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Oral administration of palatinose vs sucrose improves hyperglycemia in normal C57BL/6J mice

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ABSTRACT

Palatinose is a sucrose analog with a slower digestion rate than that of sucrose. For this reason, palatinose shows better effects on hepatic lipogenesis and cholesterol homeostasis compared with sucrose. We hypothesized that supplementation with palatinose instead of sucrose improves postprandial hyperglycemia and hyperinsulinemia in mice. Herein, we compared the digestion rates in vitro and observed physiological changes in vivo between sucrose- and palatinose-containing diets given to mice. Palatinose was hydrolyzed only by enzymes of the small intestine and was digested more slowly compared with sucrose in vitro. In mice, a diet containing palatinose resulted in significantly lower body weight gain and food efficiency rate values than those given a diet with sucrose. In this study, changes in serum biochemistry; hepatic fatty acid synthesis; cholesterol homeostasis; glucogenic, proinflammatory cytokines; and oxidative stress-related genes and proteins in the palatinose- and sucrose-fed mice were measured. Compared with the mice fed the sucrose diet, the palatinose diet resulted in lower serum glucose, insulin, and total cholesterol levels, as well as lower expression of several lipogenesis-related genes and proteins. Histological analysis of hepatic cells of palatinose-fed mice showed normal morphology. In conclusion, palatinose intake results in lower hepatic lipogenesis and better cholesterol homeostasis than the effects from sucrose.

Abbreviations: ACC, acetyl-CoA carboxylase; ALT, alanine aminotransferase; AST, serum aspartate aminotransferase; AUC, area under the curve; CYP7A1, cholesterol 7 alpha-hydroxylase; FAS, fatty acid synthase; FER, food efficiency ratio; GLUT2, glucose transport 2; H&E, hematoxylin and eosin; HDL-C, high-density lipoprotein cholesterol; HMGCR, HMG-CoA reductase; OGTT, oral glucose tolerance test; PPARγ, peroxisome proliferator-activated receptor-gamma; PBS-T, phosphate-buffered saline with 0.05% TWEEN 20; qPCR, quantitative polymerase chain reaction (qPCR); SOD1, superoxide dismutase 1; SREBP-1C, sterol regulatory element-binding protein-1C; TCHO, total cholesterol; TG, triglyceride; TNF-α, tumor necrosis factor-alpha.

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1. Introduction

Lifestyle-related diseases, such as obesity, hyperlipidemia, diabetes, hypertension, and atherosclerosis, are considered to be associated with the intake of some nutrients [1]. Among these, sucrose consumption increases the risk factors for developing both obesity and its related chronic diseases [2]. Compared with a similar starch diet, a high-sucrose diet fed to rats induced a time-dependent, non–insulin-dependent diabetes syndrome characterized by insulin resistance [2]. In addition, rats fed a sucrose-rich diet showed glucose intolerance, hyperinsulinemia, and so on are markers of insulin resistance [3, 4]. Therefore, alternative sweeteners need to be developed to lower the risk factors for chronic disease in humans.

Palatinose, a sucrose analog composed of α-1-6–linked fructose and glucose, tastes and appears similar to sucrose and is used as a sucrose substitute in most sweet foods [5]. Palatinose is regarded as a healthier sugar than sucrose for several reasons. Most importantly, it is completely hydrolyzed and absorbed in the small intestine but at a much slower rate than that of sucrose [5]. It therefore causes an attenuated blood glucose and insulin response [6]. Oral administration of palatinose resulted in significant improvements in diet-induced metabolic abnormalities, which would help to prevent obesity and its complications [7, 8].

Many studies have clearly indicated that diets rich in sucrose or fructose contribute to the development of obesity and insulin resistance [9]. The consequence of lasting hyperglycemia and hyperinsulinemia is type 2 diabetes. This insulin-related disorder is attributed to many factors, including oxidative stress and inflammation, and intricately connects many diseases [10]. Moreover, type 2 diabetes stimulates de novo lipogenesis, inhibits glucose uptake, and increases triglyceride (TG) production, which alter the lipid metabolic parameters and lead to an increase in the levels of atherogenic cholesterol in blood [11].

