Sains Malaysiana 43(5)(2014): 649–654

Effect of Acute Stevia Consumption on Blood Glucose Response in Healthy Malay Young Adults

(Kesan Pengambilan *Stevia* Akut ke atas Tindak Balas Glukosa Darah dalam Kalangan Orang Melayu Dewasa yang Sihat)

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ABSTRACT

Previously, researchers had initiated investigation to find an alternative drug that can treat diabetes mellitus without dragging patients into more complicated health problems. After many studies, they found a new and high potential plant-based drug named stevia that is able to reduce diabetic patients' blood glucose. This study aimed to determine the effect of stevia on blood glucose of healthy subjects. The study was carried out by comparing the glycemic response between sucrose and stevia (500 and 1000 mg) among 32 subjects aged between 18 and 23 years old. Subjects were required to fast 8 to 10 h prior to each test which was done on different days. Finger prick test were done on 0, 30, 60, 90 and 120 min to construct a blood sugar response curve for 2 h period. There is a significant difference between the glycemic response of sucrose and stevia 500 mg. Sucrose significantly increased the post prandial blood glucose while stevia 500 mg reduced blood glucose after 30 min of consumption. Sucrose also produced higher glycemic response at min-30 when compared with stevia 1000 mg. There is no significant difference between the glycemic response of stevia of different dose, 500 and 1000 mg. No dose-dependent effect was observed in this study. In conclusion, stevia does not raise blood glucose significantly when consumed in short period. Stevia is effective to be used by healthy people to maintain blood glucose even when consumed in short length of time.

Keywords: Glycemic response; natural sweetener; stevia rebaudiana

ABSTRAK

Sebelum ini, para penyelidik telah menjalankan kajian bagi mencari ubat alternatif yang mampu merawat diabetes melitus tanpa menyebabkan masalah kesihatan yang lebih rumit dalam kalangan pesakit. Kajian ini dijalankan bertujuan untuk menentukan kesan stevia *ke atas kandungan glukosa dalam darah subjek sihat. Kajian ini telah dijalankan dengan membandingkan tindak balas glisemik antara sukrosa dengan* stevia *(500 dan 1000 mg) dalam kalangan 32 subjek berumur 18 hingga 23 tahun. Subjek dikehendaki berpuasa 8 hingga 10 jam sebelum setiap ujian dijalankan. Ujian cucuk jari telah dijalankan pada min 0, 30, 60, 90 dan 120 untuk membina lengkuk tindak balas gula dalam darah dalam tempoh dua jam. Terdapat perbezaan yang bererti antara tindak balas glisemik dengan* stevia *500 mg. Sukrosa meningkatkan glukosa darah pos prandial secara signifikan sementara* stevia *500 mg menurunkan glukosa darah selepas 30 min pengambilan. Sukrosa juga menghasilkan tindak balas glisemik pada min ke 30 berbanding* stevia *1000 mg. Tiada perbezaan yang signifikan antara tindak balas glisemik* stevia *yang berlainan dos, 500 dan 1000 mg. Tiada kesan kebergantungan kepada dos diperhatikan dalam kajian ini. Kesimpulannya,* stevia *tidak meningkatkan glukosa darah dengan signifikan apabila diambil dalam tempoh masa yang singkat.* Stevia *adalah efektif untuk digunakan oleh individu sihat yang mahu mengawal glukosa darah walaupun diambil dalam tempoh masa yang singkat.*

Kata kunci: Pemanis semula jadi; stevia rebaudiana*; tindak balas glisemik*

INTRODUCTION

Diabetes mellitus is a metabolic disease which is indicated by the high level of blood glucose in body and there are few main types of diabetes mellitus (DM) including Type 1, Type 2 and Gestational diabetes (Mahan & Escott-Stump 2008). According to American Diabetes Association (2011), 1.6 million cases are diagnosed in people aged 20 years old and above each year. Diabetes is later classified as the seventh leading cause of death in U.S. and in 2010, diabetes mellitus already affected 25.6 million of this population (National Diabetes Information Clearinghouse 2011).

