

Applied nutritional investigation

# Effects of a nutritional supplement containing *Salacia oblonga* extract and insulinogenic amino acids on postprandial glycemia, insulinemia, and breath hydrogen responses in healthy adults

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## Abstract

**Objective:** This study evaluated the postprandial glycemic, insulinemic, and breath hydrogen responses to a liquid nutritional product containing *Salacia oblonga* extract, an herbal  $\alpha$ -glucosidase inhibitor, and two insulinogenic amino acids.

**Methods:** In a randomized, double-masked, crossover design, 43 healthy subjects were fed the following meals on separate days after overnight fasting: control (C; 480 mL of a study beverage containing 82 g of carbohydrate, 20 g of protein, and 14 g of fat), control plus 3.5 g each of phenylalanine and leucine (AA), control plus 1000 mg of *S. oblonga* extract (S), and control plus S and AA (SAA). Postprandially, fingerstick capillary plasma glucose and venous serum insulin levels were measured for 180 min, and breath hydrogen excretion was measured for 480 min.

**Results:** The baseline-adjusted peak glucose response was not different across meals. However, changes in plasma glucose areas under the curve (0 to 120 min and 0 to 180 min, respectively) compared with C were  $-9\%$  and  $-11\%$  for AA ( $P > 0.05$  each),  $-27\%$  and  $-24\%$  for S ( $P = 0.035$  and  $0.137$ ), and  $-27\%$  and  $-29\%$  for SAA ( $P < 0.05$  each). Changes in insulin areas under the curve were  $+5\%$  and  $+5\%$  for AA ( $P > 0.05$  each),  $-35\%$  and  $-36\%$  for S ( $P < 0.001$  each), and  $-6\%$  and  $-7\%$  for SAA ( $P > 0.05$  each). Breath hydrogen excretion was  $60\%$  greater ( $P < 0.001$ ) in the S-containing meals than in the C- and AA-containing meals and was associated with mild flatulence.

**Conclusions:** *Salacia oblonga* extract is a promising nutraceutical ingredient that decreased glycemia in this study. Supplementation with amino acids had no significant additional effect on glycemia. © 2005 Elsevier Inc. All rights reserved.

## Keywords:

*Salacia oblonga*;  $\alpha$  glucosidase inhibitor; Amino acids; Glycemia

## Introduction

Type 2 diabetes mellitus (DM) has profound effects on personal health, quality of life, and economics. Between 1995 and 2025, the number of people with diabetes worldwide is projected to increase by  $122\%$  [1]. Research into this area continues because efforts at prevention are generally

unsuccessful, no cure is available, and current therapies merely delay the progression of DM at best. In addition, many current therapies to control glycemia have harmful side effects, such as hypoglycemia and liver damage. Therefore, development of novel strategies to decrease glycemic response to meals will be beneficial in the therapy of DM.

Food ingredients that delay or block absorption of carbohydrate can attenuate the rapid increase in plasma glucose that follows consumption of a carbohydrate-containing meal. In this way, an herbal extract of the plant genus *Salacia* holds promise for therapy of DM. *Salacia oblonga* is a perennial herb grown in some areas of India and Sri

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Lanka. For at least 4000 y, *Salacia* plants have been used in the traditional Ayurvedic system of medicine to manage several common ailments, including DM [2,3]. Yoshikawa et al. [4] first isolated and identified one active component of the root and concluded that its mode of action is inhibition of  $\alpha$ -glucosidase enzymes, similar to the antidiabetic drug acarbose. Animal studies have demonstrated that the extract, which contains a thio sugar, decreases glycemia after consumption of starch-containing meals [3,4]. A recent randomized, double-masked, crossover study of *S. oblonga* extract in humans tested the glycemic, insulinemic, and breath hydrogen responses to 0 (control), 500, 700, and 1000 mg of *S. oblonga* extract in a maltodextrin-based beverage [5]. The 1000-mg dose resulted in the lowest postprandial glycemia and insulinemia due at least in part to carbohydrate malabsorption, as demonstrated by linear increases in breath hydrogen excretion at every dose of *S. oblonga* extract and subjective reports of greater flatulence and distention. Aside from the effects of acute administration, Kowsalya et al. [2] reported that 2 mo of constant administration of a root bark preparation of *S. prinoidea* to human subjects with DM significantly decreased fasting blood glucose, serum total cholesterol, and triacylglycerols and increased high-density lipoprotein compared with control. From work conducted by Heacock et al [5], we chose to test the 1000-mg dose of *S. oblonga* extract.

