

# The impact of stevioside supplementation on glycemic control and lipid profile in patients with type 2 diabetes: a controlled clinical trial

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## Background

Stevia is a naturally occurring non-nutritive sweetener that has been reported as sugar substitutes for diabetic patients. We aimed to assess the impact of stevia supplementation on glycemic control in patients with type 2 diabetes mellitus (T2DM). Also, we aimed to examine the association between stevia supplementation and anthropometric measures as well as lipid profile in both obese and diabetic patients.

## Patients and methods

The controlled clinical trial included unrelated 150 participants; 40 patients with T2DM and 60 obese patients and 50 healthy controls. Obese patients were then subdivided into two subgroups according to their fasting blood sugar: nondiabetic ( $n=30$ ) and 30 patients with T2DM. The participants received stevia (4 mg/kg/body weight) as an alternative to artificial sweetener for 24 weeks.

## Results

Our results found that stevioside supplementation for diabetic patients' increased the total caloric intake and decreased BMI, waist circumference, waist-hip ratio, and fat mass index, in the obese group. Our results have shown a significant increase of BMI, waist circumference, waist-hip ratio, and fat mass index after 24 weeks of stevia supplementation. In the diabetic group, stevioside for 24 weeks improved the lipid profile and glycemic control, fasting plasma glucose, 2-h plasma glucose, fasting serum insulin, homeostasis model assessment of insulin resistance and hemoglobin A1c (HbA1c), as well as total cholesterol, triglycerides, low density lipoprotein-cholesterol, and high density lipoprotein-cholesterol in all studied intervention groups. Logistic regression test revealed that among clinical and laboratory waist circumference, fasting plasma glucose and HbA1c were independent predictors of response to stevioside.

## Conclusion

Stevioside supplementations for 24 weeks improved cardiometabolic risk in diabetic patients. However, in the obese group, stevioside supplementations increased body weight.

## Keywords:

obesity, randomized controlled trial, stevioside, type 2 diabetes

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## Introduction

The prevalence of obesity in Egypt has increased at an alarming rate during the last three decades affecting 22% of adult men and 48% of adult women [1]. It is associated with several comorbidities including hypertension, dyslipidemia, type 2 diabetes mellitus (T2DM), coronary heart disease, stroke, osteoarthritis, sleep apnea, and respiratory problems, as well as some types of cancers [2,3].

Type 2 diabetes is a metabolic disorder characterized by hyperglycemia, insulin resistance, and  $\beta$ -cell dysfunction. Its prevalence is increasing at an alarming rate worldwide [4–7]. Recent studies have explained the role of lifestyle, in particular daily diet in achieving glycemic target in patients with T2DM [7,8].

As a matter of fact, the consumption of a high sugar/high fat diet is one of the contributing factors attributed to the increase in obesity [9]. Increasing evidence points to critical roles of consumption of non-nutritive sweeteners (NNS) as an alternative to sugar intake [10]. There are eight Food Drug Administration (FDA)-approved NNS: sucralose, aspartame, saccharin, acesulfame-K, neotame, and advantame. Even more importantly, naturally derived NNS, steviol glycosides, and Luo Han Guo extract are generally recognized as safe and endorsed for use in

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food by the US FDA and the European Food Safety Authority [11].

Stevia, the common name for the naturally derived NNS, steviol glycosides is an extract from the leaves of *Stevia rebaudiana* Bertoni. Stevia is a natural, sweet-tasting calorie-free botanical that may also be used as a sugar substitute or as an alternative to artificial sweeteners. There was scattered evidence that stevia improves glycemic control in diabetic patients and increases insulin levels [12], which suggest that it may have a role in food intake regulation. In experimental studies, stevia has been found to increase insulin sensitivity [13].

Regarding the safety of stevia consumption, evidence suggested that there were no negative side effects reported. Furthermore, stevia is inexpensive and available to most consumers; thus, it has the potential to be widely used and may assist individuals in regulating their weight if it has a positive effect on caloric substitution [14].

