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Effect of acute bitter melon intake on postprandial glucose and insulin in sedentary, abdominally obese persons

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ABSTRACT

Background: Lifestyle modifications have been considered to be the primary prevention strategies for diabetes. However, there is a lack of evidence guiding the use of functional foods that potentially possess anti-hyperglycemic effects. The objective of this study was to investigate the acute effect of bitter melon intake on postprandial glucose and insulin levels in sedentary, abdominally obese persons.

Methods: In this study, 16 sedentary, abdominally obese participants were randomly assigned to receive either 100 ml of bitter melon juice or placebo juice 30 minutes prior to an oral glucose tolerance test. Plasma glucose and serum insulin were measured every 30 minutes during the 2-hour postprandial period. Two-way repeated measure ANOVA was used to test the effects of bitter melon on postprandial glucose and insulin levels after adjustment for covariates.

Results: The 2-h postprandial glucose was significantly lower in bitter melon group as compared with control group (99.5 ± 22.3 vs 133.9 ± 36.9 mg/dL, P=0.04), resulting in an absolute glucose reduction of 34.4 mg/dL (95% confidence interval, 1.7 to 67.1 mg/dL) and a relative glucose reduction of 26%. There was a fairly significant reduction in 2-h postprandial glucose incremental area under the curve (iAUC) (52.9 ± 29.5 vs 94.7 ± 47.3 mg/dL·h, P=0.052), resulting in a relative glucose reduction of 44%.

Conclusion: Our acute study demonstrated that the single-dose intake of bitter melon juice decreased postprandial glucose levels among sedentary, abdominally obese persons. Bitter melon juice appears to be a promising functional food to manage hyperglycemia for people who are at elevated risk of developing diabetes.

Key Words: Functional Food; Momordica Charantia; Hyperglycemia; Sedentary; Obese

BACKGROUND

Lifestyle modifications are the cornerstones of the primary prevention of diabetes. Current nutrition research, a key component of healthy lifestyles, has largely focused on energy balance, macronutrients, and food groups for managing diabetes risk. But there is a lack of scientific evidence of functional food that potentially possesses anti-hyperglycemic effects. However, a great number of consumers are using functional foods with the purpose of improving glucose regulation despite limited scientific evidence. Accordingly, there is a need to examine the effects of functional food on glucose regulation with rigorously designed studies.

This study emphasizes the acute effect of a promising functional food, bitter melon, on postprandial glucose and insulin levels in sedentary, abdominally obese persons. Bitter melon is a natural food used for the management of diabetes in tropical regions which showed particular promise for glucose control. The glucose-lowing effect of bitter melon has been tested in many in vitro studies and animal models [1]. A study revealed that the extract of bitter melon decreased ATP-dependent active transport of glucose cross the rat intestine under in vitro conditions, suggesting that bitter melon may decrease blood glucose by suppressing the glucose absorption in the gastrointestinal tract [2]. Studies in rats revealed that bitter melon improved insulin resistance and β-cell dysfunction, the two most important pathogenic causes of type 2 diabetes [3, 4], indicating a potential application of bitter melon in the prevention of diabetes. Nonetheless, high-quality evidence supporting the beneficial effect of bitter melon on glucose regulation in human participants is limited. Few studies have tested the acute effect of bitter melon in sedentary, abdominally obese individuals, a population at increased risk of cardiometabolic diseases.

Therefore, the objective of this study was to investigate the acute effect of a single-dose intake of bitter melon juice on postprandial glucose and insulin levels in sedentary, abdominally obese persons.

METHODS

Participants

Sedentary persons with abdominal obesity who were physically inactive were recruited through an online pre-screening survey. All participants provided written informed consent before participation. The inclusion criteria were an age of 18 years or above; a large waist circumference (men $\geqslant$ 102 cm, women $\geqslant$88 cm); and physical inactivity (not engaged in regular recreational physical activity/exercise). Exclusion criteria were diabetes or other metabolic diseases; the use of medications that could interfere with blood glucose metabolism; food allergy or medical conditions that impact normal functioning of the gastrointestinal tract; and pregnancy.

Research Design

We performed a randomized, double-blind, placebo-controlled trial at the Healthy Lifestyles Research Center in Arizona State University (ASU). All eligible participants were randomly assigned to receive either 100 ml of bitter melon juice or placebo according to 1:1 ratio. The randomization sequence number was generated by a computer program. The treatment allocation was concealed by electronically sealed envelopes. Study participants, outcome assessors, and data

entry operators were blind to treatment allocation. The trial protocol was reviewed and approved by the institutional review board at ASU.

