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Effects of *Cucurbita ficifolia* Intake on Type 2 Diabetes: Review of Current Evidences

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Context: Type 2 diabetes mellitus (DM) is one of the most common chronic diseases worldwide. In recent years, *Cucurbita ficifolia* intake has been identified as one of the most widely used herbal medications in treatment of DM. Since previous studies have suggested the benefits of C. *ficifolia* intake in treatment of DM, we reviewed available literature concerning effects of C. *ficifolia* on Type 2 DM.
Evidence Acquisition: Databases such as PubMed, Scopus, and Google scholar were searched. Key words included type 2 diabetes, blood glucose, hyperglycemia, insulin resistance, and C*ucurbita*. After removing irrelevant article, ten articles were reviewed.
Results: Studies reported beneficial effects of C. *ficifolia* on serum insulin and glucose level. Some of the studies showed a correlation between low level of lipid profiles and plasma glucose and increase intake of C. *ficifolia*. Although the exact role of C. *ficifolia* intake on DM has not been identified, the benefits might be due to the effects of active compounds such as flavonoids, alkaloids, polyphenolic components, glutathione peroxidase, and superoxide dismutase.
Conclusions: *Cucurbita ficifolia* intake might have useful effects on prevention and treatment of DM. C*ucurbita ficifolia* has beneficial effects on insulin sensitivity and risk factors of DM; however, due to the small number of available studies, more researches are needed in this field.

*Keywords:*Type II diabetes; Cucurbita; Hyperinsulinism; Hyperglycemia

1. Context

Diabetes mellitus (DM) is a chronic disorder of carbohydrate, fat, and protein metabolism (1). This disease is characterized by high levels of blood glucose due to absence of insulin secretion or insulin resistance (2). Type 2 DM is due to decrease peripheral glucose uptake and increase blood glucose level. Since type 2 DM causes serious nervous system, renal, and ophthalmologic complications, its prevention and treatment has urgent priority. The prevalence of Type 2 DM is predicted to increase dramatically in the next few years. DM affects approximately 4% of the population worldwide and is expected to increase by 5.4% in 2025 (3). Moreover, DM is one of most common chronic disease in Iran. Its prevalence is 7% and 8% among Isfahan and Tehran residents, respectively (3).

Traditional medicine is considered in treatment of numerous diseases, especially chronic diseases. Recent researches have shown the beneficial effects of herbs such as vegetable in the treatment of DM. In Asia, traditional medicinal plant, *Cucurbita ficifolia* (Cucurbitaceae), popularly known as pumpkin, is one of the most widely used herbal medications in treatment of DM (4). In recent years, *C. ficifolia* intake is commonly used as antidiabetic and antihyperglycemic agent in Asia (5); however, the mechanisms of antidiabetic action of this plant are unknown (6). Some evidence has shown an association between higher intake of C. ficifolia marrow and lower levels of glucose and lipid profile (7); however, there are controversial evidences concerning the difference effects of C. ficifolia marrow on DM. In this review study, we discussed the different effect of this vegetable on diabetes and lipids profile.

2. Evidence Acquisition

The search was conducted in the following databases: PubMed, Scopus, and Google Scholar. Keywords such as "type 2 diabetes", "blood glucose", hyperglycemia, "insulin resistance", "*cucurbita*", and "*cucurbita* marrow" were used. Human and animal studies, English language, and clinical trials that investigated the effect of C. *ficifolia* intakes on type 2 DM were included. Titles and abstracts of papers were screened and relevant papers were selected. Then, full texts of relevant papers were read and findings rescreened. Finally, we evaluated ten studies

3. Results

Cucurbitaficifolia contain water (94%), fiber (3%), vitamin B1 (0.03 mg), calcium (17 mg), iron (0.6 mg), and vitamin C (7 mg) (8). One Study showed C. *ficifolia* extract had impressive effect of lipid profile and serum insulin of mice with streptozocin-induced DM (9).

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Most of the animal studies showed beneficial effects of C. *ficifolia* on diabetic animals. Xia et al. (10) reported that in mice, C. *ficifolia*-rich diet reduced blood glucose and improved glucose tolerance significantly after 28 days. Another studies showed that C. *ficifolia* extract decreased blood glucose concentration after 60, 90, and 120 minutes of intake in diabetic rats and 30 minutes after glucose loading, blood glucose level in C. *ficifolia* group was significantly lower than in control group (11). Acosta-Patino et al. (6) investigated effect of *C. ficifolia* on pancreas β cells and showed *C. ficifolia* could significantly improve function of β cells, and the number of insulin-positive cells per islet. These results is consistent with findings that suggested incidence of DM in treated mice with *C. ficifolia* was lower than in controls by Kaplan-Meier analysis ($P < 0.001$) (12). In contrary, Alarcon-Aguilar et al. (13) found that plasma glucose concentration was significantly increased in *C. ficifolia*-intake group. Oral glucose tolerance test showed that in comparison with the controls, seeds of all species except *C. ficifolia* caused significant drop in blood sugar ($P < 0.05$).

Animal studies have shown that *C. ficifolia*-rich diet markedly reduced lipid peroxidation in pancreas and decreased malondialdehyde (MDA) level by 28% in diabetic rats (4). Another study found that both plasma and liver lipids decreased by 21% and 19%, respectively, in the group of animals with *C. ficifolia* diet (14). Xia et al. (10) reported that *C. ficifolia*-rich diet reduced plasma and liver total cholesterol (TC) levels by 47% and 45%, respectively. In addition, *C. ficifolia* reduced plasma and liver triglycerides (TG) levels by 47% and 15%, respectively. Moreover, serum TC and atherogenic index were significantly lower in the *C. ficifolia* group than in controls ($P < 0.05$) (14). Makni et al. (8) showed the serum TG level did not differ between the control and pumpkin groups although the nonesterified fatty acid (NEFA) level was significantly lower in the *C. ficifolia* group in comparison with the control group ($P < 0.05$) (15). While studies have shown that *C. ficifolia* caused decrease lipid parameters, effect on the high density lipid cholesterol (HDL) has not been specified (Table 1).