The pandemic of obesity represents a major public health concern, as this disorder is associated with an increased risk of medical comorbidities contributing to a significant rise in mortality. Despite a wide range of research being conducted, till now the treatment of obesity is still suboptimal. To our knowledge, no study to date in our region especially our country, Egypt evaluated the impact stevia supplementation on health and disease. Thus the aim of our study was to assess the impact of stevia supplementation on glycemic control in patients with T2DM. Also; we aimed to examine the association between stevia supplementation and anthropometric measures as well as lipid profile in both obese and diabetic patients.

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## Patients and methods

The controlled clinical trial included unrelated 150 participants: 40 patients with T2DM and 60 obese patients (BMI  $\geq$  30). The patients were recruited from Diabetes and Endocrinology Outpatient Clinic of Internal Medicine Department of Zagazig University Hospitals. Obese patients were then subdivided into two subgroups according to the American Diabetes Association [15]: nondiabetic ( $n=30$ ) and 30 patients with T2DM, in addition to 50 healthy controls who were matched to case groups as regards sex, age, and ethnicity. The participants received stevia (4 mg/kg/body weight) as an alternative to an artificial sweetener for 24 weeks.

At the beginning, the protocol and the aim of study were fully explained to the participants and written

informed consent was obtained from each volunteers. The Ethics Committee of Faculty of Medicine, Zagazig University approved our study protocol. Any subjects with a history of cardiovascular disease and stroke, liver, renal disease, and chronic inflammatory or thyroid disease were excluded from the study. Also, all participants were not allowed to be vegetarians, vegans, or smoker. None of the participants had a history of abdominal surgery that could have an impact on abdominal fat distribution, as well as participating in a dietary or exercise programs during the preceding 6 months. The participants were also excluded if they had a diagnosable eating disorder or were disliking of or allergy to stevia, or were taking any medications or dietary supplements that could influence weight, appetite, hunger, or satiety. Acceptance of the supplements was investigated via weekly phone calls. During these calls possible problems such as supplement intolerance and medication use, possibly changes in food consumption, getting a new disease, or a change in physical activity was followed and if this situation occurred, the patient were excluded. Body weight was measured with light clothing but no shoes on a digital balance (with 0.1 kg sensitivity).

Height was assessed by using a stadiometer that measured to the nearest 0.1 cm. BMI was estimated as the ratio of body weight to height squared and expressed as  $\text{kg}/\text{m}^2$ . Waist circumference (with 0.1 cm sensitivity) was measured at the minimum circumference between the iliac crest and the last rib cage at the end of exhalation. The hip circumference was measured using tape as the maximal circumference over the hip and waist-to-hip ratio (WHR) was calculated. The participants were asked to maintain their normal physical activity during the study.

At baseline and at the end point of the 6-month study, anthropometrical measurements were estimated and blood samples were collected for biochemical analyses.

## Nutrition education intervention

The nutrition intervention was designed based on macronutrient and micronutrient requirements; three 45–60 min training sessions were conducted at the beginning of the intervention. The described diet was based on the American Diabetes Association guidelines. A total energy of about 1600–200 kcal/day was calculated according to the Harris–Benedict equations revised by Mifflin *et al.* [15] [men  $\text{BMR} = (10 \times \text{weight in kg}) + (6.25 \times \text{height in cm}) - (5 \times \text{age in$

years)+5] and [women BMR=(10×weight in kg)+(6.25×height in cm)-(5×age in years)-161].

The diet including six meals per day, a macronutrient distribution of 50% total caloric value from carbohydrates, 20% proteins and 30% lipids, healthy fatty acids 30%, and a cholesterol consumption lower than 300 mg/day.

#### Blood sampling

Blood samples were drawn from all subjects after an overnight fast and were divided into three portions: 1 ml of whole blood was collected into evacuated tubes containing EDTA, for hemoglobin A1c (HbA1c) and 1 ml of whole blood was collected into evacuated tubes containing potassium oxalate and sodium fluoride (2 : 1) for fasting blood glucose. Serum was separated immediately from the remaining part of the sample and stored at -20°C until analysis.