Insulin secretagogues are another method of controlling postprandial glycemia. Several researchers have reported increases in insulin secretion after coadministration of carbohydrate with protein or protein hydrolysates or free amino acids compared with carbohydrate alone [6–12]. Van Loon et al. [13] found that consumption of a beverage containing  $0.8 \text{ g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$  of carbohydrate and  $0.4 \text{ g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$  of an amino acid and protein hydrolysate mixture resulted in an 88% higher plasma insulin response over 5 h and a significantly lower glucose response when compared with a response to carbohydrate alone. Ingestion of several individual amino acids, including leucine, phenylalanine, arginine, glycine, and ornithine, have been implicated in the protein-mediated stimulation of insulin secretion and/or attenuation of postprandial hyperglycemia [14–21]. However, plasma levels of phenylalanine and leucine showed the strongest correlations with stimulation of insulin secretion [17]. In one study, a drink containing a combination of phenylalanine, leucine, wheat protein hydrolysate, and carbohydrate was found to strongly promote insulin secretion without significant side effects [14]. In this study, a subject who weighed 70 kg would have received a 245-mL solution containing 3.5 g of phenylalanine, 3.5 g of leucine, 7 g of wheat hydrolysate, and 28 g of carbohydrate four times over a 90-min period (totals of 14 g of phenylalanine, 14 g of leucine, 28 g of wheat hydrolysate, and 112 g of carbohydrate). We chose a smaller dose (approximately 3.5 g each) of additional phenylalanine and leucine because the product to which the *S. oblonga* extract and amino acids were added is a medical food that was designed to assist in the dietary

management of DM. Thus, there were concerns regarding the limitation of stress on renal function in patients with DM and for product palatability.

The objectives of this study were three-fold: 1) to determine the glucose and insulin responses of healthy adults without DM to test meals containing *S. oblonga* extract and/or phenylalanine and leucine; 2) to ascertain the degree to which the carbohydrate from the test meals was malabsorbed versus simply delayed in its absorption; and 3) to quantify the extent of nausea, cramping, distention, and flatulence experienced by healthy adults after the test meals.

## Materials and methods

### Subjects

A power analysis determined that 36 subjects (nine in each treatment sequence) would provide 85% power to detect a difference between a product (such as the control) with a mean of 3.012 mmol/L and three other products with the same mean of 2.560 mmol/L (15% difference) for the primary variable, i.e., change from baseline for peak glucose concentration, by using a single-group repeated measures analysis of variance with a 0.05 significance level (nQuery Advisor 4.0) [22]. Fifty-one subjects (22 men and 29 women) from the community of the The Ohio State University (Columbus, OH, USA) were eligible and randomized, and 43 subjects (20 men and 23 women) completed the protocol. Reasons for attrition included intolerance to the pre-visit standard meal, discomfort during blood drawing, antibiotic therapy, and scheduling conflicts. The 43 subjects who completed the study had the following characteristics: mean age of  $23.5 \pm 0.6$  y, mean weight of  $70.8 \pm 1.9$  kg, mean body mass index of  $23.9 \pm 0.4 \text{ kg/m}^2$ , and mean fasting plasma glucose level of  $4.8 \pm 0.1$  mmol/L. Ethnic makeup of the sample was 29 Caucasians (67%), 7 Asians or Pacific Islanders (16%), 6 African Americans (14%), and 1 Latino (2%). All subjects were healthy, free from infectious, metabolic, and gastrointestinal diseases, and were not taking medications or dietary supplements at doses that are known to affect glycemia or gastric motility. In addition, subjects did not use antibiotics for 3 wk before or during the study. The study protocol was approved by the Western Institutional Review Board (Olympia, WA, USA), and all subjects provided informed consent.

