ORIGINAL ARTICLE

Acute Effect of Stevia on Glycemic and Insulin Responses in Obese Patients: A Randomized Double-Blind Placebo-Controlled Crossover Study

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Objective: Artificial sweeteners like sucralose cause glucose intolerance in obese patients, whereas stevia, a natural sweetener, is metabolically inert. The present study aimed to assess the acute effects of stevia on glycemic and insulin responses in obese patients.

Materials and Methods: Obese patients underwent a 75-gram oral glucose tolerance test (OGTT) preceded by consuming pills containing either 200 mg of stevia or a placebo for 60 minutes prior to the test on two separate occasions, one week apart, in a randomized crossover design. Blood samples were obtained for glucose and insulin at 0, 30, 60, 90, and 120 minutes. The area under the curve (AUC) of glucose and insulin responses was calculated. Indices for insulin sensitivity, the Matsuda index, and Insulin secretion, the insulinogenic index, were calculated using minimal models of glucose and insulin kinetics.

Results: Twenty obese patients, with a BMI of 28.75±3.68 kg/m^2, were recruited to the study. There were no significant differences in AUC of glucose and insulin between stevia and placebo with glucose at 15,285±4,531 versus 15,101±3,955 (p=0.89) and insulin at 8,507±5,858 versus 7,652±5,020 (p=0.62). Insulin sensitivity derived from OGTT using Matsuda index was not significantly different between stevia and placebo at 4.74±1.86 versus 5.84±2.96 (p=0.09). Insulin secretion using Insulinogenic index was not significantly different between stevia and placebo (p=0.155).

Conclusion: Stevia did not affect the acute glycemic and insulin responses to OGTT in obese patients. It is necessary to conduct a long-term ingestion study to ascertain these findings.

Keywords: Stevia; Nonnutritive sweeteners; Oral glucose tolerance test; Obese patients; Matsuda index; Insulinogenic index

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Obesity is a global health crisis that leads to metabolic disorders, including type 2 diabetes mellitus (T2DM), and increases the risk of mortality due to cardiovascular diseases[1-3]. Obesity is associated with metabolic syndrome, a condition where the accumulation of both visceral and subcutaneous fat leads to the development of insulin resistance and atherosclerosis, primarily due to elevated levels of free fatty acids[4,5].

In recent years, there has been a growing concern regarding health issues, notably obesity, which is significantly influenced by dietary choices and beverage consumption. The increased intake of unhealthy foods is widely recognized as a primary contributing factor. In Thailand, the trend of sugar consumption is rapidly growing. Between 1983 and 2009, sugar consumption in Thailand rose from 12.7 to 31.2 kg per person per year[6].

In response to the adverse effects of sugar, artificial non-nutritive sweeteners (NNS) are gaining popularity in limiting calorie intake in place of diets and beverages with added sugar, particularly among individuals with obesity[7,8]. The U.S. Food and Drug Administration (FDA) has approved eight artificial NNS, which include two artificial NNS of natural origin, stevia, and monk fruit extract, and six synthetically derived artificial NNS, namely, aspartame, acesulfame potassium (Ace-K), neotame, saccharin, sucralose, and advantame[9]. Studies have indicated that synthetically derived artificial NNS, similar to diets with added sugar, can contribute to

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an increase in weight, metabolic syndrome, risk of T2DM, and cardiovascular diseases[10-14].

Stevia contains steviol glycosides, a group of chemical compounds including stevioside, Rebaudioside A through F, Dulcoside A, Rubusoside, and Steviolbioside[15]. In vitro studies have highlighted stevia potential in glycemic control. For instance, Rebaudioside A has been shown to stimulate insulin secretion in the islet cells of mice, directly affect insulin secretion from beta cells, enhance insulin sensitivity, and increase insulin production[16-19]. Studies have investigated stevia's effects on glycemic control in individuals with and without T2DM. A 3-month randomized controlled trial (RCT) involving patients with T2DM who received 1,500 mg of Rebaudioside A revealed no statistically significant reduction in HbA1c levels compared to a placebo[20]. Additionally, Barriocanal et al. found no significant difference in plasma glucose levels and HbA1c after participants received stevioside[21]. These findings suggest that stevia does not worsen glycemic control and may improve insulin sensitivity, offering a benefit for obese individuals at high risk of T2DM development, seeking to limit calorie intake with an alternative sweetener.