#### Biochemical analysis

We measured fasting plasma glucose (FPG) levels using the glucose oxidase method (Spinreact, Girona, Spain). Total cholesterol, high density lipoprotein-cholesterol (HDL-C), and triglycerides levels were measured by routine enzymatic methods (Spinreact). The low density lipoprotein-cholesterol (LDL-C) level was calculated using the Friedewald formula [16].

#### Immunochemical assays

Fasting serum insulin concentrations were measured using the high-sensitivity-linked immunosorbent assay kit provided by Biosource Europe SA (Nivelles, Belgium). A homeostasis model assessment of insulin resistance (HOMA-IR) was calculated.

#### Dual-energy X-ray absorptiometry

The accurate and precise values of body composition parameters were estimated from dual-energy X-ray absorptiometry scan of the total body. They included fat mass (FM) and fat-free mass (FFM). Additionally, we calculated the fat mass index (FMI); fat mass/square height, and fat-free mass index (FFMI); fat-free mass /square height (kg/m<sup>2</sup>), was calculated.

#### Statistical analysis

Statistical analyses were performed using the statistical package for the social sciences for Windows (version 21.0; SPSS Inc., Chicago, Illinois, USA). Data were expressed using descriptive statistic (mean±SD) and were analyzed using *t*-test. Logistic regression analysis was done to evaluate the association of sativoid

supplementation with clinical, anthropometric, and biochemical parameters of the studied groups. We considered *P* to be significant at less than 0.05 with a 95% confidence interval.

## Results

### Clinical, anthropometric, and laboratory characteristics of the studied groups at baseline

Clinical, anthropometric, and laboratory characteristics of the studied groups at baseline as shown in Table 1. In the intervention group, we found significant higher levels of body composition parameters: BMI, waist circumference, WHR, FM, FFM, FMI%, and FFMI%. Also, the levels of triglycerides, LDL-C, FPG, fasting serum insulin, HbA1c (%), and HOMA-IR were significantly higher in the intervention group compared with the control group. On the other hand, there were significant lower values

**Table 1 Clinical, anthropometric, and laboratory characteristics of the studied groups at baseline**

Variables	Control group (n=50) (mean ±SD)	Intervention group (n=100) (mean ±SD)	<i>P</i>
Age (years)	39.34±6.4	40.56±6.18	0.467
Systolic blood pressure (mmHg)	122.44±4.68	126.7±17.58	0.340
Diastolic blood pressure (mmHg)	78.142±4.68	79.47±9.361	0.610
Waist circumference (mm)	99.9±4.698	121.77±19.639	<0.001*
BMI (kg/m <sup>2</sup> )	24.47±0.867	34.51±8.73	<0.001*
Waist/hip ratio	0.99±6.046	1.21±0.196	<0.001*
FM	13.44±1.031	18.03±3.831	<0.001*
FMI%	4.89±0.17346	6.9±1.746	<0.001*
FFM	53.74±4.125	72.14±14.9	<0.001*
FFMI%	19.58±0.693	27.615±6.98	<0.001*
Total cholesterol (mg/dl)	183.73±3.75	193.68±32.54	0.260
Triglycerides (mg/dl)	114.1±1.406	135.71±31.4	<0.05*
LDL cholesterol (mg/dl)	85.88±0.187	103.4±35.2	0.071
HDL cholesterol (mg/dl)	55.11±3.281	41.72±14.344	<0.01*
Fasting plasma glucose (mg/dl)	87.11±3.28	98.21±19.17	<0.001*
HbA1c (%)	5.09±0.150	7.24±2.194	<0.001*
2-h blood glucose (mg/dl)	109.8±3.45	158.8±19.87	<0.001*
HOMA-IR	1.13±0.098	2.84±1.23	<0.001*
Fasting serum insulin (μU/ml)	7.48±0.141	10.43±2.65	<0.001*

FFM, fat-free mass; FFMI, fat-free mass index; FM, fat mass; FMI, fat mass index; HDL, high density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; LDL, low density lipoprotein. \**P*<0.05.

of HDL in the case group compared with the control group ( $P<0.05$ ).