### Feeding protocol

Subjects prepared for each meal glucose tolerance test by consuming at least 150 g of carbohydrate for each of 3 d before the study visit (verified by self-recorded, 3-d food records), abstaining from smoking and exercise the day before the visit, and by consuming only a low-residue standard meal between 4:00 and 9:00 PM on the evening before the study visit. The standard meal consisted of 240 mL of

Table 1  
Nutrient composition of study beverages

	C	AA	S	SAA
Portion fed (mL)	480	480	480	480
Energy (kcal)	534	562	534	562
Carbohydrate (g)	82	82	82	82
Maltodextrin (g)	50	50	50	50
Fructose (g)	18.9	18.9	18.9	18.9
Maltitol (g)	16.4	16.4	16.4	16.4
FOS (g)	3.3	3.3	3.3	3.3
Soy fiber (g)	2.5	2.5	2.5	2.5
Protein (g)	20	27	20	27
Caseinates (g)	16	16	16	16
Soy (g)	4	4	4	4
Fat (g)	14	14	14	14
High-oleic safflower oil (g)	11.9	11.9	11.9	11.9
Canola oil (g)	1.4	1.4	1.4	1.4
Soy lecithin (g)	0.7	0.7	0.7	0.7
<i>Salacia oblonga</i> extract (mg)			1000	1000
Additional phenylalanine (g)		3.5		3.5
Additional leucine (g)		3.5		3.5

AA, amino acids phenylalanine and leucine; C, control; FOS, fructo-oligosaccharide; S, *Salacia oblonga* extract; SAA, *S. oblonga* extract plus amino acids

Ensure Plus liquid product and a variable quantity of Ensure Nutrition and Energy Bars (Ross Products Division, Columbus, OH, USA), calculated such that the meal met one-third of each subject's daily caloric needs, based on the Harris-Benedict equation [23]. Consumption of water during visit preparation was encouraged. With a washout period of 3 to 14 d between visits, subjects underwent four meal glucose tolerance tests in random order: control (C), control plus amino acids (AA), control plus *S. oblonga* extract (S), and control plus *S. oblonga* extract and amino acids (SAA). Table 1 lists the nutrient composition of the study products. Phenylalanine and leucine were also components of the protein matrix of the control formulation, so 3.5 g of each amino acid was included with approximately 1.0 g of phenylalanine and 1.8 g of leucine per serving.

Subjects consumed the entire study product within 10 min, and the time the subject began consuming the study product was considered time 0 or baseline for subsequent measurements. During the first 3 h of the meal glucose tolerance test, subjects were limited to 240 mL of water, but consumed water ad libitum for the remainder of the treatment. At 4 h postprandial, subjects were permitted to consume 0, 240, or 480 mL of Ensure Plus liquid to alleviate hunger during the prolonged fast. Previous studies of similar low-residue enteral formulas have shown negligible hydrogen production [24].

#### Data collection and analysis

##### Plasma glucose.

Plasma glucose was collected at 0 (baseline) and 15, 30, 45, 60, 90, 120, 150, and 180 min after administration of the

study product. Subjects provided fingerstick capillary blood samples for measurement of plasma glucose. Samples were analyzed on site with an AccuChek Advantage Blood Glucose Monitoring System (Roche Diagnostics, Indianapolis, IN, USA). The AccuChek monitor measures glucose concentration of whole blood by bioamperometry but is calibrated to report plasma-like values [25]. Thus, glucose concentrations are reported as plasma glucose levels, although they were measured in whole blood. A previous study showed that plasma glucose measured by AccuChek correlates well with measurements by the YSI 2300 Stat Plus glucose analyzer (YSI Incorporated, Yellow Springs, OH, USA), a standard laboratory glucose analyzer [26].

##### Serum insulin.

Serum insulin was collected at 0 (baseline) and 15, 30, 45, 60, 90, 120, 150, and 180 min postprandially and measured from venous blood. A registered nurse obtained all venous blood samples from an indwelling catheter that was inserted into the antecubital vein. Blood was allowed to clot in serum separator tubes at room temperature and then centrifuged at 1168g for 15 min (Clay Adams Compact II centrifuge, Becton Dickinson Scientific, Franklin Lakes, NJ, USA). Each insulin sample was analyzed by radioimmunoassay (Laboratory Corporation of America, Dublin, OH, USA).