Procedures

Fresh bitter melon fruit was purchased from a certified local grocery. The seed was removed, and juice was obtained from the fruit pulp through blending. We obtained 100 ml of bitter melon juice from every 140 g of bitter melon pulp. A packet of sweetener (Splenda, Heartland Food Products Group, Carmel, Indiana) was added to each cup (100 ml) of bitter melon juice to improve palatability. The placebo was a sham drink that has a similar color, taste, and texture as bitter melon juice.

All included participants attended a familiarization visit to our lab. During the familiarization visit, anthropometric measures including body weight, height, and waist circumferences were recorded. On the experiment day, participants arrived at our lab at 8:00 am after a 9-hour overnight fast. Upon arrival, all participants sat still for 30 min to avoid the influence of physical activity on postprandial glucose levels. Then, the participants consumed a cup (100 ml) of bitter melon juice or placebo within 3 minutes. After 30 minutes of the bitter melon or placebo intake, a 75-gram oral glucose tolerance test (OGTT) was administered. The exact point in time when the subject began to consume the glucose beverage was marked as 00:00. All participants consumed the glucose beverage within 3 minutes. All participants sat still throughout the 2-hour period of the OGTT.

Measures

We collected blood samples for plasma glucose and serum insulin measurement at the time -00:10, 00:30, 1:00, 01:30, and 02:00 respectively. All the measures occurred in the research laboratory at ASU. A registered nurse was responsible for blood collection. Whole blood was collected by venipuncture and centrifuged for 15 minutes at 3000rpm. Glucose was measured in plasma with an automated chemistry analyzer (Cobas C111; Roche Diagnostics, Indianapolis, IN) using colorimetric enzymatic reagents. Insulin was measured in plasma using the ultrasensitive human radioimmunoassay kit (Millipore Corporation, Billerica, MA).

Statistical Analysis

All data were expressed as mean ± standard deviation. Descriptive statistics were used to present demographic information. Shapiro-Wilk test was used to determine whether the data had a normal distribution. The independent t-test was used to compare the mean differences in glucose and insulin levels at each time point. Two-way repeated measure ANOVA was used to test the effects of treatment (bitter melon, and control), time (baseline, 30 min, 60 min, 90 min, and 120 min), and treatment x time interaction on postprandial glucose and insulin levels after adjustment for covariates (i.e., age, sex, etc.). The two-way repeated measure ANOVA with power transformation of the variables or the Mann-Whitney test was used if the assumption of normality was unjustified. All statistical procedures and analyses were conducted with SAS (version 9.3, PROC GLM in SAS) software.

RESULTS:

A total of 15 women and 1 man participated in this study. Of these, 8 were randomly assigned to the bitter melon group and 8 were assigned to the control group. There were no significant differences in patients' characteristics between the two study groups at baseline (Table 1). The mean age of the participants was 29.5 years. The mean waist circumference was 117.4 cm. The mean fasting blood glucose was 93.5 mg/dL. The mean systolic and diastolic blood pressures of the participants at baseline were 117.2 mmHg and 76.1 mmHg, respectively.

The difference in 2-h postprandial glucose incremental area under the curve (iAUC) between groups was nearly significant (52.9 ± 29.5 vs 94.7 ± 47.3 mg/dL·h, P=0.052) (Figure 1). When comparing the glucose levels between the two groups at each time point, significant differences were found at 120 minutes (99.5 ± 22.3 vs 133.9 ± 36.9 mg/dL, P=0.04), but not at 30 minutes (140.3 ± 24.1 vs 150.5 ± 23.3 mg/dL, P=0.4), 60 minutes (124.9 ± 24.2 vs 153.2 ± 38.3 mg/dL, P=0.1), or 90 minutes (118.7 ± 19.8 vs 145.1 ± 33.1 mg/dL, P=0.07).

Table 1. Baseline characteristics of participants. Data are mean ± standard deviation, or n (%).

Variable	Bitter Melon Group (n=8)	Control Group (n=8)	P value
Age (years)	31.3 ± 9.3	27.7 ± 11.1	0.50
Height (cm)	171.6 ± 9.7	166.1 ± 8.8	0.26
Weight (kg)	105.3 ± 28.4	94.8 ± 18.6	0.40
Body Mass-Index (kg/m^2)	35.3 ± 7.5	34.5 ± 7.5	0.83
Waist circumference (cm)	122.1 ± 13.9	112.6 ± 13.9	0.19
Number of Female	8 (100%)	7 (88%)	-
Systolic blood pressure (mmHg)	118.5 ± 13.7	115.9 ± 10.4	0.67
Diastolic blood pressure (mmHg)	77.3 ± 13.4	75.0 ± 7.7	0.69
Fasting blood glucose (mmol/L)	93.7 ± 4.6	93.4 ± 5.4	0.86