#### Macronutrient and micronutrient intakes before and after 24 week's intervention by stevioside supplementation

In the control group, there were nonsignificant changes regarding energy (kcal/day), total carbohydrate (g), total protein (g), and total fat (g) in diet intakes before and after 24 week's intervention by stevioside supplementation. However, in the intervention group, there were significantly higher values of total energy (kcal/day), total carbohydrate (g), total protein (g), and total fat (g) in diet after 24 week's intervention by stevioside supplementation compared with the diet regimen before the intervention (Fig. 1).

#### The impact of stevioside supplementations on clinical and anthropometric parameters

We tested the role of stevioside supplementations as an alternative to sugar sweetener in intervention groups. The case groups were subclassified into obese, obese diabetic, and diabetic groups. In the obese group, our results showed significantly increased body composition parameters by using stevia as NNS; the parameters were: BMI, waist circumference, and WHR. Additionally, FM, FMI, FFM, and FFMI were significantly increased after stevia supplementation (Table 2).

Among the obese diabetic group, there were significant differences between baseline and after 24 weeks of stevioside supplementation as regards waist circumference, BMI, and FMI, FFM, and FFMI. As regards the diabetic group, supplementation with

stevioside for 24 weeks had significant effects on BMI, waist circumference, WHR, and FMI (Table 2).

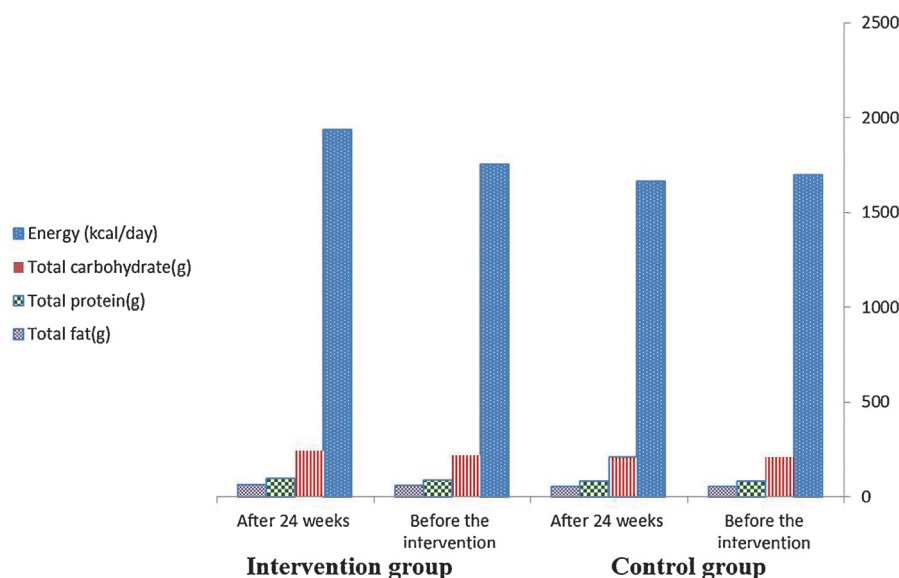
#### The impact of stevioside supplementations on the biochemical variable of the studied case group

The impact of stevioside supplementations on the biochemical variable of the studied case group as shown in Table 3. Regarding the diabetic group, supplementation with stevioside for 24 weeks had significant improvement on FPG ( $128.1\pm 28.1$  vs.  $141.7\pm 34.6$ ), 2-h plasma glucose ( $198.2\pm 53.02$  vs.  $251.5\pm 59.2$ ), HOMA-IR ( $5.8\pm 2.2$ ), HbA1c ( $8.3\pm 1.1$  vs.  $7.9\pm 0.9$ ), and total cholesterol ( $158.9\pm 24.5$  vs.  $167.1\pm 30.9$ ), LDL-C ( $100.91\pm 39.53$  vs.  $125.8\pm 33.6$ ), and HDL-C ( $36.2\pm 8.267$  vs.  $34.79\pm 11.56$ ; Fig. 2).