Table 1. Summary of Some Studies on *Cucurbita* Intake and Glycemic Effect [a]

Author	Duration of Study	*Cucurbita* Intake Dose	Population of Study	Result
Teugwa et al. (16)	**7 days**	295.11 mg/g dry Matter *C. Ficifolia*	Male Mice (n = 24)	*Cucurbitaceae* Seeds Contained globulins with significant antihyperglycemic activity.
Diaz-Flores et al. (9)	**4 weeks**	200 mg/kg *C. Ficifolia* Aqueous Extract	Male Mice (n = 14)	*Cucurbita ficifolia* Intake Enhanced Activity of Glutathione Peroxidase and Glutathione Reductase in Liver, Pancreas, and Kidney. It Significantly Reduced Hyperglycemia, Polydipsia, hyperphagia, and Plasma Lipid Peroxidation.
Jiang et al. (15)	**4 weeks**	105 mL/min and 800 rpm Extract of *C. Ficifolia*	Male Mice (n = 10)	Extracts Significantly Decreased Blood Glucose.
Makni et al. (8)	**2 weeks**	Flax and *C. Ficifolia* Seed Mixture Powder (2g/kg BW)	Male Wistar rat (n = 6)	The powder Significantly Decreased Glycemia, Plasma and Liver Lipid Parameters Such as TC and TG, and mda, and increased Antioxidant enzymes.
Yoshinari et al. (17)	**3 days**	600 g *C. ficifolia*	Male Wistar Rat	*Cucurbita Ficifolia* Increased Insulin level over 120 min and Improved Insulin Resistance. Serum and Liver TG levels and Hyperphagia Decreased.
Xia et al. (11)	**4 weeks**	300 mg/kg body weight extract of *C. ficifolia*	Male rat	Extract significantly diminished Hyperglycemia and Lipid Peroxidation in the Pancreatic Tissue. Level of Plasma Insulin Markedly Decreased by 41% ($P < 0.01$) in Comparison With Control.
Liu et al. (4)	**4 weeks**	pumpkin polysaccharides	Diabetic rats	Pumpkin Polysaccharides Can Decrease The Blood Glucose And Lipids Levels.
Quanhong et al. (18)	**10 days**	high dose PBPP (1000 mg/kg body weight) small dose PBPP group (500 mg/kg body weight)	Male rat (n = 16)	Blood Glucose Significantly decreased after *C. Ficifolia* Intake. The Results Suggest That the Hypoglycemic Effect of PBPP Depends on the Dose and it Can Develop into a New Antidiabetic Agent.
Alarcon-Aguilar et al. (13)	**2 weeks**	Freeze-dried juice of *C. ficifolia* (1000 mg/kg body weight/day)	Male mice (n = 5)	Study Showed an Acute Hypoglycemic Effect in Animals and Significant Reduction of Glycemia.
Acosta-Patino et al. (6)	**8 weeks**	75 mL of the *C. ficifolia* extract	Female and male subject (n = 10)	Blood Glucose Level Decreased Significantly.

[a] Abbreviation: TC, total cholesterol; TG, triglyceride; MDA, malondialdehyde; and PBPP, protein-bound polysaccharide from pumpkin fruits.

4. Discussion

We assessed the association between consumption of pumpkin and diabetes in several studies. Most of these studies were done on animals. The antiglycemic effect of *C. ficifolia* was seen in patients with type 2 DM with moderate hyperglycemia (7, 15, 16, 18, 19). The strongest antiglycemic effect was obtained after three to five hours of oral administration (9). Evidence showed that an aqueous extract of this plant significantly decreased blood sugar and glycosylated hemoglobin. Another characteristic of *C. ficifolia* extract is its effect on the distribution and number of pancreatic β cells in the diabetic rats, that is, *C. ficifolia* intake positively affects the β cell in pancreas (8, 9, 11). It has been reported that phenols in *C. ficifolia* can inhibit lipid peroxidation and demonstrate antioxidant activity that also have antiglycemic and antilipemic properties. Therefore, *C. ficifolia* may have antioxidative activity (4); these finding showed that *C. ficifolia* extract would help to achieve good glycemic control.

It was also shown that 20 mg/kg of *C. ficifolia* natural extract was slightly more useful than chemically synthesized *C. ficifolia* extract at the same dose. It may be the result of natural components in C. *ficifolia* natural extract, ie, active compounds such as flavonoids, alkaloids, polyphenolic components, glutathione peroxidase, and superoxide dismutase (5).

Results confirmed antiglycemic effects of C. *ficifolia* oral administration in healthy and alloxan-induced diabetic rabbits (5). Studies presumed that myo-inositol might have contributed to the glucose lowering effects of the *C. ficifolia* extract by conversion to chiro-inositol in vivo (19). Serum and liver TG levels were downregulated in the process of type 2 DM improvement that was closely related to the regulation of glucose uptake or gluconeogenesis (8, 11). These results suggested that regulation of these enzymes by trigonelline and *nicotinic acid* in *C. ficifolia* might play a crucial role in mitigating progression of diabetes in rats; however, the precise mechanisms should be determined (15, 17).

5. Conclusions

Studies showed that pumpkin extract has positive effects on glycemic control, lipid profile, and pancreatic β cells; however, most of the studies were done on animals. Due to the small number of available studies, more research, especially human study, are needed in this field.

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