitus among Mexican American Patients

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Introduction

The incidence of type 2 diabetes mellitus has substantially increased in the United States with 1.5 million new cases of diabetes diagnosed in 2005 (Center for Disease Control and Prevention 2005). Mexican Americans, the largest Hispanic subgroup, are 1.7 times as likely to have diabetes as non-Hispanic whites (Center for Disease Control and Prevention). The American Diabetes Association showed that approximately two million Hispanics were diagnosed with type 2 diabetes mellitus (American Diabetes Association 2002).

A study by Coronado et al. (2004) on the beliefs and attitudes of Mexican Americans towards diabetes demonstrated that diet and exercise, oral medication, and subcutaneous insulin injections were acknowledged forms of medical treatment for diabetes. Additionally, participants in this study identified natural therapies as effective complements to treatments prescribed by allopathic physicians. The use of natural remedies to treat illnesses is consistent with the general health-seeking practices of Hispanics, as demonstrated in data from the Hispanic Health and Nutrition Examination Survey (see Coronado et al.). Najm et al. (2003) found that lack of health insurance, recent immigration, and frequent physician visits were strong predictors of patients incorporating natural remedies into their health management.

Various herbals are known for their apparent hypoglycemic activity in the management of diabetes, including aloe vera, fenugreek seeds, karela, ginseng, and prickly pear cactus as noted by Shapiro and Gong (2002a). The prickly pear cactus constitutes the herbal most commonly used for its hypoglycemic properties by persons of Mexican descent (Shapiro and Gong 2002b). Its cultural popularity in addition to its hypoglycemic properties makes the prickly pear cactus an ideal dietary constituent among Mexican Americans in their management of type 2 diabetes mellitus.

Historical Use of Prickly Pear Cactus

The prickly pear cactus is a member of the *Opuntia* genus and is known in Mexico as the *nopal*. This plant can be found dotting the landscape throughout the dry regions of the Western Hemisphere. The flattened stems, or cladodes popularly named *pencas*, of the prickly pear cactus have been traditionally used to maintain optimal health among the native Nahuatl populations of Mexico (Trejo-Gonzalez et al. 1996) and Native Americans in the United States (Wolfram et al. 2003). This popular herbal is also a food source and largely consumed in Mexican cuisine—used in salads, soups, casseroles, sandwiches, and blended in drinks. When used purposely for its hypoglycemic characteristics, the cactus is prepared in any of the previously described manners or is available as a dried powder in bulk form and capsules.

Evidence for Hypoglycemic Effects

Both animal and human studies have demonstrated the hypoglycemic properties of the prickly pear cactus. Although the methodology employed throughout older studies is not always uniform, the hypoglycemic characteristic of this plant is revealed. Trejo-Gonzalez et al. demonstrated the ability of purified *Opuntia fuliginosa* extract to regulate glucose levels in rats. In their controlled study, four groups of seven to ten diabetic rats were given either no treatment, 1 mL oral *Opuntia* daily, 3 to 5 units of NPH insulin subcutaneously daily, or insulin plus 1 mL oral *Opuntia* daily. In the *Opuntia*-plus-insulin group, insulin treatment was ceased after week eight due to the development of hypoglycemia; normal blood glucose values were further maintained among this treatment group for seven additional weeks using the *Opuntia* alone.

Treatment with *Opuntia* extract alone achieved normalized glucose levels by week fifteen. The control groups retained similar glucose levels throughout the study.

In a crossover, placebo-controlled human study of eight patients with type 2 diabetes mellitus, Frati-Munari, Rios Gil et al. (1989) compared serum glucose levels after patients consumed 500 grams of broiled *Opuntia streptacantha* stems, crude extracts, or only water for control purposes. Serum glucose levels among the group consuming the crude extracts were not significantly different from glucose levels among the control group. However, the intake of broiled plant stems caused a mean peak decrease in levels of serum glucose levels of 48.3 ± 16.2 mg/dL versus basal levels at three hours post-ingestion. This finding suggests that heating the prickly pear cactus may be necessary for attaining the plant's hypoglycemic effect.