In the obese group, our results revealed significantly improved lipid profile: total cholesterol ( $188.2\pm 25.9$  vs.  $210.5\pm 47.4$ ), triglycerides ( $144.7\pm 30.6$  vs.  $150.9\pm 35.9$ ), LDL-C ( $102.9\pm 31.1$  vs.  $121.9\pm 47.6$ ), and HDL-C ( $36.25\pm 17.09$  vs.  $33.6\pm 8.44$ ). Furthermore, fasting serum insulin was significantly decreased after stevia supplementation (Fig. 3).

In the obese diabetic group, stevioside supplementation for 24 weeks led to significant improvement of glycemic control tests; FPG ( $183.2\pm 53$  vs.  $196.5\pm 59.2$ ), 2-h plasma glucose ( $183.1\pm 28.1$  vs.  $293.7\pm 34.64$ ) HOMA-IR ( $3.2\pm 0.9$  vs.  $3.7\pm 1.28$ ) and HbA1c ( $8.56\pm 0.9$  vs.  $9.7\pm 1.1$ ). Interestingly, lipid profile parameters also improved after stevioside supplementation for 24 weeks of these parameters: total cholesterol, LDL-C, and HDL-C (Figs 2 and 3).

Figure 1



Mean of macronutrient and micronutrient intakes before and after 24 weeks' intervention by stevioside supplementation.

**Table 2 The effect of stevioside supplementation on clinical and anthropometric parameters of intervention groups**

Variables	Obese group (n=30)	Obese diabetic group (n=30)	Diabetic group (n=40)	P <sub>1</sub>	P <sub>2</sub>
Waist circumference (mm)					
Baseline	125.2±18.51	128.3±17.71	137.9±16.80	<0.001*	<0.001*
Week 24	131.3±23.8	135.1±15.3	133.1±17.1	<0.001*	<0.001*
P	<0.001*	<0.001*	<0.001*		
Waist/hip ratio					
Baseline	1.22±0.15	1.35±0.12	1.24±0.09	<0.001*	<0.001*
Week 24	1.46±0.21	1.41±0.33	1.01±0.07	<0.001*	<0.001*
P	<0.001*	<0.001*	<0.001*		
BMI					
Baseline	37.1±5.16	37.64±4.12	27.23±3.65	<0.001*	<0.001*
Week 24	40.8±5.50	41.09±4.01	25.98±3.52	<0.001*	<0.001*
P	<0.001*	<0.001*	<0.001*		
FM					
Baseline	20.5±2.04	19.3±1.79	15.8±1.6	<0.001*	<0.001*
Week 24	23.3±2.06	20.9±1.91	15.7±1.48	<0.001*	<0.001*
P	<0.01*	0.760	0.564		
FMI%					
Baseline	7.57±1.03	5.61±0.8	6.4±0.73	<0.001*	<0.01*
Week 24	8.87±1.1	6.93±0.81	4.39±0.71	<0.001*	<0.001*
P	<0.05*	<0.05*	<0.05*		
FFM					
Baseline	81.08±8.16	79.54±7.17	62.52±6.4	0.760	<0.001*
Week 24	83.3±8.25	81.6±7.86	61.98±5.9	<0.001*	<0.001*
P	<0.05*	<0.05*	0.670		
FFMI%					
Baseline	30.75±4.12	28.75±3.20	21.74±2.92	0.814	<0.001*
Week 24	32.51±4.4	30.47±3.21	21.59±2.82	<0.001*	<0.001*
P	<0.05*	<0.05*	0.078		

FFM, fat-free mass; FFMI, fat-free mass index; FM, fat mass; FMI, fat mass index. \*P<0.05

**Table 3 Logistic regression analysis evaluating the association of stevioside supplementation with clinical, anthropometric, and biochemical parameters of the studied groups**