The 2-h postprandial insulin iAUC was not significantly different between groups (213.7 ± 167.4 vs 200.3 ± 58.5 uIU/mL·h, P=0.83) (Figure 2). When comparing the insulin levels between the two groups at each time point, there were no significant differences at 30 minutes (158.9 ± 88.3 vs 124.4 ± 48.5 uIU/mL, P=0.35), 60 minutes (162.1 ± 111.2 vs 151.9 ± 58.7 uIU/mL, P=0.82), 90 minutes (126.5 ± 108.3 vs 144.9 ± 31.7 uIU/mL, P=0.65), or 120 minutes (116.4 ± 127.6 vs 130.2 ± 38.6 uIU/mL, P=0.77). The postprandial insulin sensitivity was not significantly different between the two study groups (0.052 ± 0.102 vs 0.077 ± 0.025 $umol \cdot kg^{-1} \cdot min^{-1} \cdot pM^{-1}$, P=0.52).

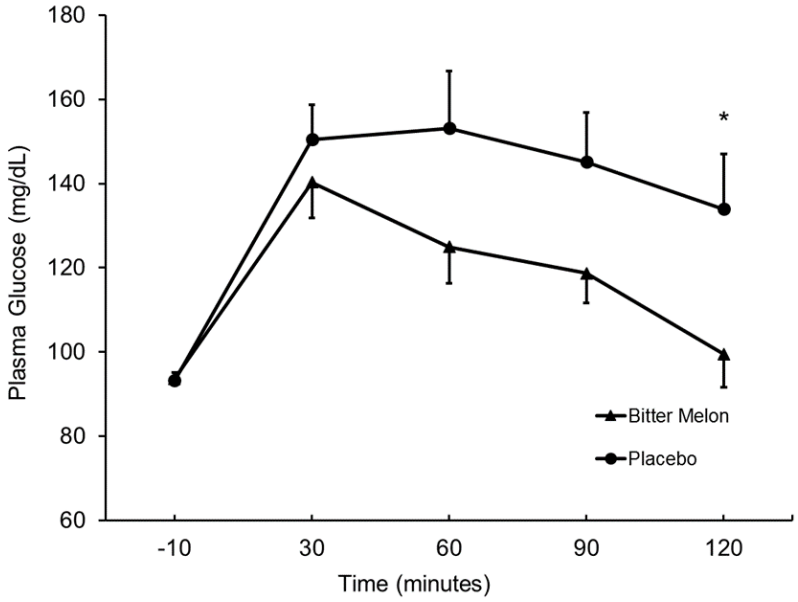

Figure 1. Postprandial glucose responses to bitter melon and control. Baseline measures were taken 10 minutes prior to the consumption of the oral glucose solution. Data present mean ± standard error. * Significantly different between two conditions ($P < 0.05$).

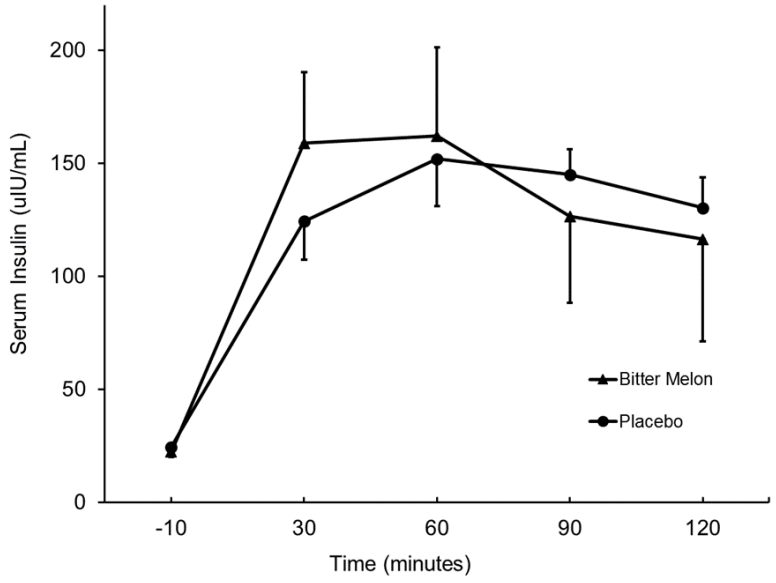

Figure 2. Postprandial glucose responses to bitter melon and control. Baseline measures were taken 10 minutes prior to the consumption of the oral glucose solution. Data present mean ± standard error. * Significantly different between two conditions ($P < 0.05$).