In this study, we hypothesized that oral supplementation of palatinose instead of sucrose improves postprandial hyperglycemia and hyperinsulinemia in normal C57BL/6J mice. The objective of this study is to compare hyperglycemia-related index between sucrose and palatinose in vitro and in vivo. We measured digestion rates because slow digestion attenuated blood glucose and insulin response. We measured body weight, food efficiency rate, and biochemical changes in serum for comparing the effect of obesity. To compare the relationship between diets and diabetes, we investigated hepatic fatty acid synthesis; cholesterol homeostasis; and glucogenic, proinflammatory cytokine and oxidative stress-related genes and proteins. The hepatic expression levels of oxidative stress markers are superoxide dismutase 1 (SOD1) and tumor necrosis factor-alpha (TNF-α). We also measured the expression levels of several lipogenic and cholesterol homeostasis-related genes, namely, fatty acid synthase (FAS), peroxisome proliferator-activated receptor-gamma (PPARγ), sterol regulatory element-binding protein-1C (SREBP-1C), acetyl-CoA carboxylase (ACC), HMG-CoA reductase (HMGCR), and cholesterol 7 alpha-hydroxylase (CYP7A1) [12].

2. Methods and materials

2.1. Hydrolysis of palatinose by digestive enzymes in vitro

To measure the digestion of palatinose in vitro, we prepared gastric and small intestinal enzymes. The gastric enzyme was pepsin from the porcine gastric mucosa (Sigma-Aldrich Co, St Louis, MO, USA). In brief, 0.1 g of pepsin was suspended in 1 mL of saline, and the pH was adjusted to 2.0. The small intestinal enzyme solution, prepared from rat intestinal acetone powder, contained maltase, sucrase, isomaltase, and glucoamylase, with specific activities of 0.70, 0.34, 0.20, and 0.45 U/mL, respectively (Sigma-Aldrich Co). In brief, 0.1 g of rat intestinal acetone powder was suspended in 1 mL of saline, and the suspension was sonicated 12 times for 30 seconds at 4°C. Then, the solution was centrifuged at 10,000×*g* for 30 minutes at 4°C, and the resulting supernatant was used for the assay. The gastric and small intestinal enzymes were individually incubated with 1 mg/mL of substrate (sucrose or palatinose) for 3 hours at 37°C. The enzymatic reaction was terminated by heating the mixture at 99°C for 10 minutes, and the pH was adjusted to 7.0. The amount of glucose produced was measured with a Medi-Check glucose oxidase–based glucometer (Infopia Co, Anyang, South Korea).

2.2. Mice and diets

Male C57BL/6J mice (5 weeks old), purchased from Daehan Biolink Co (Seoul, South Korea), were housed in a specific pathogen-free room maintained at a constant temperature (24°C ± 1°C) and humidity (55%) on a clean rack with 12-hour cycles of light and dark. The mice were fed modified AIN-76A diets (Feed Lab Co, Hanam, South Korea); the ingredient compositions of the diets are shown in Table 1. The palatinose was provided from Mitsui Sugar Co Ltd (Tokyo, Japan). Water and each experimental pellet diet were supplied ad libitum. Mice are killed by cervical dislocation. All experimental procedures were approved by the Institutional

Table 1 – Ingredient composition of the mouse diets used in the study

Ingredients (g/kg diet)	Control [a]	Sucrose	Palatinose
Casein	200	200	200
Corn starch	650	0	0
Sucrose	0	650	0
Palatinose	0	0	650
Cellulose	50	50	50
Corn oil	50	50	50
Mineral mix	35	35	35
Vitamin mix	10	10	10
DL-Methionine	3	3	3
Choline bitartrate	2	2	2
Composition (kcal%)			
Protein	20.8	20.8	20.8
Carbohydrate	67.7	67.7	67.7
Fat	11.5	11.5	11.5

[a] Modified AIN-76A control diet.