Egypt. J. Chem. Environ. Health, 7(2):1- 9(2021)
On line ISSN: 2536-9164

Comparative Study on The Effect of Two Sweeteners, Stevia and Sucrose, on Blood Glucose Levels in Healthy Individuals

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ABSTRACT

There have always been concerns about the effect of sugar intake on health, especially in individuals suffering from diabetes. Attempts have been made to replace sugar with safe and healthy sweeteners. Owing to its low-calorie content, stevia has attracted much attention as a sugar replacement. The aim of this study was to examine the effects of two sweeteners namely: stevia and sucrose on blood glucose levels in healthy individuals. It has been established to help reduce blood glucose levels. The influence of sucrose and stevia on healthy individuals (n = 33; aged 12-55; body mass index 24.4 ± 8 kg/m^2) was studied. Participants were allowed to oral consumption of 100 mL of three beverages containing 0.2 mg/mL of sucrose, 5 mg/mL of stevia, or 10 mg/mL of stevia on different experimental days. The results showed a significant difference in glycemic response on days, when sucrose and stevia were consumed, while no significant differences were recorded between the two doses of stevia. Based on our findings, it could be concluded that that consumption of stevia in a short time period does not raise blood glucose in healthy individuals.

Keywords : Diabetes, Blood glucose, Natural Sweetener, Stevia, sucrose.

INTRODUCTION

Diabetes is a lifelong metabolic disease characterized by elevated blood glucose levels. It can cause serious harm to the heart, blood vessels, skin, kidneys, and the nervous system over time. Type 2 diabetes mellitus is recognized as a worldwide health hazard[1]. In 2019, nearly 463 million adults were diagnosed to have diabetes, and this number is expected to increase to 578 million by 2030. Other than the cases that are diagnosed and reported, many go unnoticed. By an estimate, in actuality, diabetes affects one out of every two people, i.e., 232 million people globally suffer from diabetes. This is particularly common in the elderly, where one in every five diabetic individuals is 65 years old. Type 2 diabetes mellitus is becoming more prevalent with time worldwide as behavioral and environmental risk factors keep changing with the current times[2]. Another major factor in the occurrence of diabetes is genetic predisposition, especially in combination with behavioral and environmental risk factors. Although the genetic causes of Type 2 diabetes are yet to be discovered, there is clear

evidence that non-genetic determinants, such as obesity and physical inactivity, are the most important non-genetic causes[3]. The intake of sugar-sweetened beverages (SSB) is linked to the development of metabolic syndromes and Type 2 diabetes, as well as weight gain. Specifically, SSB consumption has been associated with the risk of obesity-related chronic metabolic diseases[4]. Despite these risks, the high consumption of SSBs that includes soft drinks, fruit drinks, iced tea, energy and vitamin drinks has increased worldwide[2,5]. Devising sweeteners, other than sucrose, is particularly important for diabetic patients because they have low glucose tolerance, and their blood glucose levels increase dramatically after eating sucrose[6].

Non-nutritive sweeteners (NNS) are sugar replacements and have increased in popularity over the last two decades. These sugar replacements appeal to a large clientele because they provide a strong sweetening effect without contributing any sugar or processed-food energy to the diet. Aspartame, saccharin, sucralose, stevia, cyclamate, and acesulfame K are popular examples of NNS. Stevia extract, also known as stevia, is a natural sweetener made from the leaves of Stevia plant. This plant is native to South America, where it has been used as a sweetener by populations for over a century. Studies testing stevia, its usefulness, and safety have been sparse and inconclusive[7]. As stevia is cheap and readily available, it is an attractive option for sugar replacement that can be widely adopted. Furthermore, if it can have a positive influence on calorie substitution, it may even aid in weight loss[5]. According to previous studies, stevia does not increase blood glucose levels when ingested[2].

Keeping in view the aforementioned key strengths of stevia, we have tested its influence on the blood sugar levels of healthy peoples, majorly by monitoring blood glucose levels after consumption. Based on our results, we strongly recommended that diabetic and healthy individuals both should incorporate stevia sweetener to their lifestyle to prevent and/or better manage Type 1 and Type 2 diabetes mellitus.

MATERIALS AND METHODS

1. Participants

This study was performed on 33 healthy participants: six males and 27 females, aged 12-55. The participants were chosen based on the following inclusion criteria: Body mass index (BMI) ranging from 16.4 to 32.1 kg/m^2. The participants did not have a chronic disease, especially diabetes, and were tested to have a normal fasting blood glucose level. Fasting blood glucose levels were recorded to exclude any subject that had more than 7 mmol/L of blood glucose in order to ensure that already present conditions did not interfere with the objectives of this study. Written consent was obtained from all subjects.

2. Stevia extracts and reference beverages

A commercial stevia product by Oladole Natural was used in this study to compare its effect on blood glucose, along with sucrose, which is known to be the most consumed sugar. The concentrations of the test beverages were as follows: 0.2 mg/mL of sucrose, 5 mg/mL of stevia, and 10 mg/mL of stevia.