However, the impact of stevia on individuals with obesity, especially in Thailand, remains underexplored. The present study aimed to investigate stevia's utility in dietary interventions targeting obesity. The findings may provide valuable insights for clinicians, dietitians, and patients seeking alternative sweetening options to improve metabolic health.

Materials and Methods

Study design

A randomized, double-blind, placebo-controlled crossover study was conducted at the Obesity Clinic, in a tertiary hospital, Bangkok, Thailand, to evaluate the effects of stevia on glycemic and insulin responses in obese patients.

Study population

The present study enrolled twenty eligible obese patients from the Obesity Clinic at Phramongkutklao Hospital. Before providing informed consent, each subject was thoroughly informed about the study's purpose and procedures.

Inclusion criteria:

1. Healthy individuals with BMI of 25 kg/m² or greater
2. Aged older than 18 years old
3. Obtained informed consent.

Exclusion criteria:

1. Individuals diagnosed with all types of diabetes.
2. Individuals currently taking medication affecting plasma glucose levels.
3. Individuals with chronic medical conditions
4.. Pregnancy

Study protocol

The Institutional Review Boards of the Phramongkutklao Hospital approved the study (Approved No. IRBRTA408/2560). Moreover, the study was approved by the Thai Clinical Trial Registry (ID: TCTR20190825001, available at https://www.thaiclinicaltrials.org/show/TCTR201900825001). Upon obtaining written informed consent, eligible subjects underwent a comprehensive evaluation, including history taking, physical examination. Baseline characteristics, including gender, age, body weight, height, systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate, underlying disease, history of smoking, family history of diabetes mellitus (DM), frequency of exercise, sweetener consumption behavior, and volume of consumption were obtained using questionnaire. Baseline laboratory of the participants including fasting plasma glucose (FPG), HbA1c level, hematocrit (Hct) level, creatinine (Cr) level, glomerular filtrate rate (GFR), serum uric acid, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglyceride level, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were obtained from medical record. They were then randomly allocated into two groups, A and B, using a block randomization method with blocks of four. The intervention comprised 200 mg of stevia, specifically Thai FDA-approved pure extracted Steviol glycosides provided by Sugavia Co., Ltd. Participants in group A received 200 mg of stevia, while those in group B received placebo pills, designed to be visually identical and without any effects on glucose metabolism. Both were administered 60 minutes prior to a 75-gram oral glucose tolerance test (OGTT). A similar study investigating the acute effects of sucralose on glucose metabolism administered the sweetener ten minutes before conducting OGTT[22]. However, an in vivo study by Koyama et al. demonstrated rapid absorption of steviol, with peak plasma concentrations observed 15 minutes after oral administration and a steady increase over an 8-hour period[23]. In the present

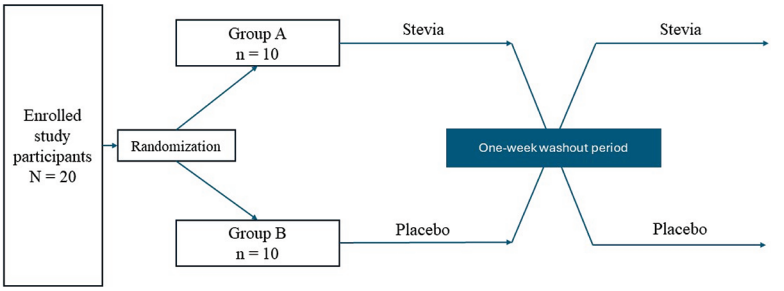

Figure 1. Study protocol.

study, stevia was administered one hour prior to the OGTT to allow sufficient time for its effects to manifest. Blood samples were taken at baseline and 30, 60, 90, and 120 minutes post-OGTT to measure plasma glucose and insulin levels. After a one-week washout period, participants received the opposite intervention, with the same pre-testing procedure and timing for blood sample collection following the 75-g OGTT. Administering stevia too close to the OGTT may not provide adequate time for its metabolic changes to take effect, while a longer interval could attenuate its acute effects. Plasma glucose and insulin levels were measured simultaneously with the initial phase (Figure 1).