Recently, the number of Type 2 diabetes mellitus (Type 2 DM) patients in Malaysia is alarmingly increasing. Based on the outcome of the 2011 National Health and Morbidity Survey (NHMS), the prevalence of Malaysians suffering from diabetes has increased from 14.9% in 2006 to 20.8% now (Zainal Ariffin 2013). According to the

Malaysian Diabetes Association (2008), 98% from the total of 1.2 million of diabetic patient in Malaysia were diagnosed with Type 2 DM. Apart from the physiological cause of diabetes, excess intake of sugar added foods and beverages may also contribute to this problem (Mahan & Escott-Stump 2008). Sugar or its scientific name, sucrose is the most commonly used sweetener nowadays. One tablespoon of sugar contains 60 kilocalories (Suzana et al. 2009) so a gram of sugar is equal to 4 kcal, hence when consumed in large amount it may significantly contributes to the total energy intake. Many people are looking for alternatives for sweetener and it leads to the consumption of artificial sweeteners such as aspartame and saccharine. However, issue regarding its safety rose in the world of researches and created huge concern. Side effects were found in aspartame, in which consumers reported of having headache and some other neuropsychiatric disorders. In addition, those who consume saccharine stated that they experienced dermatologic reactions including pruritus and eczema (Hull 2002).

When the controversies regarding these sweeteners rose, people start searching for other alternatives that is stevia, a natural sweetener that may be an ideal substitute to sugar. Stevia is a type of leaf that has the unique sweet taste and is 70 to 400 times sweeter than sucrose (Elkins 1997). The component that is responsible for the sweet taste of stevia is steviol glycoside and it has two primary compounds, stevioside and rebaudioside A. Stevioside is 300 times sweeter than sucrose in 0.4% solution (Geuns 2003) while rebaudioside A. is 250 to 450 times sweeter (Chatsudthipong & Muanprasat 2009). Even though the after taste of stevia is bitter but it is still well tolerated by all subjects. Stevia with its therapeutic properties has been proven to be safe and efficient for diabetic patient (Elkins 1997). It may also be beneficial for others who prefer to stay healthy and at the same time reduce the risk of having this metabolic disease due to its non-caloric properties (Elkins 1997). Hence, the main concern of this study was to determine the effect of stevia on blood glucose in healthy individuals. This may help healthy people to choose healthier sweetener to be used in their daily meal and at the same time will reduce the risk for diabetes mellitus.

METHODS

SELECTION AND EXCLUSION OF SUBJECTS

The subjects were young adults from International Islamic University Malaysia (IIUM) Kuantan and Centre for Foundation Studies (CFS IIUM) Petaling Jaya, Selangor. Inclusion criteria were subjects should be healthy (Non-diabetic and normal BMI), free from any underlying medical illness especially diabetes and willing to participate in the study. Subjects with known medical illness and random blood glucose equal to or more than 11.1 mmol/L or fasting blood glucose more than 7.0 mmol/L were excluded from this study. This is to avoid the results of study from being interfered by other health conditions. Participation is voluntary and subjects need to fill in the consent form prior to the test.

STEVIA EXTRACTS

The leaves extracts of *Stevia rebaudiana* plant were processed at Stevialeaf Co. a company from Kedah and is a commercialized product. The plants used for the production originated from Paraguay.

REFERENCE DRINK

This study compares stevia with sucrose as it is the most common sweetener used by the nation. An experiment was done to study the sweetness equivalent of stevia with sucrose (Savita et al. 2004). We found out that 1000 mg of curded stevia leaf in 100 mL of water is equivalent to 20 g of sucrose in 100 mL of water. Sucrose (20 g) and stevia (500 and 1000 mg) solution were prepared by solving them in 100 mL of water for subject to drink.

STUDY PROCEDURE

SUBJECTS

The study design was approved by the IIUM Ethical Committee. Subjects were briefed regarding the procedures of the experiment and written informed consent was taken from subjects. Basic details of subjects were obtained prior to the study such as subjects' name, age, race and gender. Initially, subjects have to ensure they fulfill the inclusion criteria which is free from any underlying medical illness. Height and weight were taken during subject selection and BMI is then calculated. Random blood glucose was taken to ensure subjects have no diabetic background.

EXPERIMENTAL DETAILS

The experiment has three parts of tests. Subjects were required to drink sucrose, stevia 500 mg and stevia 1000 mg solution. Subjects were informed that they can withdraw from the study at any time. Subjects were then required to fast 8-10 h prior to each test. Peripheral capillary blood was obtained by standard finger-prick procedure. Site of pricking was cleaned with alcohol swab before and after each pricking. During the first test, fasting blood glucose reading was taken and recorded. After that, subjects were given a sucrose solution made of 20 g of sucrose and 100 mL of water. Finger prick test were taken five times, on 0, 30, 60, 90 and 120 min and readings were recorded. Later, for the second and third test on two different days, subjects were given 500 and 1000 mg of stevia solution, also dissolved in 100 mL of water (Table 1) and the glycemic response was recorded with the same technique. These blood samples were used to construct a blood sugar response curve for 2 h period for area under curve (AUC) calculator to compare the glycemic response between sucrose, stevia 500 mg and stevia 1000 mg.

