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Short communications

Weight reducing effect and safety evaluation of rare sugar syrup by a randomized double-blind, parallel-group study in human

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ABSTRACT

Rare sugar syrup is a sweetener obtained from high-fructose corn syrup under slightly alkaline conditions, which promotes the formation of rare sugars. Here, the physiological impact and safety of rare sugar syrup in humans was investigated by a randomized double-blind parallel experiment. Thirty-four subjects with an average body mass index of 25.6 kg/m^2 were divided into two groups. Subjects consumed either a test drink containing rare sugar syrup or an isocaloric control drink containing high-fructose corn syrup on a daily basis for 12 weeks. Results showed significant decreases in body weight, body fat percentage and waist circumference in the rare sugar syrup group compared to the control. No adverse events with regard to hepatic and renal function or blood parameters were observed. Our study conclusively suggests, for the first time, that rare sugar syrup is a safe sweetener, and that continuous consumption of this syrup could help weight management.

1. Introduction

High-fructose corn syrup (HFCS) and high intensity sweeteners are used in a wide range of food and beverage products. The rise in these consumption, however, is reported to be associated with the growing risk of diabetes and obesity in the United States (Gross, Li, Ford, & Liu, 2004; Swithers, 2013). Because these issues relate to complex factors, such as appetite, excessively consumed amount, kinds of carbohydrate, and genetic or social background of consumer, it is needed to cautiously discuss and propose a solution to the social demand that is the development of better sweeteners smoothing these problems.

Recently, some interesting biological properties have been reported for rare sugars. 'The International Society of Rare Sugars' defined rare sugars as monosaccharides and their derivatives that are present in limited quantities in nature. For

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example, allulose (psicose) is a rare sugar that has been well-studied in terms of its efficacy, safety and production using microorganisms. Allulose has nutritional benefits such as prevention of diabetes (Chung, Oh, & Lee, 2012; Matsuo & Izumori, 2009) and improvement of lipid metabolism (Matsuo et al., 2001). In addition, the inclusion of around 4% allulose in HFCS suppresses abdominal fat accumulation caused by the long-term ingestion of HFCS (Yamada et al., 2010).

As a natural and economically-feasible method for obtaining syrup containing around 5% allulose, the quantity of which is sufficient to suppress fat accumulation, we reisomerized HFCS under mildly-basic conditions, similar to those used in food processing applications such as sugar refining. This method produces other monosaccharides, such as allose, sorbose and mannose, which have been reported to improve lipid and carbohydrate metabolism or immune function (Kimura et al., 2005; Toyota, Fukushi, Katoh, Orikasa, & Suzuki, 1989; Yamada et al., 2014).

The obtained syrup containing rare sugars, called rare sugar syrup (RSS), has 90% of the sweetness of sucrose, and with a richer and cleaner taste than HFCS. Accordingly, we reasoned that RSS might provide an alternative to HFCS, which may reduce the likelihood of obesity caused by the consumption of HFCS.

We previously tested the safety and efficacy of RSS for daily use as a sweetener in a series of feeding experiments using rats. Our study showed ingestion of RSS caused a reduction in body weight and abdominal fat with no detectable adverse effects (Iida et al., 2013; Matsuo et al., 2011). However, detailed information concerning the safety and efficacy of RSS for humans is being reported now for the first time. Based on our previous animal study, we conducted this experiment in humans to know more about an effective safe dose of rare sugar syrup, and to evaluate biomarkers during long-term consumption.

2. Materials and methods

2.1. *Subjects*

This study was approved by the ethics committee of Isogo Central Hospital (Kanagawa, Japan) in accordance with the spirit of the Declaration of Helsinki, and conducted under the supervision of the principle investigator. Informed consent was obtained from 34 volunteers (17 males and 17 females) with an average BMI score of 25.6 kg/m^2 (22–63 years old). A BMI score of more than 25 kg/m^2 is considered as obese as defined by the Japan Society for the Study of Obesity. Exclusion criteria included people with hepatic or renal dysfunction. Subjects participating in this study were randomly divided into two groups by the minimization method based on inspected medical centers, age, gender, BMI, body weight, body fat ratio and waist circumference. Other background details for each group are given in Table 1.

Table 1 – Background of the subjects.

	Control	RSS
Number of subjects	17	17
Male–female ratio	Male: 9, female: 8	Male: 8, female: 9
Age (years)	42.4 ± 2.6	41.7 ± 2.8
Weight (kg)	70.4 ± 2.5	70.2 ± 3.0
Height (cm)	165.8 ± 2.6	165.7 ± 2.5
BMI (kg/m^2)	25.6 ± 0.6	25.4 ± 0.6
Body fat ratio (%)	28.4 ± 1.7	28.2 ± 2.1
Waist circumference (cm)	83.9 ± 2.6	84.7 ± 2.7

Data are expressed as mean ± SEM.

2.2. *Experimental diets*

The compositions of RSS and HFCS were analyzed by high performance liquid chromatography with a MCI GEL CK 08EC column (8 i.d. × 300 mm; Mitsubishi Chemical Corporation) and refractive index detector. RSS was composed of 44.3% glucose, 31.9% fructose, 6.0% allulose and 17.8% other saccharides, in which 7.5% mannose and sorbose were detected as non-dividable peaks and 4.6% oligosaccharides were also detected. The oligosaccharides analyzed were primarily disaccharides (3.7%) including 0.7% maltose, 1.2% isomaltose, and 0.9% maltulose derived from oligosaccharides in HFCS (Osaki & Yoshino, 1982; Shiraishi, Kawakami, & Kusunoki, 1985). As a reference, we confirmed around 1% allose in RSS using other method. HFCS was composed of 41.8% glucose, 52.3% fructose and 5.9% oligosaccharides.

The energy exchange ratios of glucose and fructose are 4 kcal/g, and that of allulose is 0 kcal/g. Other saccharides for which the energy exchange ratios were not determined were calculated as 4 kcal/g based on the maximum calorie obtained for the carbohydrate. The test drink containing 30 g of RSS (114 kcal) and the control drink containing 28 g of HFCS (114 kcal) as dry solid base were then used as the experimental diets. Each experimental diet had the same calorific value and was prepared in the form of an identical 200 g jelly drink, with an indistinguishable flavor and color.

HFCS used as the sweetener for the control drink was purchased from Nihon Shokuhin Kako Co., Ltd. (Tokyo, Japan). RSS used for the test drink was made by Matsutani Chemical Industry, Co., Ltd. (Hyogo, Japan).

2.3. *Study design*

The experiment was based on a randomized double-blind, two-group parallel, placebo-controlled comparison study. The 20-week study period comprised 4 weeks for pre-treatment observation, 12 weeks for treatment, and 4 weeks for post-treatment observation. During the treatment phase the subjects consumed either a test drink or a control drink 30 minutes before breakfast on a daily basis. Subjects were instructed to make seven scheduled visits to the medical center for testing as follows: firstly at the beginning of the pre-treatment observation period and then during weeks 0, 2, 4, 8 and 12 of the treatment period, and finally at the end of the post-treatment observation period.

During each visit body weight, body fat ratio, waist circumference, hip circumference, systolic blood pressure and diastolic blood pressure were measured and blood and urine samples were collected. Each subject was interviewed by a doctor to investigate any subjective symptoms in body condition (e.g.,