Outcome measurement

The area under the curve (AUC) for plasma glucose and insulin levels was measured to assess the effects of stevia versus placebo over two hours. The AUC was calculated using the formula:

$$\text{Area} = \left(A+B+C+\frac{D}{2}\right)t + \frac{(D+E)T}{2} + \frac{(E^2T)}{2(E+F)}$$

Insulin sensitivities were evaluated using the Matsuda index, which was calculated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), while insulin secretion was evaluated using the insulinogenic index. Both indices for insulin sensitivity and secretion were calculated using minimal models for glucose and insulin kinetics.

Sample size calculation and statistical analysis

The sample size for the RCT was calculated using a standard formula for comparing two means.

$$\text{ntrt} = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 \times (\sigma^2_{\text{trt}} + \sigma^2_{\text{con}}/r)}{\Delta^2}$$

This formula incorporates key parameters, including the critical values from the standard normal distribution corresponding to the desired significance level of α at 0.05, and power of 80%. Based on the previous study of NNS effect on hormonal response, the means for the treatment and control groups were 68,647 and 57,192, respectively, with standard deviations of 7,610 for the treatment group and 5,644 for the control group[24]. The pooled standard deviation was 5.36, and the effect size (Δ) was set at 2.50. Using these values, along with Z(0.975) = 1.959964Z(0.975) = 1.959964Z(0.975) = 1.959964 and Z(0.800) = 0.841621Z(0.800) = 0.841621 and Z(0.800) = 0.841621, the sample size required for both the treatment and control groups was determined to be six participants each.

Data were analyzed using IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA). Categorical data were presented as numbers and percentages, whereas continuous data were shown as means and standard deviations for normally distributed data, or medians and interquartile ranges (IQRs) for non-normally distributed data. The mean AUCs for plasma glucose and insulin levels between the two groups were compared using the paired t-test or Wilcoxon test as appropriate. Within-group comparisons were done using repeated measures ANOVA. The analysis was conducted on a per-protocol basis, with p-values less than 0.05 considered statistically significant.

Results

Characteristics of study participants

Twenty obese patients were recruited for the present study, 85% female. Participants had a mean age of 43±12.16 years, ranging from 26 to 71 years. The subjects' mean body mass index (BMI) was 28.75±3.68 kg/m², with 60% falling within the 25 to 29.9 kg/m² range. Subjects exhibited a mean SBP of 125.6±10.93 mmHg, a DBP of 77.35±10.36 mmHg, and a heart rate of 73.69±12.71 bpm. Hypertension and dyslipidemia were comorbidities in 10% and 15% of participants, respectively. Seventeen

Table 1. Baseline characteristics of enrolled participants

Variable	Total n=20
Sex; n (%)	
Male	3 (15.0)
Female	17 (85.0)
Age (years); mean±SD	46.3±12.16
Body weight (kg); mean±SD	74.75±10.79
Height (cm), mean±SD	160.75±7.45
Body mass index (kg/m^2); n (%)	
25 to 30	13 (65.0)
>30	7 (35.0)
Mean±SD	28.75±3.68
Systolic blood pressure (mmHg); mean±SD	125.6±10.93
Diastolic blood pressure (mmHg); mean±SD	77.35±10.36
Heart rate (bpm); mean±SD	73.69±12.71
Underlying disease; n (%)	
None	17 (85.0)
Hypertension	2 (10.0)
Dyslipidemia	3 (15.0)
Smoking; n (%)	
None	17 (85.0)
Stopped smoking	2 (10.0)
Still smoking	1 (5.0)
Family history of diabetes mellitus; n (%)	
Relatives have diabetes mellitus	10 (50.0)
Gestational diabetes mellitus	2 (10.0)
Exercise; n (%)	
None	8 (40.0)
1 to 2 days a month	4 (20.0)
1 to 2 days a week	4 (20.0)
3 to 4 days a week	1 (5.0)
5 to 6 days a week	2 (10.0)
Everyday	1 (5.0)
Sweetener consumption behavior; n (%)	
None	10 (50.0)
Drink, coffee, tea	10 (50.0)
Food, snack	2 (10.0)
Volume of consumption (n=10); n (%)	
1 glass/pack	5 (25.0)
2 glasses/pack	2 (10.0)
4 glass/pack	1 (5.0)
5 glass/pack	1 (5.0)
More than or equal 7 glass/pack	1 (5.0)

