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Nutrition Research 31 (2011) 836–841

Nutrition Research

www.nrjournal.com

Combination of erythritol and fructose increases gastrointestinal symptoms in healthy adults

Yeonsoo Kim[a,*], Sonhee C. Park[b], Bryan W. Wolf[c], Steven R. Hertzler[d]

[a]Louisiana Tech University, School of Human Ecology, Ruston, LA 71272, USA
[b]The Ohio State University, Department of Human Nutrition, Columbus, OH 43210, USA
[c]International Mission Board, Southern Baptist Convention, Vallenar, Chile
[d]Abbott Nutrition, Abbott Laboratories, Columbus, OH 43215, USA

Received 16 May 2011; revised 25 September 2011; accepted 29 September 2011

Abstract

Consumption of a large amount of dietary fructose induces gastrointestinal intolerance, and glucose has been known as an enhancer of fructose absorption. Erythritol is a nonglycemic sugar alcohol, and it has been suggested that erythritol is absorbed paracellularly. It was hypothesized that paracellular absorption of erythritol could also enhance paracellular absorption of fructose in healthy adults. This is one of the proposed pathways for how additional glucose enhances the absorption of fructose. Thirty-seven nondiabetic, healthy adults participated in a randomized, double-masked, controlled crossover study. After an overnight fast, participants consumed beverages containing either 50 g fructose and 50 g glucose, 50 g fructose and 33.3 g erythritol (an equimolar concentration of fructose), or 50 g fructose alone. Breath hydrogen response was determined for 8 hours postprandially. Gastrointestinal intolerance symptoms and the number and consistency of bowel movements were recorded for 24 hours postprandially. The breath hydrogen area under the curve (AUC) of the fructose and erythritol beverage was 2 times the AUC of the fructose beverage and 8.75 times the AUC of the fructose and glucose beverage ($P < .001$, respectively). Compared with fructose and glucose beverage and fructose alone, frequency of watery stools increased ($P < .05$) and gastrointestinal tolerance worsened ($P < .05$) when participants consumed fructose and erythritol. These data suggest that coingestion of equimolar concentrations of fructose and erythritol increased carbohydrate malabsorption.

Keywords: Fructose; Erythritol; Carbohydrate absorption; Breath hydrogen; Gastrointestinal symptoms; Flatus; Human study

Abbreviations: BMI, body mass index; GLUT, glucose transporter; AUC, area under the curve.

1. Introduction

Fructose absorption is known to be affected by other monosaccharides when ingested simultaneously [1-8]. Most of these studies reported that the simultaneous intake of fructose with an equimolar concentration of glucose increased fructose absorption dramatically, whereas fructose alone is poorly absorbed when consumed in large concentrations [1-4].

A potential problem associated with increased fructose intake is gastrointestinal intolerance [1,2,9-12]. When fructose is not absorbed in the small intestine, malabsorbed fructose is fermented by colonic bacteria, resulting in production of hydrogen, carbon dioxide, methane, and short-chain fatty acids. In addition, unabsorbed fructose causes gastrointestinal symptoms such as abdominal pain,

* Corresponding author. School of Human Ecology, Louisiana Tech University, PO Box 3167, Ruston, LA 71272, USA. Tel.: +1 318 257 3237; fax: +1 318 257 4014.
E-mail address: kim@latech.edu (Y. Kim).

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doi:10.1016/j.nutres.2011.09.025

bloating, and discomfort [9,11,13,14]. Moreover, unabsorbed fructose in the colon increases osmotic load, which draws fluid into the intestinal lumen leading to watery bowel movements [11].

Erythritol is a 4-carbon sugar alcohol [15]. Erythritol is naturally found in some fruits, mushrooms, and fermented foods, such as wine, sherry, and soy sauce [16]. Because of its almost noncaloric (0.84 kJ/g) and nonglycemic effect [15], erythritol has been recently used in chewing gum, confectionery, beverages, and sugar substitutes in Japan and the United States [17,18]. The use of erythritol has been growing in the development of healthier and tastier products.

More than 90% of ingested erythritol is absorbed from the human small intestine without any gastrointestinal intolerance symptoms [15]. It has been suggested that erythritol may be absorbed via paracellular route [19]. Paracellular diffusion is the major pathway of hydrophilic molecules and is regulated by tight junctions [20].