Variables	B	SE	t	P value	Odds ratio	95% CI	
						Lower	Upper
Systolic blood pressure	-0.020	0.030	0.435	0.510	0.980	0.924	1.040
Diastolic blood pressure	0.023	0.052	0.192	0.661	1.023	0.924	1.132
BMI	-0.009	0.059	0.021	0.883	0.991	0.884	1.112
Waist circumference	0.046	0.020	4.974	0.026	1.047	1.006	1.090
Triglycerides	-0.012	0.009	1.623	0.203	0.988	0.970	1.006
FPG	0.025	0.012	4.161	0.041	1.026	1.001	1.051
HbA1c	-1.022	0.375	7.429	0.006	0.360	0.173	0.750
TC	-0.017	0.009	3.644	0.056	0.984	0.967	1.000
HDL	-0.007	0.019	0.133	0.715	0.993	0.957	1.031
Constant	6.280	3.532	3.161	0.075	533.806		

CI, confidence interval; FPG, fasting plasma glucose; HDL, high density lipoprotein; SE, standard error; TC, total cholesterol.

#### Assessment of stevioside supplementation as non-nutritive sweeteners in the improvement of anthropometric and biochemical variable of the studied group

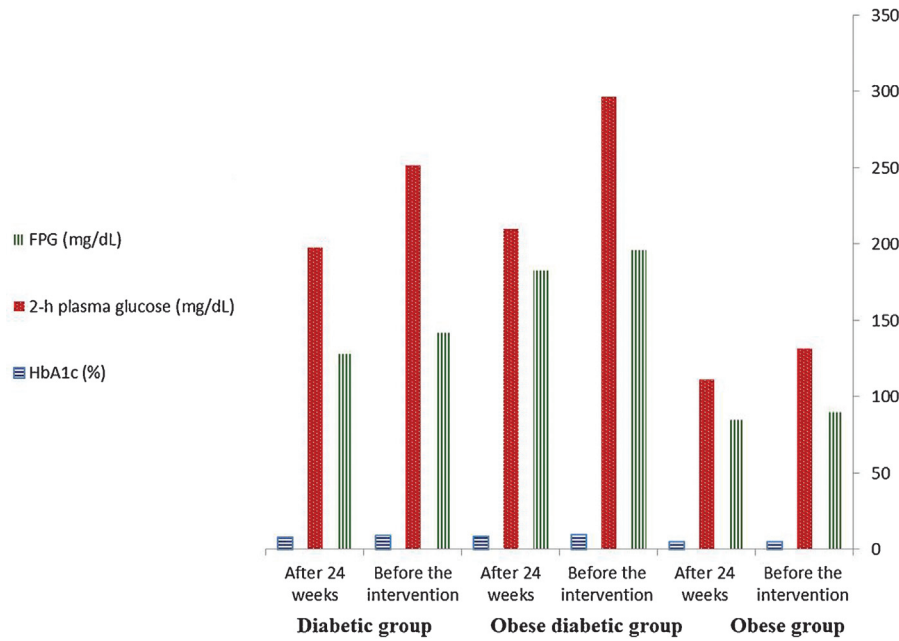
Logistic regression analysis was performed to detect the main predictors associated with stevioside supplementation in the diabetic group. Our findings have shown that among clinical and laboratory waist circumference, FPG and HbA1c were independent positive predictors of response to stevioside supplementation with odds ratios of 1.047, 1.026,

and 0.360, respectively (P<0.05, <0.05, and <0.01, respectively; Table 3).