##### Breath gas analysis.

Breath hydrogen responses were monitored hourly for 480 min postprandially, with the last five samples collected off-site. Subjects were instructed to use an alveolar air sampling device (QuinTron Instrument Company, Milwaukee, WI, USA), and they collected their own samples in approximately 15-mL evacuated tubes (Becton Dickinson). Samples were extracted from the tubes by using the SamplXtractor device (QuinTron Instrument Company) and analyzed for CO<sub>2</sub>, CH<sub>4</sub>, and H<sub>2</sub> content by gas chromatography using the Microlyzer Model SC (QuinTron Instrument Company). Observed H<sub>2</sub> values were corrected for atmospheric contamination of alveolar air by normalization of observed CO<sub>2</sub> to 40 mmHg (5.3 kPa), the partial pressure of CO<sub>2</sub> in alveolar air [27]. An increase in breath hydrogen concentration of more than 10 ppm over basal nadir value (lowest measurement at baseline, 60 min, or 120 min) led to classification of positive breath hydrogen test, indicative of carbohydrate malabsorption [28].

##### Gastrointestinal tolerance.

For 24 and 48 h after each study visit, subjects recorded the frequency and intensity of any nausea, cramping, distention, or flatulence they experienced by using a 100-mm visual scale that ranged from 0 (usual or absent) to 100 (severe). This scale has been used to measure subjective gastrointestinal tolerance in previous studies [26].

Table 2

Postprandial plasma glucose, serum insulin, and breath hydrogen responses (peak and AUC values) to a medical food containing *Salacia oblonga* extract and insulinogenic amino acids\*

	Treatment			
	C	AA	S	SAA
Peak glucose, baseline-adjusted (mmol/L)	2.76 ± 0.21 <sup>a</sup>	2.71 ± 0.20 <sup>a</sup>	2.35 ± 0.17 <sup>a</sup>	2.50 ± 0.17 <sup>a</sup>
Plasma glucose AUC, 0–120 min (mmol · min <sup>-1</sup> · L <sup>-1</sup> )	160.4 ± 16.8 <sup>a</sup>	146.3 ± 9.8 <sup>a,b</sup>	117.4 ± 10.9 <sup>b</sup>	117.3 ± 10.6 <sup>b</sup>
Plasma glucose AUC, 0–180 min (mmol · min <sup>-1</sup> · L <sup>-1</sup> )	201.9 ± 21.2 <sup>a</sup>	179.1 ± 12.7 <sup>a,b</sup>	152.7 ± 12.5 <sup>a,b</sup>	142.8 ± 12.6 <sup>b</sup>
Peak insulin, baseline-adjusted (pmol/L)	341.1 ± 31.0 <sup>a</sup>	357.4 ± 29.0 <sup>a</sup>	265.7 ± 28.2 <sup>b</sup>	347.4 ± 33.7 <sup>a</sup>
Serum insulin AUC, 0–120 min (pmol · min <sup>-1</sup> · L <sup>-1</sup> )	18 328 ± 1692 <sup>a</sup>	19 181 ± 1585 <sup>a</sup>	11 959 ± 1407 <sup>b</sup>	17 161 ± 1617 <sup>a</sup>
Serum insulin AUC, 0–180 min (pmol · min <sup>-1</sup> · L <sup>-1</sup> )	23 020 ± 2148 <sup>a</sup>	24 197 ± 1959 <sup>a</sup>	14 726 ± 1644 <sup>b</sup>	21 493 ± 1941 <sup>a</sup>
Breath hydrogen AUC, 0–480 min (ppm/h)	154.8 ± 15.1 <sup>a</sup>	146.0 ± 15.5 <sup>a</sup>	248.3 ± 23.4 <sup>b</sup>	247.8 ± 30.3 <sup>b</sup>

AA, amino acids phenylalanine and leucine; AUC, area under the curve; C, control; S, *Salacia oblonga* extract; SAA, *S. oblonga* extract plus amino acids

\* Values represent mean ± standard error of the mean. Analysis of variance was run on square-root transformed data for each variable to stabilize variance (plasma glucose,  $n = 43$ ; serum insulin,  $n = 43$ ; breath hydrogen,  $n = 31$ ). Values within a row not sharing the same letter are significantly different ( $P < 0.05$ ).

### Calculation of area under the curve.

Positive incremental area under the curve (AUC) was calculated geometrically, accounting only for area above baseline [29], for 120- and 180-min glucose and insulin concentrations, and for 480-min breath hydrogen concentrations.