TABLE 1. Experimental procedure

Test	Test drink
Day I	Sucrose 20 g
Day II	Stevia 500 mg
Day III	Stevia 1000 mg

BLOOD SAMPLING

The glucose measured was taken from capillary blood samples using Accu-Check Advantage II Glucometer by following the manufacturer's protocol. This method is preferable than venous blood glucose since glycemic response measured using venous plasma showed higher variability (Wolever 2004). Sensitivity of measurement was also greater when using the capillary blood samples (Brouns et al. 2005).

STATISTICAL ANALYSIS

All the data obtained from the test were analyzed using SPSS version 12.0. Basic details of subjects including age, course of study and year of study were analyzed using descriptive statistic. Paired T-test was used to compare the glycemic response between sucrose and stevia 500 mg, sucrose and stevia 1000 mg and between stevia 500 mg and stevia 1000 mg. This study was designed to provide 90% power. Differences were considered significant at $p<0.05$. The results were expressed as mean ± standard deviation (SD).

AUC is calculated to measure the glycemic response in test drinks within 2 h of each test. It is automatically calculated using the AUC calculator only by entering the values of mean blood glucose during each blood sampling. Low value of AUC shows that the test food gives minimal increase in the blood glucose while higher value of AUC indicates higher blood glucose response.

RESULTS

DEMOGRAPHIC DATA

Thirty two subjects were recruited and no subject withdraws from the study. All subjects are Malays (n=32), where 87.5% subjects were female (n=28) and 12.5% were male (n=4). Subjects' age ranges from 18 to 23 years old and the mean age was 21.25 ± 1.11. According to the year of study, 18.8% (n=6) were first year students, 34.4% (n=11) were second year students, 43.8% (n=14) were third year students and 3.1% (n=1) were fourth year students. The mean body weight is 54.3 ± 8.5 kg while the body mass index (BMI) of subjects ranged from 16.4 to 32.1 kg/m^2 with the mean of BMI 21.6 ± 3.3. Random blood glucose (RBG) in all subjects is within the normal range. RBG ranges from 4.7 to 7.6 mmol/L with the mean of 5.6 ± 0.7 (Table 2).

BLOOD GLUCOSE RESPONSE AFTER CONSUMPTION OF SUCROSE AND STEVIA

Changes of mean blood glucose response after consumption of sucrose, stevia 500 mg and stevia 1000 mg are shown in Figure 1. Table 3 shows the mean blood glucose value after consumption of sucrose and stevia at 0, 30, 60, 90 and 120 min.

COMPARISON OF GLYCEMIC RESPONSE BETWEEN SUCROSE AND STEVIA 500 MG

When comparing between sucrose and stevia 500 mg, after 30 min of consumption, there is a significant difference in the glycemic response, with $p<0.001$. Sucrose increased the blood glucose to 7.1±0.8 mmol/L from baseline while stevia 500 mg reduced blood glucose from 5.2 ± 0.5 to 5.1±0.3 mmol/L.

Sucrose reached its peak at min 30 and drops at min 60 and decreased below baseline value at min 120 (Figure 2). Blood glucose response was significantly lower at min 30 ($p<0.05$). It dropped after min 30, 60 and 90, before returning to baseline at min 120. There is also a significant difference in blood glucose response after min 120 ($p<0.05$) but with smaller mean difference.

COMPARISON OF GLYCEMIC RESPONSE BETWEEN SUCROSE AND STEVIA 1000 MG

When comparing the blood glucose response between sucrose and stevia 1000 mg, the pattern of glycemic response seen was slightly different. Blood glucose

TABLE 2. Demographic characteristics of the subjects for gender, year of study and course of study

Characteristics	N (n = 32)	%
Race		
Malay	32	100.0
Gender		
Male	4	12.5
Female	27	87.5
Mean ± SD (Min - Max)		
Age	21.3 ± 1.1	18.0 – 23.0
BMI	21.6 ± 3.3	16.4 – 32.1
RBG (mmol/L)	5.6 ± 0.7	4.7 – 7.6