SD=standard deviation

Table 2. Laboratory results of enrolled participants

Variable	
FPG (mg/dL); mean±SD	85.58±9.43
HbA1c; n (%)	
<5.7%	15 (75.0)
5.7% to 6.4%	5 (25.0)
Mean±SD	5.39±0.36
Hct (%); mean±SD	38.25±3.7
Serum creatinine (mg/dL); mean±SD	0.77±0.16
eGFR (mL/min/1.73 m^2); mean±SD	91.9±15.68
Uric (mg/dL); mean±SD	5.28±1.05
Total cholesterol (mg/dL); mean±SD	203.6±42.48
Triglyceride (mg/dL); mean±SD	118.8±34.58
HDL-C (mg/dL); mean±SD	54.95±14.02
LDL-C (mg/dL); mean±SD	137.47±41.04
AST (U/L); mean±SD	19.1±5.76
ALT (U/L); mean±SD	19.6±12.19

FPG=fasting blood sugar; SD=standard deviation; Hct=hematocrit; eGFR=estimated glomerular filtration rate; HDL-C=high density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; AST=aspartate aminotransferase; ALT=alanine aminotransferase

participants (85%) did not use tobacco. Half of the participants reported a family history of T2DM, and two participants (10%) had a history of gestational diabetes. Two-fifths of the participants did not engage in physical activity, whereas 15% exercised three to six times weekly. Half of the participants never consumed NNS. Among those who did, 50% added NS to coffee or tea once a week, while 30% and 20% consumed it more than four and two times a week, respectively (Table 1).

Baseline laboratory tests for the study participants revealed the mean FPG level was 85.58±9.43 mg/dL. The subjects were free from diabetes, evidenced by mean HbA1c levels of 5.39±0.36%, however, 25% of participants had HbA1c levels ranging from 5.7% to 6.4%, indicating a higher risk for diabetes. No cases of anemia were observed among the study participants, as indicated by a mean Hct level of 38.25±3.7%. Renal function tests showed normal results for all participants, with mean serum Cr levels of 0.77±0.16 mg/dL and a mean glomerular filtration rate (GFR) of 91.9±15.68 mL/min/1.73 m². Lipid profiles revealed that participants had a mean total cholesterol of 203.6±42.48 mg/dL and a mean triglyceride level of 118.8±34.58 mg/dL. The mean HDL-C was 54.95±14.02 mg/dL, and the mean LDL-C was 137.47±41.04 mg/dL. Liver function tests were normal for all participants, with mean AST levels of 19.1±5.76 U/L and mean ALT levels of 19.6±12.19 U/L (Table 2).

Glucose and insulin responses

Participants in both groups underwent an OGTT 60 minutes after receiving 200 mg of stevia for the intervention group and a placebo for the control group. Plasma glucose and insulin levels were measured at

Table 3. Plasma glucose at baseline and 30, 60, 90, 120 post-OGTT

Plasma glucose (mg/dL)	Stevia mean±SD	Placebo mean±SD	p-value†
Basal	88.85±10.98	86.70±10.46	0.114
30 minutes	129.80±25.93	127.60±23.57	0.692
60 minutes	146.65±49.75	139.30±39.15	0.354
90 minutes	130.65±46.71	131.85±45.20	0.873
120 minutes	115.95±46.34	122.55±37.41	0.404
p-value¥	<0.001*	<0.001*	

SD=standard deviation

† Data were analyzed by paired t-test, ¥ Data were analyzed by repeated measure ANOVA, * Statistically significant at 0.05 level

