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Review Article

The Effectiveness of Stevia in Diabetes Mellitus: A Review

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ABSTRACT

Stevia is a sweet calorie-free plant used in food industry as a sweetener in beverages and foods. Lots of studies have been done on its efficacy, including its effects on weight, blood glucose, lipid profile, inflammation, etc. Recently, this plant has attracted diabetics, due to its low calorie sweetness. Diabetes is a chronic metabolic disease with an increasing prevalence, that the government and patients spend a great deal of money on treatment each year. Therefore, in this study, we aimed to investigate the effects of stevia supplementation in diabetic patients. Studies have shown that only a few studies have been conducted on diabetic patients, while many animal studies are available. Our review of these studies showed that stevia is a safe herb for diabetics and may have therapeutic effects, if used at a pharmacological dose, although more detailed studies are needed.

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Introduction

Diabetes is the most common cause of blindness and the most important cause of chronic renal failure (1). It is known as the most important cause of amputation in the world (2). Diabetes is a metabolic disorder mainly caused by insulin deficiency or dysfunction that results in hyperglycemic condition. Increased blood glucose in this disease for a long time causes many disorders such as heart disease, stroke, neuropathy, retinopathy, and renal problems (3). It was shown that insulin resistance is the most important factor in promoting type two diabetes mellitus (T2DM). It is strongly linked to diet, obesity, especially abdominal obesity and physical activity (4).

Lifestyle modification with proper diet, weight loss in overweight and obese patients and regular physical activity are the most important principles in managing diabetes (5). To improve glycemic status glucose lowering medications are used such as metformin, biguanides, thiazolidinediones, and also insulin (6). In recent years, herbal remedies have attracted much attention. Some herbal drugs became popular because of low side effects in comparison to chemical drugs (7). Researchers investigated a lot of studies in recent decades about the effect of different herbs on diabetes. Stevia is also one of the herbs that a large number of studies have been done to investigate its effectiveness on different issues (8).

Stevia rebaudiana belongs to the family *Asteraceae*. It is native to the northeast of Paraguay, but is cultivated in other regions around the world like

Europe, Asia, and North America. Stevia is famous because of its high sweetness which is about 250-300 times more than sucrose. Its sweet taste is related to the steviol glycosides that are commonly used as non-caloric sweeteners and substitutes for sugar. The Joint Expert Committee on Food Additives (JECFA) has established the accepted daily intake of purified steviol glycosides extracts which is 4 mg/kg/day (9).

Also, the European Food Safety Authority (EFSA) declared the safety of purified steviol glycosides to be used in food and beverages as a sweetener or additive. Further to stevia sweetness, it contains other components that have therapeutic properties including flavonoids and phenolic components (9). Considering the importance of diabetes and the beneficial effects of the stevia, as stated in various studies, we decided to investigate the effect of stevia on diabetes.

The Effect of Stevia on Glycemic Profile

Few clinical trial studies investigated the effect of stevia in diabetes (10-12), while most of the studies in this subject are conducted on animal models (13-16). Some of the studies are in Table 1. In human studies (10, 12), stevia consumption had no significant effect on HbA_{1c} (hemoglobin A1c), FBS (fasting blood sugar) levels, while animal studies indicate the effectiveness of stevia on FBS and insulin status (13, 17-19). This may be due to the use of the whole extract of stevia (20, 21) that contains other compounds like polyphenols and also using stevioside at higher doses (17), whereas human studies used stevioside in allowed limited doses (10, 12). Moreover, some studies have also demonstrated the beneficial effects of stevia on postprandial glucose (11, 22).

The Effect of Stevia on Calorie Intake and Weight

Obesity especially abdominal obesity is the most important risk factor in diabetes mellitus that can cause insulin resistance (4). On the other hand, weight loss is associated with improved glycemic profile. Therefore, considering the importance of weight loss, calorie and sugar restriction using products that are sweet, but low in calories and sugar is important for diabetic patients (23). Stevia along with sweet, but calorie-free flavors has shown beneficial effects on food intake and weight loss. Although two human (22, 24) and animal studies (25) have illustrated such effects; there are also several clinical trials that have not found a significant effect on BMI (26-28) (Table 2).