#### Discussion

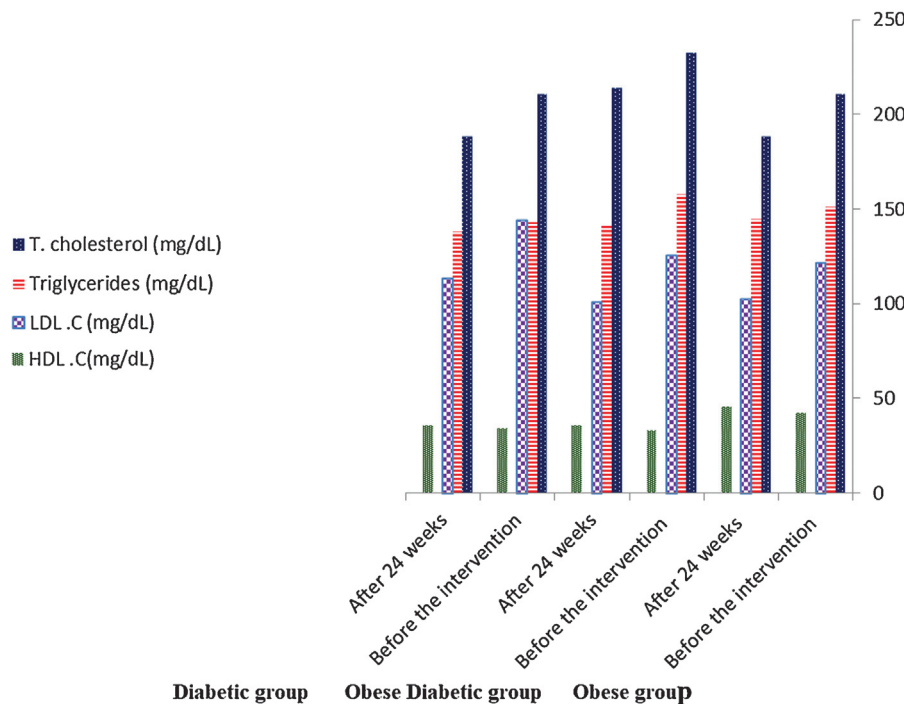
Obesity is a complex, multifactorial, and largely preventable disease, affecting, along with overweight, over a third of the world's population today [17]. Over the past decade, a close association between obesity and diabetes has become increasingly clear. Childhood obesity results in the same conditions,

Figure 2



The effect of stevioside supplementation on the glycemic profile in the studied groups.

Figure 3



The effect of stevioside supplementation on the lipid profile in the studied groups.

with premature onset, or with greater likelihood in the adulthood [18].

It is also well established that the consumption of foods and beverages containing NNS has dramatically increased over the past few decades [19]. There is controversy regarding the consumption of NNS; one

of the most popular NNS is stevia. Stevia was recently approved for use as a sweetener by the Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives (Joint Food and Agriculture Organization/World Health Expert Committee on Food Additives, 2005) [20] and by the FDA. Stevia is a naturally sourced, zero-calorie

sweetener that has been used as a natural sugar substitute and flavoring ingredient for 100's of years. The acceptable daily intake is 4 mg/kg of body weight per day for steviol equivalents [19].

Low-calorie artificial sweeteners can help to decrease blood glucose levels and can inhibit metabolic disorders. The effects of artificial sweeteners on obesity and related metabolic disorders remain controversial. We in this study attempted to pierce out the impact of stevia supplementation on glycemic control, and lipid profile in patients with type 2 diabetes. Also, we aimed to examine the association between stevia supplementation and anthropometric measures in both obese and diabetic patients.

It would be of considerable practical issues to test the metabolic effects of NNS. Among NNS, we tested the role of stevioside supplementations as an alternative to sugar sweetener in obese, obese diabetic, and diabetic patients.

The interesting result of our study was the effect of stevioside supplementation for 24 weeks on anthropometric measures. According to our results, stevioside supplementation for diabetic patients increased total caloric intake and decreased BMI, waist circumference, WHR, and FMI. Even more interestingly, in the obese group, our results have shown significant increase of BMI, waist circumference, WHR, and FMI after 24 weeks of stevia supplementation.

There is no clear evidence that NNS augment appetite by activating cephalic phase responses, altering osmotic balance, or enhancing food palatability. Indeed, there is emerging evidence that selected NNS may stimulate the release of satiety hormones, although the link between these hormones and energy intake in free-living individuals is also open to debate. With respect to energy intake, there is no substantive evidence that an inherent liking for sweetness or NNS activation of reward systems is problematic.

In a human clinical intervention study conducted by Parker and his colleagues they found that the participants who used NNS were significantly more likely to gain weight than were nonusers. However, the weight gain was less than 2 lb ( $\approx 0.9$  kg) between users and nonusers [20].