DISCUSSION

Our findings revealed that, among sedentary participants with abdominal obesity, the intake of 100 ml of bitter melon juice 30 minutes prior to a 75-gram OGTT significantly reduced the 2-h postprandial glucose by 34.4 mg/dL compared with the placebo juice, suggesting a potent glucose-lowering effect of acute bitter melon intake. Although statistical significance was not reached, the 2-h glucose iAUC was lowered by 44% (Cohen's d, 1.06) in the bitter melon group compared to the control group, indicating that the magnitude of the glucose-lowering effect was substantial and clinically significant. Additionally, the absolute reductions in plasma glucose at 60 minutes (28.3 mg/dl or 1.6 mmol/L) and 90 minutes (26.4 mg/dL or 1.5 mmol/L) did not reach statistical significance but had tendencies of being clinically meaningful.

The glucose-lowering effect of bitter melon in the present study was in agreement with existing evidence. In a repeated-measures study, Ahmad and colleagues showed that the single intake of bitter melon juice lowered 2-h glucose by 35.3 mg/dL (1.96 mmol/L) among 100 patients with type 2 diabetes [5]. The dose of bitter melon in that study was 2 g of bitter melon pulp per Kg of body weight, which was similar to the dose applied in the present study. In a cross-over study, Welihinda and colleagues also found a significant reduction in postprandial glucose AUC ($P<0.01$) after the intake of 100 ml of bitter melon juice compared with the control condition, among 18 newly diagnosed type 2 diabetic patients [6].

To date, the underlying mechanisms of the glucose-lowering effect of bitter melon have not been fully explained. Animal model studies have shown that bitter melon extract inhibited the glucose uptake in the small intestine by suppressing ATP-required glucose transport [2], which might be responsible for the lower postprandial glucose levels after bitter melon in our study. Another study revealed that bitter melon extract decreased hepatic glucose production by inhibiting gluconeogenesis [7], which lowered the postprandial glucose by limiting endogenous glucose release. Additionally, bitter melon can increase the peripheral glucose uptake via the activation of the adenosine monophosphate-activated protein kinase (AMPK) pathway [8], a common pathway through which exercise decreases blood glucose [9]. In summary, the intake of bitter melon could influence the postprandial glucose through multiple mechanisms. Further study using isotope glucose tracer is needed to identify the primary mechanism of the glucose-lowering effect in human participants.

In this study, the overall postprandial insulin responses were not significantly different between the two treatment groups. In a previous study, Lim et al. showed that a single dose of bitter melon extract (100 mg of extract/Kg of body weight) that was consumed immediately prior to a standardized meal significantly increased insulin levels at 15 minutes in patients with type 2 diabetes [10]. An in vitro study revealed that the aqueous extract of bitter melon stimulated the release of insulin from beta cells by affecting the membrane functions to release the stored insulin [11]. It is possible that bitter melon intake can only stimulate insulin release in diabetics and has little effect in non-diabetics. Clinical and basic science studies are needed to verify the insulin-stimulating activity of bitter melon among different populations.

We did not find a significant improvement in insulin sensitivity in the bitter melon group, as compared with the control group. This finding was expected because the improvement in insulin sensitivity has only be observed in chronic feeding study [4, 12]. We hypothesize that the single dose of bitter melon intake was not sufficient to induce a noticeable increase in insulin sensitivity.

The major strength of our study is the randomized, placebo-controlled design. Our study has limitations. We only measured postprandial glucose and insulin levels, making it difficult to explain the primary mechanism of the observed glucose-lowering effect. An isotope glucose tracer study would be helpful to depict the influence of bitter melon on postprandial glucose metabolism. Secondly, we only monitored glucose and insulin levels for 2 hours. A study has suggested that the glucose-lowering effect of bitter melon may last up to 3.5 hours in rat models [13]. The duration of this effect in human participants requires further investigation.

CONCLUSION

In conclusion, the single-dose intake of bitter melon juice significantly decreased 2-h glucose among sedentary, abdominally obese persons. Bitter melon juice appears to be a promising functional food to manage hyperglycemia for people who are at elevated risk of developing diabetes.

List of Abbreviations: AMPK, adenosine monophosphate-activated protein kinase; ASU, Arizona State University; iAUC, incremental area under the curve; OGTT, oral glucose tolerance test

Author's Contribution: C.L. conceived of the idea. T.M. and C.L. designed the study and obtained research fund. T.M. recruited participants and completed data collection. T.M. and C.L. performed data analysis. T.M. and C.L. wrote the manuscript. All authors read and approved the final version of the manuscript.

Competing Interests: There are no conflicts of interest to declare.

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