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### Original article

# Zùsto: A new sweetening agent with low glycemic index

Joeri Jan Pen <sup>a, 1</sup>, Galina Khorosheva <sup>a, 1</sup>, Ursule Van de Velde <sup>a</sup>, Corinne Debroye <sup>a</sup>, André Huyghebaert <sup>b</sup>, Raoul Rottiers <sup>c</sup>, Bart Keymeulen <sup>a, \*</sup>

- <sup>a</sup> Diabeteskliniek UZ Brussel, Vrije Universiteit Brussel (VUB), Brussels, Belgium
- <sup>b</sup> Food Safety and Quality, Faculty Bioscience Engineering, Ghent University (UGent), Ghent, Belgium
- <sup>c</sup> Dienst Endocrinologie, UZ Gent, Universiteit Gent (UGent), Ghent, Belgium

#### ARTICLE INFO

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#### SUMMARY

Background & aims: Sweetening agents are sugar substitutes with a low glycemic index, used to obtain a better glycemic control in diabetes patients. However, they also may have a role in other subjects, as a high glycemic index is thought to cause many pathological conditions. Unfortunately, not all artificial sweeteners are perceived as sweet as sugar by patients. Consumers refer often to an after taste present in foods sweetened with intensive sweeteners. The objective of this study was to explore whether Zùsto<sup>®</sup> had a low glycemic index, to replace glucose as a sweetener.

Methods: In this study, the glycemic index (GI) of a new sweetening agent, Zùsto<sup>®</sup>, is compared to that of glucose 25 g, a standard sugar-loaded drink used in the oral glucose tolerance test to detect diabetes, as primary endpoint. Zùsto<sup>®</sup> is composed of non-digestible, water soluble fibers and sweeteners. 10 healthy, female non-obese volunteers received glucose and Zùsto<sup>®</sup>, albeit by an interval of a week. Evolution of glycemia, C-peptide and insulin release was measured at different time-points after intake.

Results: The results show that, when calculating the mean incremental Area Under the Curve (AUC), the AUC of glucose was around five times as high as that of Zùsto<sup>®</sup>; a GI of 22 for Zùsto<sup>®</sup> was calculated. Furthermore, Zùsto<sup>®</sup> had no significant effect on the glycemia, contrary to glucose, for at least 60'. This was also the case concerning C-peptide and insulin release, but the difference lasted even for 180'. Moreover, Zùsto<sup>®</sup> was perceived as sweet by all volunteers, with no particular aftertaste.

Conclusion: Zùsto<sup>®</sup> could be a viable alternative for fast sugars and other sweetening agents, both for diabetic patients and other subjects, requiring however a larger trial to confirm these results. Clinicaltrials.gov: NCT02607345.

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#### 1. Introduction

The glycemic index (GI) is a tool to rank the capacity of foods to raise glycemia after a meal. Food with a low GI is preferred in diabetic patients, as regulation of the glycemia is primordial. High GI-containing food is known to lead to fast, high and longstanding postprandial hyperglycemia, making it more difficult to control diabetes and prevent complications [1-4].

Sweetening agents are sugar substitutes that are artificially designed to replace fast sugars. They are generally used in diabetic patients due to their low GI and their sweet taste. They do not cause a postprandial hyperglycemia and are therefore good agents to

\* Corresponding author.

E-mail address: Bart.Keymeulen@uzbrussel.be (B. Keymeulen).

obtain glucose control, contrary to fast sugars. One problem with these agents is that in some cases, health concerns on the long term have been raised. Also, these agents are not all perceived as sweet by all patients, as sweetness can be accompanied by other tastes, inherent to the molecule [5,6].

A higher GI is also linked to many pathological conditions in non-diabetic individuals, and is thought to give rise to obesity and diabetes (even after risk correction for obesity) [7–9], cancer [10] and cognitive functioning [11], also in children [12]. Moreover, in pregnancy, food intake with a higher GI is linked to the development of obesity and metabolic disturbances in the newborn [13,14]. This appears also to be the case with sugar-sweetened beverages. Sweetening agents have been shown to diminish those risks, even in the absence of diabetes [15–18].