Mechanism of Hypoglycemic Activity

The decrease in serum glucose levels observed upon ingestion of *Opuntia* may be due to two different mechanisms: the postprandial effect attributable to dietary fibers and the hypoglycemic effect due to specific hypoglycemic substances in the ingested plant. While the dietary fiber is neither digested by gastrointestinal enzymes nor absorbed, it does modify the absorption of certain substances such as biliary salts, cholesterol, and glucose (Frati-Munari, Fernandez-Harp et al. 1983). In a crossover study, Chandalia et al. (2000) demonstrated a 10% reduction in 24-hour plasma glucose concentration in patients on a high soluble fiber diet compared with the standard diet previously recommended by the American Diabetes Association. Soluble fibers, such as the large quantities of pectin and mucilage found in the prickly pear cactus, increase the viscosity of food in the gut, slowing or reducing sugar absorption (Shapiro and Gong 2002a). Furthermore, Frati-Munari, Gordillo et al. (1991) found that when cactus stems were ingested simultaneously or immediately prior to an oral glucose test, a decrease in glycemic serum peak was observed.

Frati-Munari, Del Valle-Martinez et al. (1989) has hypothesized that the hypoglycemic effects observed upon the ingestion of *Opuntia streptacantha* were aside from the effects attributed to the dietary fiber. In order to rule out the hypoglycemic effect of dietary fiber, Frati-Munari, Licona-Quesada et al. (1990) parenterally administered 500mLs of 20% dextrose versus 400mLs of water after initial ingestion of 500g of *Opuntia streptacantha* among different groups of patient subjects. Blood glucose levels were significantly different among treatment and control groups at 90 minutes after the dextrose or water infusion (143.4 ± 58 versus 192.5 ± 9 mg/dl, respectively). Additionally, since a significant decrease in serum insulin level was observed after *Opuntia* intake among their study subjects, the hypoglycemic effect was hypothesized to involve an enhancement of cellular sensitivity to insulin and not to an increase in insulin release. No substance, however, was ever identified.

Recently, polysaccharides of *Opuntia ficusindica* (POLOF) and *Opuntia streptacantha* (POLOS) were isolated and evaluated for their hypoglycemic properties by Alarcon-Aguilar et al. (2003). When each of the two polysaccharides was injected intraperitoneally in healthy mice, no hypoglycemic activity was observed. POLOF administered orally caused a significant hypoglycemic effect in orally-induced hyperglycemic mice. Due to the oral administration of both POLOF and the hyperglycemic-inducing agent, the hypoglycemic effect of POLOF may function similar to dietary fiber in reducing the intestinal absorption of glucose. On the other hand, POLOS produced a significant decrease in serum glucose levels in mice with subcutaneously-induced hyperglycemia. Considering that subcutaneously-induced hyperglycemia bypassed the intestinal absorption of glucose, POLOS may be a hypoglycemic

agent possibly working by increasing insulin sensitivity, as previously hypothesized by Frati-Munari, Del Valle-Martinez et al.

Hypoglycemic Activity of Different Preparations

Different preparations of the prickly pear cactus have been studied in order to make the medicinal properties of this plant most accessible to patients. Frati-Munari, Altamirano-Bustamante et al. (1989) prepared *Opuntia* extracts by raw homogenization of the cactus cladode. Their patient study compared the effects of consuming different components of homogenized preparation (pure supernatant, pure precipitate, or whole homogenized preparation) to consuming equivalently measured broiled plant stems, or water for control purposes. They found that the raw homogenized preparations did not produce the hypoglycemic activity obtained by the broiled plant stems. Subsequently, Frati-Munari, Vera Lastra et al. (1992) found that consumption of 100 g of broiled prickly pear three times daily before meals for ten days resulted in a decrease of fasting glucose levels in patients with diabetes.