In animal and cell culture studies, fructose absorption appears to be coupled with glucose via an apical glucose transporter (GLUT) 2 pathway [6-8]. However, Shi et al [3] suggest that the facilitation of fructose absorption by glucose occurred via the paracellular route in humans. An intestinal perfusion study with a triple lumen tube in healthy adults demonstrated that the presence of free glucose enhanced fructose absorption by 19% via the paracellular pathway [3]. Glucose on the apical membrane of epithelial cells increases tight junction permeability via the condensation of the perijunctional cytoskeleton. The enhanced tight junction permeability increases local osmotic pressure in the lateral intercellular spaces and generates the osmotic force to drive paracellular flow, which may contribute to fructose absorption [21].

Although erythritol is being used in food applications in industries, little is known about the interaction of erythritol and other food components. Fructose is a natural monosaccharide of fruits and is commonly used as an additive in confectionery and soft drinks, possibly in combination with erythritol. Information on interaction between erythritol and fructose appears to be an important consideration when making recommendations for preventing potential gastrointestinal distress in healthy persons and people with irritable bowel syndrome.

Because erythritol is presumed to be absorbed via paracellular pathway, it opens tight junctions of the small intestine, which may facilitate fructose transport [3]. We, therefore, hypothesized that erythritol increases fructose absorption. The primary objective of the present study was to determine if the simultaneous ingestion of erythritol with an equimolar concentration of fructose increases fructose absorption as measured by breath hydrogen concentrations in healthy, nondiabetic adult participants. The secondary objective was to evaluate the subjective gastrointestinal tolerance of nondiabetic, healthy adults to beverages containing 50 g fructose with or without an equimolar concentration of erythritol (33.3 g) or glucose (50 g).

2. Methods and materials

2.1. Participants

Study participants were recruited through advertising in The Ohio State University community (Columbus, Ohio, USA). Participant eligibility criteria included the following: age between 18 and 75 years; male or nonpregnant, nonlactating female greater than 6 weeks postpartum; body mass index (BMI) of 18 to 28 kg/m^2 or a BMI up to 30 kg/m^2 if waist circumference was less than 88.9 cm for females or less than 101.6 cm for males [22]; no tobacco use; fasting plasma glucose 5.56 mmol/L or less; no previous diagnosis of diabetes mellitus or other metabolic or gastrointestinal diseases; no infection, surgery, or corticosteroid treatment within the past 3 months or antibiotic therapy within the past 3 weeks; and excretion of hydrogen (>10 ppm above baseline) in the breath after oral lactulose challenge and greater hydrogen than methane excretion [23,24]. Weight and height were measured at the study site, and BMI was calculated as weight (in kilograms)/height^2 (in square meters). Waist circumference was gauged at 3 cm above the umbilicus without pushing the skin. Fasting glucose concentrations were determined in the capillary whole blood using a portable blood glucose monitor (Accu-Chek Advantage Blood Glucose Monitoring System, Roche Diagnostics, Indianapolis, Ind., USA).

The study was approved by the Western Institutional Review Board (Olympus, Wash., USA), and informed consent was obtained from all participants before the start of the study. This study followed Good Clinical Practice (GCP) guidelines.

2.2. Feeding protocol

The study was a randomized, double-masked, controlled, crossover design in which participants participated in 3 separate 3-hour beverage tolerance tests. The tolerance tests were spaced 3 to 14 days apart for each participant. To ensure that participants had similar glycogen stores on the test days, participants were instructed to consume at least 150 g of carbohydrate per day for 3 days before each visit (verified by 3-day food records) and to refrain from exercise the day before each visit. In addition, participants were asked to consume a low-residue, low-fiber (≤5 g per dinner) standard dinner provided to them between 4 and 7 PM on the day before each visit. The standard low-residue, low-fiber dinner consisted of 240 mL of Ensure Plus along with variable quantities of Ensure Nutrition and Energy Bars (Abbott Nutrition, Abbott Laboratories, Columbus, Ohio) calculated to provide a total energy value equal to one third of each participant's estimated daily energy requirement (based on the Harris-Benedict equation multiplied by a light activity factor of 1.3) [25]. At each visit, participants consumed 1 of the 3 test beverages administered in random order, consisting of