### Statistical analysis.

Outcomes included change from baseline for peak glucose and insulin, AUC for glucose and insulin over 120 and 180 min after administration of treatments, glucose and insulin concentrations at individual time points, AUC for breath hydrogen over 480 min after administration of treatments, and tolerance of the study products. Classification-evaluable and intent-to-treat analyses were run for all data; however, only the classification-evaluable analyses are considered in this report because results were similar. Shapiro-Wilk tests for normality indicated non-normal distribution of glucose, insulin, breath hydrogen, and gastrointestinal tolerance data. Square root transformations improved normality of the data for glucose at individual time points, glucose and insulin AUC, change from baseline for peak glucose and insulin, and breath hydrogen. Log<sub>10</sub> transformations improved normality of insulin data at individual time points. For gastrointestinal tolerance data, rank transformations were employed. Repeated measures analysis of variance was performed on transformed data by using Tukey's  $P$ -value adjustments for pairwise comparisons among treatments. No significant interactions were observed between *S. oblonga* extract and amino acids, so statistical tests examined the significance of main effects of treatments. Non-transformed data are reported as the mean ± standard error and  $P < 0.05$  was considered statistically significant.

## Results

### Plasma glucose

There were no significant differences in baseline plasma glucose across treatments. Analysis of variance indicated

that neither *S. oblonga* extract nor the amino acids had a significant effect on change from baseline for peak plasma glucose (Table 2). However, for the change from baseline at the 45-, 60-, 90-, and 120-min time points, *S. oblonga* extract elicited a lower glycemic response than did treatments without *S. oblonga* extract (Figure 1). In addition, the 0- to 120-min AUCs were decreased by 27% for the S and SAA treatments compared with the control ( $P = 0.035$  and  $P = 0.046$ , respectively; Table 2). The trend was similar for the 0- to 180-min AUC data, such that the SAA meal decreased the glucose AUC by 29% compared with control ( $P = 0.039$ ). However, the 24% decrease observed with S versus C did not reach significance ( $P = 0.137$ ). The presence of AA alone decreased the 0- to 120-min and 0- to 180-min glucose AUC values by 9% to 11%, respectively, but the decreases were not significant ( $P = 0.998$  and  $P =$

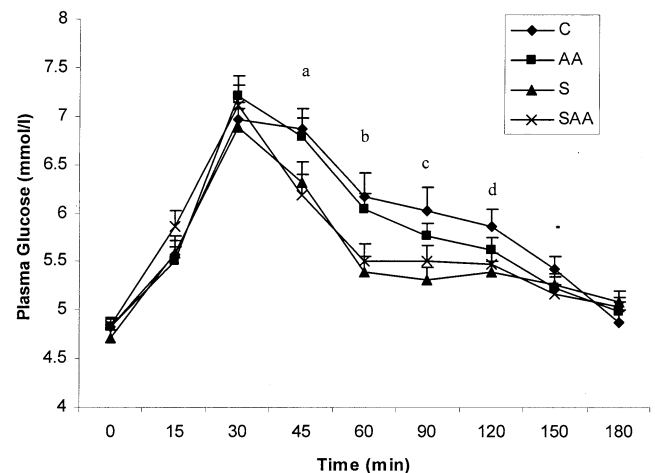


Fig. 1. Effects of S and AA treatments on plasma glucose concentrations over a 3-h meal glucose tolerance test. Values represent mean ± standard error of the mean ( $n = 38$ –44). Analysis of variance was run on square-root transformed data, but untransformed data are presented. <sup>a</sup>C > S ( $P = 0.006$ ), C > SAA ( $P < 0.001$ ), AA > SAA ( $P = 0.004$ ); <sup>b</sup>C > S ( $P < 0.001$ ), C > SAA ( $P < 0.001$ ), AA > S ( $P = 0.001$ ), AA > SAA ( $P = 0.002$ ); <sup>c</sup>C > S ( $P < 0.001$ ), C > SAA ( $P = 0.001$ ), AA > S ( $P = 0.015$ ); <sup>d</sup>C > S ( $P = 0.003$ ), C > SAA ( $P = 0.019$ ). AA, amino acids; C, control; S, *Salacia oblonga* extract; SAA, *S. oblonga* extract plus amino acids.