Similar results were obtained by previous animal studies. Researchers have suggested that the intake of NNSs may promote weight gain, either by

increasing energy intake [21], or by decreasing energy expenditure [22–26].

Previous researches reported that premeal consumption of high calories leads to reduced food intake, a process known as caloric compensation [27]. Thus, it is possible that the controls fed on high-calorie sugars were subjected to caloric compensation and consumed less food and this led to reduced weight gain when compared with the treated groups.

Similarly, Abo Elnaga *et al.* [27] observed administration of stevia sweetener at doses of 25 mg/kg, body weight decreased feed intake as compared with the control group. There is scattered evidence that found decreased rat weight after supplementation of stevia. They explained that these changes in body weight of rats could be due to the absence of quick glucose-releasing source or due to decrease in the caloric intake by rats [28,29].

Stevia is inexpensive and available to most consumers; thus, it has the potential to be widely used and may assist individuals in regulating their weight if it has a positive effect on caloric substitution. However, no study to date has examined the effect stevia has on food intake and satiety levels.

The main finding of the present study is that there were significant improvement in lipid profile; total cholesterol, triglycerides, LDL-C, and HDL-C as well as fasting serum insulin in all studied intervention groups.

Similar to our results, the experimental study of Abo Elnaga *et al.* [27] observed that the groups of rats treated with stevia sweetener had improvement in lipid profile levels compared with the negative or positive control group.

Our finding adds to the growing body of evidence implicating the need for stevioside supplementation for lean and obese patients with T2DM. In both groups, stevioside supplementation for 24 weeks led to significant improvement of glycemic control tests: FPG, 2-h plasma glucose, HOMA-IR, and HbA1c.

Our findings are in concordance with Anton *et al.* [30], who conducted their study to evaluate the effects of stevia, aspartame, and sucrose on food intake, satiety, and postprandial glucose as well as insulin levels and they observed that consumption of stevia in preloads significantly lowered postprandial insulin levels compared with both aspartame and sucrose, as well

as postprandial glucose levels compared with sucrose. These effects on postprandial glucose levels are likely due in large part to the lower caloric and carbohydrate intake of stevia supplementation compared with other artificial sweeteners.

In agreement with our results, Viswanathan *et al.* [31] found that stevia may be helpful in managing postprandial hyperglycemia, insulin resistance, and T2DM.

Our findings are in concordance with Saltiel *et al.* [32] which suggest that the presence of pharmacological concentrations of sucralose and stevioside on the basolateral membrane may increase GLP-1 secretion. However, given the high concentrations needed to stimulate secretion, this finding is probably of limited clinical relevance.

Similar results confirmed by the Romo-Romo *et al.* [33] results revealed stevia consumption as one of the natural NNS that led to lower glucose and insulin concentrations compared with sucrose.

As a consequence of our studies, we further evaluated our results by the logistic regression test which revealed that among clinical and laboratory waist circumference, FPG, and HbA1c were independent predictors of response to stevioside.

Anton *et al.* [30] observed that the participants did not compensate by eating more at either their lunch or dinner meal and reported similar levels of satiety when they consumed lower calorie preloads containing stevia or aspartame than when they consumed higher-calorie preloads containing sucrose.

Tey *et al.* [34] suggested that the consumption of NNS is not encouraged, but they could be considered a useful tool in the nutritional treatment of certain metabolic diseases as sugar substitutes as long as the quantity consumed is within the acceptable daily intake and without compensation by ingesting other energy-rich foods.

Paula Neto *et al.* [35] detected that sweeteners, which are freely used by obese and diabetic patients had hazards effect on the gut microbiota, which contributed to the development of insulin resistance and weight gain.

## Conclusion

Stevioside supplementations to T2DM decreased anthropometric measures and cardiometabolic risks. Notwithstanding, in obese patients the consumption

of stevia as NNS increased body composition values; thus, these additives should not be considered as safe and must have their use controlled and labeled with regard to the possible undesirable effects.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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