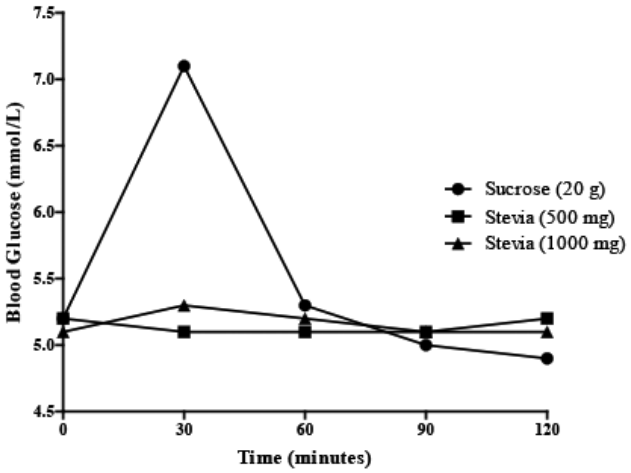

FIGURE 1. Mean blood glucose response after consumption of sucrose, stevia 500 and 1000 mg

TABLE 3. Mean fasting blood glucose and blood glucose at minute 30, 60, 90 and 120 after consumption of sucrose, stevia 500 and 1000 mg

Test	N	FBG (mmol/L)	30 min (mmol/L)	60 min (mmol/L)	90 min (mmol/L)	120 min (mmol/L)
Sucrose drink (20 g)	32	5.2 ± 0.50	7.1 ± 0.79	5.3 ± 0.84	5.0 ± 0.84	4.9 ± 0.44
Stevia 500 mg	32	5.2 ± 0.52	5.1 ± 0.34	5.1 ± 0.40	5.1 ± 0.38	5.2 ± 0.58
Stevia 1000 mg	32	5.1 ± 0.46	5.3 ± 0.49	5.2 ± 0.55	5.1 ± 0.44	5.1 ± 0.43

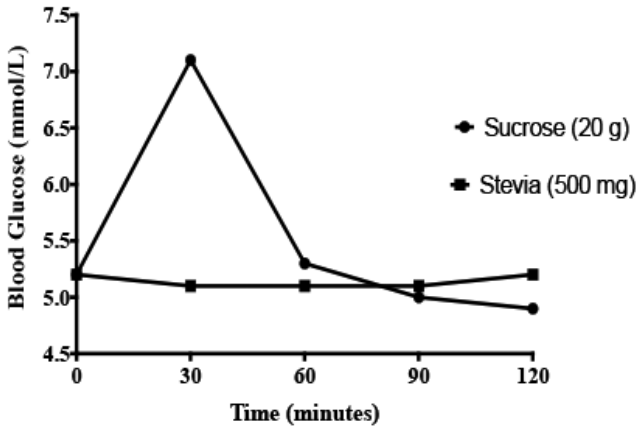

FIGURE 2. Mean blood glucose response after consumption of sucrose and stevia 500 mg

increased after 30 min of stevia 1000 mg consumption, before decreased at baseline at min 120 (Figure 3). Stevia raises blood glucose with higher dosage; therefore it is important to note that there is a significant difference between the glycemic response of sucrose and stevia 1000 mg (p<0.05). At min 30, blood glucose increased from 5.1±0.5 to 5.3±0.5 mmol/L (p<0.001). After 2 h of stevia 1000 mg consumption, the blood glucose returned to baseline.

COMPARISON OF GLYCEMIC RESPONSE BETWEEN STEVIA 500 AND 1000 MG

When performing test to compare the glycemic response between stevia 500 and 1000 mg, no significant difference was seen. However, short term consumption of stevia reduces mean blood glucose when consumed at dose of 500 mg, while 1000 mg stevia slightly increases the blood glucose. No significant dose-dependent effect was observed in this study.

AREA UNDER CURVE (AUC) FOR BLOOD GLUCOSE RESPONSE OF SUCROSE AND STEVIA

From the result shown in Table 3, sucrose has higher glycemic response with AUC value 59, followed by stevia 1000 and 500 mg. The AUC value for stevia 500 mg is 0 which shows that the curve has no increment and stevia 500 mg did not raise the post-prandial blood glucose. AUC value for stevia 1000 mg is 5 indicating a minimal increment in blood glucose response (Table 4).

DISCUSSION

HYPOGLYCEMIC EFFECT OF STEVIA

From this study, it can be seen that short term consumption of stevia 500 mg did not increase blood glucose. It shows minimal reduction in blood glucose after 30 min. Contrary, sucrose shows higher peak of glycemic response within the 2 h of test. The result may be statistically significant but medically insignificant for a blood glucose response. According to Barriocanal et al. (2008) medically significant difference for blood glucose is defined as 50 mg/dl or 2.8 mmol/L. Duration of study might be one of the influencing factors of such result. This experiment is a short period study which supplemented each dose of stevia to subjects for only one day. It may not represent the actual stevia effect that does not increased blood glucose after consumption. Throughout this study, no subject complained of having hypoglycemic symptoms.