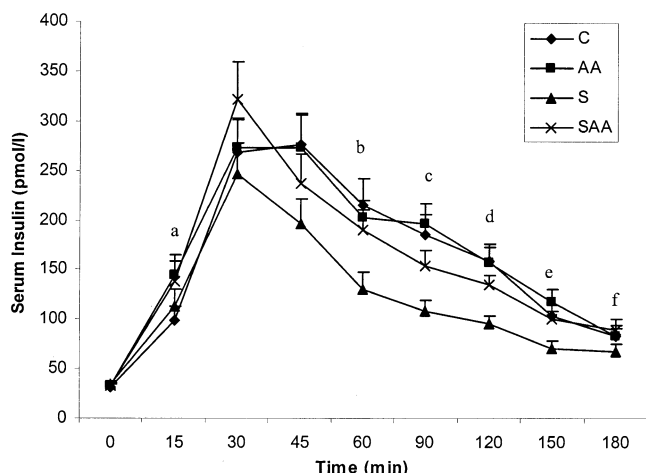


Fig. 2. Effects of S and AA treatments on serum insulin concentrations over a 3-h meal glucose tolerance test. Values represent mean  $\pm$  standard error of the mean ( $n = 39$ – $44$ ). Analysis of variance was run on  $\log_{10}$ -transformed data, but untransformed data are presented. <sup>a</sup>AA > C ( $P = 0.027$ ); <sup>b</sup>C > S ( $P = 0.006$ ), AA > S ( $P = 0.007$ ); <sup>c</sup>C > S ( $P < 0.001$ ), AA > S ( $P < 0.001$ ), SAA > S ( $P = 0.044$ ); <sup>d</sup>C > S ( $P = 0.001$ ), AA > S ( $P = 0.001$ ), SAA > S ( $P = 0.017$ ); <sup>e</sup>C > S ( $P = 0.001$ ), AA > S ( $P < 0.001$ ), SAA > S ( $P = 0.001$ ); <sup>f</sup>AA > S ( $P = 0.029$ ). AA, amino acids; C, control; S, *Salacinol oblonga* extract; SAA, *S. oblonga* extract plus amino acids.

0.996, respectively). Thus, the AA treatment had only a small effect on glycemia and a mildly additive effect when included with S that was observed in the 0- to 180-min glucose AUC but not in the 0- to 120-min AUC.

### Serum insulin

There were no significant differences in serum insulin across treatments at baseline. Analysis of variance indicated that S resulted in significantly lower baseline-adjusted peak serum insulin levels compared with C, AA, and SAA ( $P = 0.034$ ,  $0.004$ , and  $0.029$ , respectively). At 15, 60, 90, 120, 150, and 180 min, the treatments containing amino acids resulted in higher serum insulin concentrations, whereas treatments containing *S. oblonga* extract tended to decrease serum insulin (Figure 2). As presented in Table 2, S resulted in significantly lower positive incremental AUC at 120 min than did C, AA, and SAA ( $P < 0.001$ ,  $P < 0.001$ , and  $P = 0.003$ , respectively). For 180-min serum insulin AUC data, these trends were identical. The amino acids failed to increase the serum insulin AUC above the level observed with the control product, but they did blunt the *S. oblonga* extract-induced decrease in the insulin response.

### Carbohydrate malabsorption

There were no significant differences in breath hydrogen at baseline across treatments. Classification of positive or negative breath hydrogen test findings did not differentiate between treatments because all treatments resulted in an increase in

breath hydrogen excretion of more than 10 ppm above baseline in the vast majority of subjects. Analysis of variance indicated that breath hydrogen was not affected by amino acids but was significantly increased by *S. oblonga* extract (Table 2). Compared with C and AA, S and SAA resulted in significantly higher 480-min breath hydrogen AUC values ( $P < 0.001$  for each comparison). Mean ratings for the frequency of flatulence (100 mm is the maximum) were generally higher for the S-containing meals ( $22.2 \pm 4.2$  mm for S and  $26.6 \pm 4.6$  mm for SAA) than for the C ( $13.4 \pm 3.4$  mm) and AA ( $14.4 \pm 3.6$  mm) meals. The pairwise comparisons for the rank-transformed flatulence frequency data were C versus S ( $P = 0.066$ ), C versus AA ( $P = 0.916$ ), C versus SAA ( $P = 0.0580$ ), S versus AA ( $P = 0.011$ ), AA versus SAA ( $P = 0.010$ ), and S versus SAA ( $P > 0.999$ ). For other factors (intensity of flatulence and intensity and frequency of nausea, cramping, and distention), there were no significant differences across treatments.