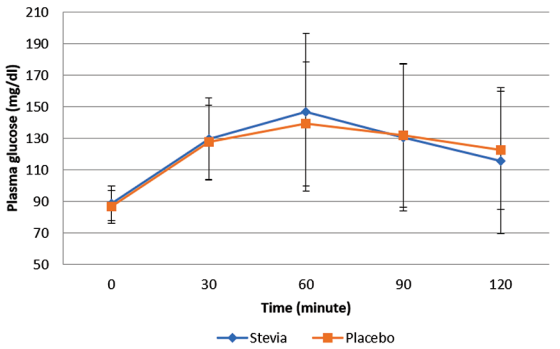

Figure 2. Plasma glucose (mg/dL) at baseline, 30, 60, 90, and 120 minutes post-OGTT.

Table 4. Insulin levels at baseline and 30, 60, 90, 120 post-OGTT

Insulin (µU/mL)	Stevia mean±SD	Placebo mean±SD	p-value†
Basal	9.12±4.58	8.20±3.65	0.334
30 minutes	63.40±38.97	37.96±27.63	0.035*
60 minutes	89.89±56.42	84.11±62.23	0.629
90 minutes	87.89±64.17	84.19±48.44	0.815
120 minutes	75.71±66.88	79.44±54.42	0.534
p-value¥	<0.001*	<0.001*	

SD=standard deviation

† Data were analyzed by paired t-test, ¥ Data were analyzed by repeated measure ANOVA, * Statistically significant at the 0.05 level

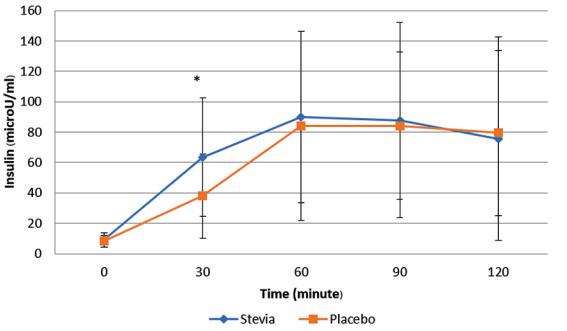

Figure 3. Insulin level (µU/ml) at baseline, 30, 60, 90, and 120 minutes post-OGTT.

* Statistically significant at 0.05 level

baseline and 30, 60, 90, and 120 minutes after the OGTT. For the intervention group, the mean plasma glucose levels were 88.85±10.98 mg/dL at baseline and then 129.80±25.93 mg/dL, 146.65±49.75 mg/dL, 130.65±46.71 mg/dL, and 115.95±46.34 mg/dL at 30, 60, 90, and 120 minutes post-OGTT, respectively. For the placebo group, the mean plasma glucose levels at baseline were 86.70±10.46 mg/dL, 127.60±23.57 mg/dL, 139.30±39.15 mg/dL, 131.85±45.20 mg/dL, and 122.55±37.41 mg/dL at 30, 60, 90, and 120 minutes post-OGTT, respectively. Significant differences in mean plasma glucose levels were observed at all time intervals within each group ($p<0.001$). However, there were no statistically significant differences in mean plasma glucose levels between the intervention and placebo groups at any time interval ($p=0.114$ at baseline, $p=0.692$ at 30 minutes, $p=0.354$ at 60 minutes, $p=0.873$ at 90 minutes, and $p=0.404$ at 120 minutes, respectively) (Table 3, Figure 2).

In the intervention group, insulin levels were measured as 9.12±4.58 µU/mL at baseline and increased to 63.40±38.97 µU/mL, 89.89±56.42 µU/mL, 87.89±64.17 µU/mL, and 75.71±66.88 µU/mL at 30, 60, 90, and 120 minutes after OGTT, respectively. For the placebo group, insulin levels started at 8.20±3.65 µU/mL at baseline and were recorded as 37.96±27.63 µU/mL, 84.11±62.23 µU/mL, 84.19±48.44 µU/mL, and 79.44±54.42 µU/mL at 30, 60, 90, and 120 minutes post-OGTT, respectively. There was a statistically significant difference in the mean insulin levels at various time intervals within each group ($p<0.001$), indicating substantial changes over time. However, between the intervention and placebo groups, no statistically significant difference in mean insulin levels was observed at baseline, 60, 90, and 120 minutes post-OGTT, with the exception of insulin level 30 min post-OGTT, where a significant difference was noted ($p=0.035$) (Table 4, Figure 3).