3. Experimental details

This study was conducted over a time period of three days. Basic information of participants was recorded, including name, age, and gender, whereas weight, height, and BMI were measured during the preselection of subjects. The participants were asked to fast for at least 8 hours before each experimental period. On the first day, fasting blood glucose of participants was measured and blood samples were collected Before beverage intake. The participants were requested to consume 100 mL of the sucrose solution followed by their blood glucose being measured at different known times (0, 30, 60, 90, and 120 min) also, in each time point blood samples were taken to determent insulin level. The participants were then requested to resume their usual routines. On the second test day, participants were given 5 mg/mL stevia solution, and on the third day, they were given a 10 mg/mL stevia solution. Blood samples were collected and Blood glucose readings were taken and written down for record on all days for each participant.

4. Blood sampling

Blood glucose was measured from capillary blood samples using Accu-Chek Performa®.

This blood was chosen instead of venous blood because of the greater fluctuations expected in venous plasma[2].

Insulin levels were determined by a sandwich ELISA technique, using a commercial ELISA kit (ab100578)

5. Statistical analyses

The data were analyzed using IBM SPSS 26. Descriptive statistics were performed on basic information of volunteers, including gender, age, BMI, and fasting blood glucose (FBG), etc. Paired t-test was applied to compare the responses of blood glucose between the first and second test days (sucrose; stevia (5 mg/mL)), between the first and third test days (sucrose; stevia (10 mg/mL)), and between the second and third test days (stevia 5 mg/mL; stevia 10 mg/mL). All results are expressed as mean ± standard deviation. The area under the curve (AUC) was calculated to compare the blood glucose response to beverages tested here over 2 hours on each test day.

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RESULTS AND DISCUSSION

Thirty-three subjects completed the study, and no volunteers complained of adverse reactions. Demographically, 81.8% of subjects were female; 18.2% were male. The mean age was 24.48 ± 9.51 and mean BMI was 21.83 ± 5.075 kg/m^2. Fasting blood glucose (FBG) ranged from 4.1 to 7.44 mmol/L and the mean FBG was 5.23 ± 0.75.The change recorded in mean blood glucose response after intake of sucrose, 5 mg/mL stevia, and 10 mg/mL after 2 h is shown in Table 1. There was a significant difference ($p < 0.001$) in the response to sucrose and 5 mg/mL stevia after 30 min of consumption ($t=4.072$, p value $=0.001$). The greatest glycemic response was exhibited by 0.2 mg/mL sucrose at 30 min, as well as insulin level was increased, while 5 mg/L stevia showed a decrease in mean blood glucose from 5.22 ± 0.82 at 0 minutes to 5.14 ± 0.67 mmol/L at 30 minutes after ingestion. Similarly, a significant difference ($p < 0.001$) was observed between the response of sucrose and 10 mg/mL stevia as well ($t= 5.150$, value $P=0.001$). It was noted that after 30 min of ingesting 100 mL of 10 mg/mL stevia, blood glucose decreased and eventually reached the highest blood glucose levels at 60 min after ingestion. It returned to baseline at 120 min. Interestingly, there was no significant difference ($p < 0.001$) in blood glucose response when 5 mg/mL or 10 mg/mL stevia were compared ($t= 1.842$, p value $=.075 > 0.05$)**.** insulin levels showed a relatively steady levels within 60 min after consuming stevia.

Areas under the curve (AUC) indicated that sucrose led to much higher blood glucose levels with an AUC value of 49.88. The AUC value for 5 mg/mL stevia was 1.38, indicating that the curve had little or no increment with time and that this solution has much lesser influence on post-ingestion blood glucose. The other stevia solution, 10 mg/mL, had an AUC of 5.07, indicating a minimal increase in blood glucose. in contrast, there is no significant different in total AUC for insulin response between sucrose and stevia doses.

Stevia was chosen in this study due to its many special characteristics. It is nontoxic and has been extensively tested as a natural sweetener[8,9,10]. Stevia contains nine known non-toxic types of steviol glycosides, numerous low-calorie compounds. Another major advantage of stevia is that it contains low calories; in case of nutritional guidelines that require added sugar to be reduced to <10% of the overall calorie intake and to replace common sugar with a low-calorie sweetener, stevia could be effective in reducing added-sugar intake[11]. Most importantly, regardless of it being 300 times sweeter than sucrose, stevia is considered safe for Type 2 diabetes patients[12]. Much research has provided evidence for the therapeutic potential of stevioside and steviol in the treatment of Type 2 diabetes[14]. There have been studies showing that incorporating stevia in everyday diet may be useful in maintaining a healthy diet, control sugar consumption[7], and in preventing health issues, especially for individuals on high-fat diets[13]. This supports studies that have advised diabetes patients specifically to keep healthy sugar levels in their diets, whether or not they consume NNS[14,15]. In addition, since plasma glucose levels are highest during the postprandial cycle, it can be safely assumed that minor lifestyle modifications may aid in lowering glycemia[16].