The Effect of Stevia on Lipid Profile

Animal studies indicated the decreasing effect of stevia on triglyceride (29). However, the effect of stevia on cholesterol level is contradictory (30). Among the investigated clinical trials, stevioside had no reducing effect on lipid profile in diabetic and healthy people (10, 27). In one study, 1g/day stevia consumption for 60 days in diabetic patients led to reduced levels of cholesterol, triglyceride, and LDL-cholesterol (31). Animal and cellular studies are in favor of stevia anti-lipid effects. They have reported increased levels of carnitine palmitoyl transferase-I and PPARα mRNA by daily administrating stevia extract. Also, reduced levels of acetyl-COA carboxylase mRNA in stevia supplemented rats might lead to lower fatty acid synthesis (32) (Table 3).

Table 1: Stevia and glycemic profile

Author/Year	Subjects	Study duration	Intervention	Outcome
Jeppesen et al., 2006 (12)	T2DM in men and women	3 months	Stevioside (1500 mg/day)	No significant result in glucose, HbA_{1c}, TG Reduced cholesterol
Barriocanal et al., 2008 (10)	Men and women with or without T1DM or T2DM	3 months	Stevioside (750 mg/day)	No significant result in BMI, glucose, HbA_{1c}, TG, cholesterol, and LDL
Gregersen et al., 2004 (11)	Overweight and obese men and women with T2DM	4 hours	Stevioside (1000 mg)	Reduced postprandial blood glucose
Bayat et al., 2017 (18)	Diabetic male Wistar rats	1 month	Stevia extract (400 mg/kg/day)	Reduced FBS and IL-6
Saleh et al., 2016 (17)	Diabetic male Wistar rats	1 month	Stevioside (300 mg/kg/day)	Reduced FBS, oxidative stress, cholesterol, TG Increased insulin, HDL
Scaria et al., 2017 (13)	Diabetic nephropathy rats	28 days	stevioside (250 mg/kg/day)	Reduced FBS, TG, cholesterol, oxidative stress

T1DM: type 1 diabetes mellitus, T2DM: type 2 diabetes mellitus, HbA_{1c}: hemoglobin A1c, TG: triglyceride, LDL: low-density lipoprotein, FBS: fasting blood sugar, HDL: high-density lipoprotein; IL: Interleukin, BMI: body mass index

Table 2: Stevia and calorie intake and weight

Author/Year	Subjects	Study duration	Intervention	Outcome
Anton et al., 2010 (22)	Healthy and obese men and women	3 days	A 400 g preload of tea and crackers with cream cheese sweetened with stevia	Feeling satiety, Reduced postprandial blood glucose and insulin levels
Duram Aguero et al., 2015 (24)	Students	1 week	Consuming food and beverages containing stevia as sweetener	Associated with normal weight and nutritional status
Ahmad et al., 2018 (25)	Hyperlipidemic rats	8 weeks	Aqueous stevia (200, 300, 400, 500 ppm/kg)	Significantly reduced food intake and weight gain
Chan et al., 2000 (26)	Hypertensive men and women	1 year	Stevioside (750 mg)	Blood pressure decreased, no changes in blood lipid and glucose
Maki et al., 2008 (28)	Men and women with T2DM	16 weeks	Rebaudioside (1000 mg)	No significant changes in glucose hemostasis or blood pressure

T2DM: type 2 diabetes mellitus

Table 3: Stevia and lipid profile

Author/Year	Subjects	Study duration	Intervention	Outcome
Barriocanal et al., 2008 (10)	Men and women with or without T1DM or T2DM	3 months	Stevioside (750 mg/day)	No significant result in BMI, glucose, HbA_{1c}, TG, cholesterol, and LDL
Silva et al., 2006 (27)	Hyperlipidemic men and women	90 days	Stevioside (200 mg)	No significant result in TG, VLDL, HDL, LDL and glucose
Ritu and Nandini, 2016 (31)	Men and women with T2DM	3 days	Stevia (1 g)	Significant reduction in TG and VLDL
Park and Cha, 2010 (32)	Mice with normal or high fat diet	15 weeks	Stevia (1 mL/kg/day)	Reduced weight gain, TG, and cholesterol

T1DM: type 1 diabetes mellitus, T2DM: type 2 diabetes mellitus, BMI: body mass index, HbA_{1c}: hemoglobin A1c, TG: triglyceride, LDL: low-density lipoprotein, VLDL: very low-density lipoprotein, HDL: high-density lipoprotein

Conclusion

Studies show that stevia at high doses can be desirable and therapeutic in diabetic patients while at doses authorized as a sweetener has no significant effects on glucose and lipid markers. Although there have been limited human studies in this area, it is suggested that, to better conclude the effects of stevia on diabetes, researchers conduct further studies with higher sample sizes.

Conflict of Interest

None declared.

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