Insulin sensitivity, insulin secretion, disposition index, and AUC

To assess the effects of stevia versus placebo on insulin sensitivity and secretion, the authors compared the mean Matsuda index, finding 4.74±1.86 in the intervention group and 5.84±2.96 in the placebo group. However, the difference in mean Matsuda index was not statistically significant ($p=0.09$). For

Table 5. Insulin sensitivity, insulin secretion, and disposition index between stevia and placebo

	Stevia	Placebo	p-value
Insulin sensitivity; mean±SD			
Matsuda index	4.74±1.86	5.84±2.96	0.090†
HOMA% IR	1.91±1.03	1.53±1.02	0.064†
Insulin secretion			
Insulinogenic index; median (IQR)	1.3 (0.14, 8.03)	0.65 (0.03, 3.63)	0.155‡
HOMA% B; mean±SD	102.25±47.80	98.53±46.25	0.677†
Insulin sensitivity × secretion; median (IQR)			
Disposition index	5.98 (0.96, 25.18)	3.71 (0.18, 38.09)	0.929‡
Area under curve 0 to 120 minutes; mean±SD			
Plasma glucose (mg/dL)	15,285±4,531.57	15,101.25±3,955.71	0.892†
Insulin (μU/mL)	8,507.92±5,858.80	7,652.42±5,020.01	0.623†
Area under curve 0 to 30 minutes; mean±SD			
Plasma glucose (mg/dL)	3,279.75±553.58	3,214.50±510.42	0.701†
Insulin (μU/mL)	1,087.95±653.22	692.4±469.17	0.034†*
Area under curve 30 to 120 minutes; mean±SD			
Plasma glucose (mg/dL)	12,005.25±3,977.99	11,886.75±3,445.29	0.920†
Insulin (μU/mL)	7,419.96±5,205.58	6,960.02±4,550.84	0.768†

HOMA=Homeostasis Model Assessment; SD=standard deviation; IQR=interquartile range

† Data were analyzed by paired t-test, ‡ Data were analyzed by Wilcoxon test, * Statistically significant at the 0.05 level

insulin resistance, measured by the mean HOMA% IR, the intervention group had a value of 1.91±1.03, while the placebo group had 1.53±1.02. No significant difference was observed in the average HOMA% IR value between the two groups (p=0.064). The median insulinogenic index, reflecting insulin secretion, was 1.3 (IQR 0.14, 8.03) for the intervention group and 0.65 (IQR 0.03, 3.63) for the placebo group. This difference was not statistically significant (p=0.155). Regarding β-cell function, measured by mean HOMA% B, the intervention group showed 102.25±47.80, compared to 98.53±46.25 in the placebo group, with no significant difference between them (p=0.677). Finally, the Disposition Index, an indicator of pancreatic β-cell functions relative to insulin sensitivity, yielded mean values of 5.98 (IQR 0.96, 25.18) in the intervention group and 3.71 (IQR 0.18, 38.09) in the placebo group, with no significant difference detected (p=0.929) (Table 5).

The AUC for plasma glucose between 0 and 120 minutes indicated a mean AUC of 15,285±4,531.57 for the intervention group and 15,101.25±3,955.71 for the placebo group, with no statistically significant difference (p=0.892). In terms of insulin levels, the intervention group had a mean AUC of 8,507.92±5,858.80 compared to 7,652.42±5,020.01 for the placebo, also without a significant difference (p=0.623). Breaking down the AUC by time intervals, for plasma glucose during the first 0 to 30 minutes, the mean AUC was 3,279.75±553.58 in the intervention group and 3,214.50±510.42 in the placebo, showing no significant difference (p=0.701). However, the insulin level during the same time frame was significantly higher in the intervention group compared to the placebo, with a mean AUC of 1,087.95±653.22 versus 692.4±469.17, respectively (p=0.034). Over the period of 30 to 120 minutes, the mean AUC for plasma glucose was 12,005.25±3,977.99 in the intervention group and 11,886.75±3,445.29 in the placebo group. This difference in mean AUC was not statistically significant (p=0.92). Regarding insulin levels over the same interval, the mean AUC was 7,419.96±5,205.58 in the intervention group, compared to 6,960.02±4,550.84 in the placebo group, with no statistically significant difference detected between the groups (p=0.768) (Table 5).