### Discussion

In vitro studies have shown that *S. oblonga* extract is an  $\alpha$ -glucosidase inhibitor [30]. The approximately 25% decrease in postprandial glycemia, coupled with the increase in breath hydrogen (an indicator of carbohydrate maldigestion) and the increased flatulence symptoms observed in the present study, supports the  $\alpha$ -glucosidase inhibitory activity of *S. oblonga* extract. The peak glucose response was unchanged in this study. However, the postprandial glucose AUC was significantly decreased for the treatments containing *S. oblonga* extract. Insulin AUC demonstrated a statistically significant decrease in postprandial insulinemia for the S treatment compared with all other treatments.

It is interesting that *S. oblonga* extract decreased the 0- to 120-min and the 0- to 180-min plasma glucose AUC values but did not affect baseline-adjusted peak glucose level. A possible explanation is that the concentration of maltase increases longitudinally along the length of the small intestine, such that most maltase activity is found in the ileum [31–33]. Perhaps the delay in an observable difference in glycemia (and insulinemia) between treatments with and without the extract was due to the time required for the digestive contents to reach the jejunum and ileum. Future studies are planned to evaluate whether prefeeding of the *S. oblonga* extract relative to the carbohydrate challenge can decrease the peak postprandial glucose response.

Compared with the control formulation, the amino acids did not significantly increase insulin secretion; and although there was a trend toward lowered glycemia with amino acids, the decrease was not significant. However, it appears that the amino acids blunted the *S. oblonga* extract-induced decrease in serum insulin when the SAA treatment is compared with the S treatment. Perhaps a larger dose of amino acids would increase insulin enough to further lower glycemia beyond the decrease induced by *S. oblonga* extract. For our protocol, the palatability of large doses of individual

amino acids was a concern, so the doses of amino acids were about 75% less than what was observed to be effective in studies by van Loon et al. [14,17] for eliciting an increase in insulin secretion accompanied by a decrease in plasma glucose. Also, the duration of the testing period may have prevented observation of a significantly different glycemic response to amino acids [9,13,34]. Perhaps if we had tested a second meal effect, we would have observed a further decrease in glycemia to accompany the increase in insulin secretion caused by the SAA treatment compared with S alone. We did not test the Staub-Traugott (second meal) effect, wherein the effect of protein on insulinemia and glycemia is more substantial at a second meal, approximately 240 min after the first [9].

Amino acid–stimulated insulin secretion is most effective in patients with uncontrolled DM. In healthy subjects, ingestion of protein with carbohydrate, although it does increase insulin AUC slightly, does not seem to affect postprandial glycemia significantly [17,18,35], whereas serum insulin increases three-fold and plasma glucose response is significantly decreased in subjects with DM [9,36,37]. This may be due to differential secretion of insulin or gut hormones (e.g., cholecystokinin and gastric inhibitory polypeptide) in response to insulinogenic amino acids between populations with and without DM [35,37,38]. Had our subject sample consisted of volunteers with DM, we might have observed a greater insulin response to the amino acids, such that postprandial glycemia would have been further decreased. However, this supposition remains to be tested in the population with DM.

The next step is to test a product containing *S. oblonga* extract in the population with DM. To our knowledge, there are no studies of the effect of *S. oblonga* extract on postprandial glycemia in patients with DM and only two studies that have evaluated the effects of longer-term therapy of other plants from the *Salacia* genus (*S. prinooides*, *S. reticulata*) in patients with DM [2,39]. Future studies are needed to determine its possible benefits in the decrease of cardiovascular disease risk, as has been recently suggested for the prescription  $\alpha$ -glucosidase inhibitor acarbose [40]. Some research has suggested that another *Salacia* species (*S. reticulata*) possesses lipase inhibitory and lipolytic activities in rats [30]. It may be interesting, therefore, to examine the effects of extracts from *S. oblonga* or from other *Salacia* species on weight control and blood lipid profiles in addition to glucose management in humans.

## Summary

Our research supports an in vivo  $\alpha$ -glucosidase inhibitory effect of *S. oblonga* extract that was fed as a component of nutritional beverage. Future studies of this promising nutraceutical ingredient are warranted in people with DM. In light of the lack of further decrease in glycemia by addition of the AA in this study, doses larger than those

used in our study may be necessary to elicit an effect on postprandial blood glucose.

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