Capsules containing dried prickly pear cactus are also commonly used as a complement to the medical treatment of diabetes, high cholesterol, and obesity. A patient study by Frati-Munari, Vera Lastra et al. assessed the effectiveness of dried *Opuntia* using 30 capsules found to contain the equivalent of 300 mg of prickly pear cactus. Although a decrease in lipid concentrations was observed, there was no decrease in serum glucose levels attributed to the intake of *Opuntia* capsules. The heating and processing of the *Opuntia* capsule content may actually degrade or diminish hypoglycemic activity to undetectable levels. Additionally, the use of 30 capsules in any treatment regimen would generate poor medical adherence by patients in the clinical setting.

Cardiovascular Benefits

In addition to its hypoglycemic properties, the prickly pear cactus has also been shown to decrease hypercholesterolemia, optimize platelet function, and decrease oxidative tissue injury. In an experiment by Budinsky et al. (2001) using guinea pigs, the ingestion of prickly pear cactus was shown to reverse the low-density lipoprotein receptor suppression induced by a hypercholesterolemic diet. The influence of *Opuntia* was also examined in patients suffering from familial heterozygous isolated hypercholesterolemia (Budinsky et al.). A daily consumption of 250 grams of broiled edible pulp of prickly pear over four weeks decreased both total cholesterol ($P < 0.01$) and LDL-cholesterol ($P < 0.04$).

Platelet function is considered to significantly contribute to the initiation and progression of atherosclerosis, often a complication found in patients with type 2 diabetes mellitus. In a recent study by Wolfram et al., the ingestion of prickly pear cactus by both healthy individuals and patients with mild familial hypercholesterolemia demonstrated optimization of platelet function. Prickly pear cactus consumption significantly reduced markers of platelet activation (platelet factor 4 and β -thromboglobulin), reduced ADP-induced platelet aggregation, and improved platelet sensitivity against PGI_2 and PGE_1 . Optimizing platelet function and thereby improving haemostatic balance would benefit patients with conditions associated with atherosclerotic risk such as that found in hyperlipidemia and diabetes mellitus.

Budinsky et al. also reported that the consumption of prickly pear cactus induces a significant decrease in plasma, serum, and urinary values of 8-epi-PGF_{2 α} , a product of lipid peroxidation and cause of oxidative damage. These findings indicate that the regular ingestion of *Opuntia* is able to significantly reduce *in vivo* oxidation injury in patients suffering from

hypercholesterolemia. Cardiovascular disease and stroke account for more than half of deaths in people with diabetes (Center for Disease Control and Prevention 2005). The regular ingestion of prickly pear cactus may possibly complement medical treatments aimed at not only optimizing serum glucose levels but also decreasing progression of vascular disease in type 2 diabetes mellitus.

Adverse Effects and Precautions

Consumption of large quantities of the prickly pear fruits containing many seeds can cause fecal impaction and has been associated with complications of colonic obstruction and perforation (Kleiner et al. 2002; Steinberg and Eitan 2003). A rare case of allergic contact dermatitis due to *Opuntia* applied to broken skin was reported by Yoon et al. (2004). Ingested in its vegetable form, large quantities of the prickly pear fiber may decrease absorption of some medications. Concomitant ingestion of prickly pear cactus with hypoglycemic medications may increase the risk of hypoglycemia, although this has not been commonly reported. As noted by Shapiro and Gong (2002a), supplement preparations may also be contaminated or simply ineffective due to the absence of *Opuntia* in the product purchased by patients. Aside from risks associated with consumption of large quantities of prickly pear fruits, there are no significant documented risks or complications associated with ingestion of the prickly pear cladodes.

Conclusions and Recommendations

The prickly pear cactus has been shown to have hypoglycemic activity likely due to both fiber content and specific hypoglycemic agents. Although its beneficial properties are marketed as raw extract and dehydrated capsule preparations, its beneficial properties are best attained by consumption of the cooked prickly pear cladodes. Additional properties that would benefit patients with diabetes mellitus include its ability to reduce hypercholesterolemia, optimize platelet function, and decrease oxidative tissue damage. Given the innate hypoglycemic properties of the prickly pear cactus, health care professionals should inquire about the use of such natural therapies among Mexican American patients with type 2 diabetes mellitus. Efforts to manage their own health should be supported by providing adequate information regarding the benefits and adverse effects of the use of prickly pear cactus to patients with type 2 diabetes mellitus.

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