Discussion

The present study constitutes the first randomized, double-blind, placebo-controlled crossover study of stevia in obese patients. The study found no significant differences in plasma glucose levels between stevia and placebo group. While insulin level differences were observed during the first 30 minutes post-OGTT, no statistically significant differences were found at the subsequent intervals of 60, 90, and 120 minutes. Regarding insulin sensitivity, no significant differences were found between the intervention and

control groups in the Matsuda index or HOMA-IR. Additionally, no significant differences were observed in the insulinogenic index and the disposition index after the OGTT. The findings suggest that stevia has a physiologically inert impact on both glycemic and hormonal responses, offering potential benefits for glycemic control in obese patients.

Similar studies conducted in obese patients have shown that synthetically artificial NNS, such as sucralose, affect the glycemic and hormonal response. Pepino et al. reported significant increases in peak plasma glucose, C-peptide, insulin concentration, and insulin AUC following sucralose ingestion compared to water after an oral glucose load[24]. Conversely, Anton et al. studied both lean and obese individuals given a preload of a certain type of sweetener before meals. This study revealed that participants who consumed stevia had lower levels of plasma glucose and insulin than those consumed sucralose and aspartame[25].

Studies have shown that high postprandial plasma glucose is associated with a higher risk of cardiovascular disease and T2DM development. Azad et al. observed that NNS is associated with increased BMI and elevated risk of cardiometabolic disease[26]. The present study suggests that stevia could be a preferable NNS, as it is not associated with increased postprandial blood glucose or disturbances in insulin sensitivity. However, the increased insulin level at 30 minutes in the intervention group may be explained by the following factors. First, stevia-induced insulin secretion, as demonstrated in the previous studies, may play a role[16-18]. Additionally, the rapid absorption of stevia, with peak plasma concentrations observed as early as 15 minutes post-ingestion, could have already begun exerting its effects on insulin secretion within the first 30 minutes of the test[23]. The significant difference at 30 minutes may also reflect a transient phase during which stevia amplifies the early-phase insulin response. This is consistent with the previous findings suggesting that sweet-tasting compounds can influence incretin release, which in turn modulates insulin secretion[27].

The primary strength of the present study is its distinction as the first RCT to explore the effects of stevia on plasma glucose and insulin levels in obese individuals. The randomized, double-blind, crossover design effectively eliminates selection bias and minimizes patient-related variations. However, the present study has limitations. It specifically focuses on obese individuals with a BMI of 25 kg/m² or higher, limiting the applicability of the findings to other populations. Additionally, the present study focuses on the acute effects of stevia preceding an OGTT. Thus, conclusions regarding the long-term effects of stevia cannot be drawn.

Conclusion

Stevia does not affect plasma glucose and insulin responses following an OGTT in obese individuals. These findings suggest potential benefits for weight management and glycemic control in obese individuals. However, additional research is necessary to explore the long-term effects of stevia consumption.

What is already known on this topic?

Synthetic NNSs like sucralose affect glycemic and hormonal responses and are associated with higher risks of cardiovascular disease and T2DM.

What does this study add?

Stevia does not significantly impact plasma glucose levels or insulin sensitivity in obese patients, suggesting it as a potentially preferable NNS for glycemic control without increasing postprandial blood glucose.

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Authors' contributions

PS, MP, CK, CS, MP, NS, and AB developed the study concept. PS collected and analyzed the data. PS and MP wrote the first draft. AB overseed all study protocols. All authors contributed to and approved the final version.

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Conflicts of interest

The authors declare no conflict of interest.

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