Long term study using stevioside was done by Barriocanal et al. (2008) and Chan et al. (2000). The study was performed on healthy subjects with no diabetic history using 750 mg stevioside for 3 months (Barriocanal et al. 2008) and for 1 year (Chan et al. 2000). Interestingly, no significant changes in blood glucose were detected. Stevioside did not cause any significant reduction in mean blood glucose. Therefore, it can be concluded that long term intake of stevia will not cause hypoglycemia in healthy people. Stevia is safe to be used as sweetener in healthy people. It does not increase post prandial blood glucose and also it does not cause hypoglycemic symptoms. In other study (Geuns et al. 2007) found no effect on blood glucose in healthy human subjects after been given stevioside 250 mg 3 times daily for 3 days. This is similar to the findings by Chan et al. (2000) who supplemented the same doses of stevioside to the non-diabetic subjects for one year. Chan et al. (2000) and Geuns et al. (2007) concluded that stevia does not elevate blood glucose thus is safe to be used as sweetener in healthy subjects.

The main factor of the different findings between the present study and previous study is possibly due to the objectives of each study itself. The present study compares the short term glycemic response between sucrose and stevia while the previous studies were comparing between the mean blood glucose of stevia before consumption and after a period of time.

There are hundreds of sweetened foods and beverages in the market today that may lead to metabolic disorders

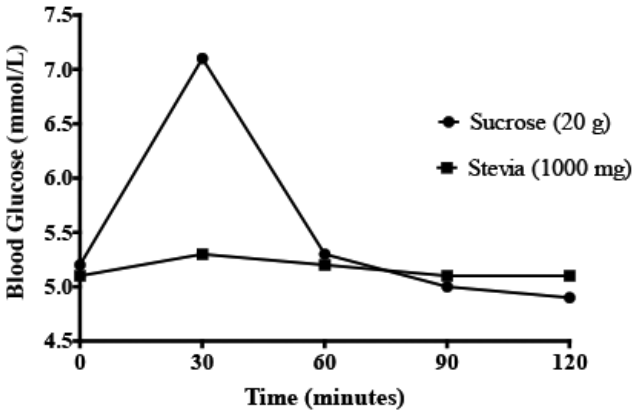

FIGURE 3. Mean blood glucose response after consumption of sucrose and stevia 1000 mg

TABLE 4. Area under curve (AUC) for 3 test drinks; sucrose, stevia 500 and 1000 mg

Test drink	Mean AUC
20 g sucrose drink	59
Stevia 500 mg	0
Stevia 1000 mg	5

such as diabetes and obesity. The manufacturers should start substituting the higher calorie sweetener to a healthier choice. In addition, there is no difference in satiety when comparing meals substituted with sucrose or stevia (Anton et al. 2010). By using lower calories sweetener, consumers can reduce the energy intake from simple sugar.

There are already abundant of stevia products produced worldwide. However, in Malaysia, stevia is not yet well-known. It is hoped that the result of this study may help people, mainly Malaysians to be aware that stevia is beneficial not only for managing diabetes mellitus, but also in preventing it from occurring. It is also an ardent hope that the information obtained from this study will be useful to the society and consumers and will provide bigger market and more demand for stevia in Malaysia. Further studies should be done by researchers in Malaysia to observe the effect of long term stevia consumption on blood glucose profile. Besides, the effect of stevia on other biochemical parameters such as blood pressure, lipid profile and renal profile should also be studied.

Conclusion

In conclusion, there is a significant difference between the glycemic response of sucrose and stevia 500 mg. Sucrose significantly increases the post prandial blood glucose while stevia 500 mg reduced the blood glucose after 30 min of consumption. Sucrose also produces higher glycemic response at min 30 when compared to stevia 1000 mg. AUC value shows that both stevia 500 and 1000 mg show minimal increment in blood glucose as compared with sucrose. Stevia does not raise the blood glucose when consumed in short period and is effective to be used by healthy people to control the blood glucose level even when consumed in a short length of time.

Acknowledgements

The authors would like to thank the International Islamic University Malaysia (IIUM) for their financial support under the Research Endowment Fund IIUM and for the laboratory facilities of IIUM.

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Received: 6 December 2012
Accepted: 31 July 2013