The present study showed that as compared to sucrose, 5 mg/mL and 10 mg/mL stevia solutions did not raise blood glucose levels. Sucrose increased glycemic response notably in patients after 30 minutes. Previous research has shown that the effect of stevia is not exclusive to maintaining blood sugar levels but also, as compared to sucrose, stevia intake may result in a significant decrease in insulin and glucose levels[5,8]. In another study, extract from *Stevia rebaudiana* was noted to enhance glucose resistance[22]. During the procedure and after an overnight fast, the extract greatly lowered plasma glucose levels in all volunteers. Consumption of stevia by 12 healthy subjects was monitored for 12 weeks to observe no differences in blood glucose or insulin response by ingestion of stevia[18]. Much similar research that has specifically focused on stevia corroborates our findings. A recent study looked at the impact of stevia on glycemic and lipid profiles of two groups of Type 2 diabetic patients. Even after two months, no statistically important variations were observed between the blood parameters of either group[19]; the authors of that research reported fasting blood sugar (FBS), HbA1c, postprandial blood glucose (PBG), triglycerides, total cholesterol, and high- and low-density lipoprotein levels to not substantially differ as well. They administered the first group with a cup of stevia three times a day and a tablet of sucralose sweetener to the other[19]. An unexpected observation was increased appetite in some participants on the second and third days. This was attributed to the tendency of stevia and other natural sweeteners to increase appetite, which may lead to overcompensation for the energy stored. However, no confirmed evidence is available for such an association between NNS intake and overcompensation for stored energy consumption.

According to our results, as well as an overwhelming majority of other studies, NNS may have a positive influence on diabetic patients' blood levels. For example, stevioside was found to lower blood glucose, when delivered intravenously[20] or orally[21], in GK mice suffering from moderate Type 2 diabetes. Another study was conducted on diabetic patients, who were given stevia leaf powder in tea three times a day for 15 days; this led to a drop in FBS and PBG levels[22]. However, some research has indicated otherwise as well. Stevioside is reported to trigger a significant increase in GK rats' insulin levels, while not decreasing blood glucose levels in normal Wistar rats[21]. Another report asserted that glycemic control in diabetic patients was not affected by NNS at all[23]. This discrepancy can be explained by certain factors. The effect of stevia on blood glucose is dictated by the timing of intake, the subject's health, and length of the study. Specifically with regard to timing, it has been reported that ingesting a beverage containing stevia prior to a meal will have a positive influence; this effect has been observed in clinical trials[24]. The study presented here was a short-term study; the subjects were given one dose of sweeteners. It is possible that different or contrary results may be observed in a similar, but long-term study. Previously in a long-term study conducted over 3 months, healthy subjects and diabetic patients were administered 250 mg of NNS dosages three times daily with no anomalous blood glucose levels.

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Conclusion

With a simple short-term study, it could be concluded that doses of 50 mg/mL and 100 mg/mL of sweeter stevia lower blood glucose levels, unlike sucrose, that has much higher probability of raising blood glucose. The blood glucose level and insulin response were not different between sucrose and stevia, and no significant differences were found in the overall effects of blood glucose and insulin response. Via tests on willing participants, it was found that stevia has a minimal influence on blood glucose, which highlights its nature as a safe sweetener for healthy peoples, as well as those suffering from diabetes. In diabetic patients specially, stevia can be incorporated in diet to regulate blood glucose levels, provided that the consumption of high-calorie sweeteners, such as sucrose is limited.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

Table 1. Mean blood glucose response after ingestion of sucrose, 5 mg/mL stevia, and 10 mg/mL stevia over a 2 h period

Test	0 min (mmol/L)	30 min (mmol/L)	60 min (mmol/L)	90 min (mmol/L)	120 min (mmol/L)
Sucrose (0.2 mg/mL)	5.15 ± 0.69	6.7 ± 1.24	5.81 ± 0.82	5.07 ± 0.66	5.09 ± 0.74
Stevia (5 mg/ml)	5.22 ± 0.82	5.14 ± 0.67	5.21 ± 0.73	5.18 ± 0.7	5.15 ± 0.75
Stevia (10 mg/mL)	5.04 ± 0.55	5 ± 0.51	5.07 ± 0.51	5.02 ± 0.6	5.07 ± 0.54

- Results are given as the mean ± SE.
- a, denote a significant change in comparison to the 0 min period at $p < 0.05$ significance*

Table 2. Mean insulin response after ingestion of sucrose, 5 mg/mL stevia, and 10 mg/mL stevia over a 2 h period

Test	0 min (mlU/L)	30 min (mlU/L)	60 min (mlU/L)	90 min (mlU/L)	120 min (mlU/L)
Sucrose (0.2 mg/mL)	11.20± 3.42	500± 343[a*]	900±705[a*]	455± 901[a*]	200± 801[a*]
Stevia (5 mg/ml)	11.40± 4.62	55±36[a*]	56±80[a*]	58±07[a*]	20±60
Stevia (10 mg/mL)	11.22± 3.72	70± 32[a*]	89± 22[a*]	34± 32	26± 01

- Results are given as the mean ± SE.
- a, denote a significant change in comparison to the 0 min period at $p < 0.05$ significance*

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