In this study, a novel sweetening agent, Zùsto<sup>®</sup>, is tested for its GI, as compared to glucose. Glycemia, C-peptide release and

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<sup>&</sup>lt;sup>1</sup> These authors contributed equally to this work.

insulinemia after ingestion are assessed. Moreover, the sweet taste of Zùsto<sup>®</sup> is tested on healthy volunteers, and no particular aftertaste is recorded.

#### 2. Materials and methods

#### 2.1. Subjects

We conducted a randomized, controlled, single-blinded trial in the University Hospital Brussel (UZ Brussel), Belgium. The study was approved by the Institutional Review Board of the hospital and performed in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was obtained from all patients.

Ten healthy female adult volunteers with normal insulin secretory beta cell function and normal insulin sensitivity, participated in the study (Table 1). Exclusion criteria were diabetes in first degree relatives, intake of medication which influences blood glucose levels, pregnancy or breastfeeding, or people following a diet for weight loss.

#### 2.2. Study design and procedures

After selection, healthy volunteers were split in two groups of five subjects. Group 1 received glucose 25 g (Glucomedics®) solved in 100 ml water (standard drink), while group 2 received 25 g Zùsto® solved in 100 ml water. Both drinks had to be taken in a time period of 5'. Subjects had to have fasted for 8 h prior to testing. Blood samples for glucose and insulin were taken at -15' and 0'. Blood samples for glucose, insulin and C-peptide were taken at 15', 30', 60', 90', 120' and 180' after the start of the intake. After one week interval, groups were switched and the same procedure took place.

#### 2.3. Properties of Zusto

Zùsto is a blend of several ingredients optimized in order to approach the sweet taste of regular sugar or sucrose (saccharose). The blend is further optimized so it can be applied in a one to one ratio to sucrose. No particular adaptation of recipes in the field of solid or semisolid sweet products, like desserts, frozen desserts or fine bakery ware, is necessary. It is not intended to be applied in liquid products.

In detail, Zùsto is a sugar substitute marketed with a proprietary formula on the EU market. It contains polydextrose, erythritol, inulin, fructo-oligosaccharides, maltodextrins, isomaltulose and sucralose in quantities that allow to mimic the organoleptic and functional properties of sugar, while providing only 97 kcal/100 g. The sweetening power is adjusted to match that of table sugar by the use of 0.14 g/100 g of Sucralose. In addition, non-digestible carbohydrates with fiber properties are added to provide bulk and mimic the technological properties of sugar. The full composition is described in the patent (World Intellectual Property

**Table 1** Subject characteristics (n = 10).

Age (y)	41,3 (5,3)
Body weight (kg)	68,0 (5,8)
BMI (kg/m <sup>2</sup> )	25 (2,7)
Fasting glycemia (mg/dL)	87 (4)
Homa	
%В	109 (29)
%S	141 (51)
IR	0.8 (0.4)

All data are expressed as mean (SD).

Organization. Patentscope). https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2015158735&redirectedID=true. Last accessed on 19 October 2018.

The individual components of the formula have all demonstrated effects on blood glucose in various trials. The aim of this study was to investigate the effect of the specific composition of Zusto on blood glucose levels. The study was designed to confirm the validity of the concept and the absence of unexpected phenomena.

In addition to the sweet taste, particular attention has been given to the functional properties of the formula. The blend shows good functional properties in terms of water solubility, texture formation, caramellisation, browning reactions and crystallization.

#### 2.4. Outcomes

The primary outcome of this study is comparison of the GI of glucose and Zùsto®, by means of calculating the AUC. The secondary endpoints are the evaluation of C-peptide and insulin levels after ingestion of either glucose or Zùsto®.

#### 2.5. Statistical analysis

Baseline subject characteristics are expressed as mean with standard deviations. The primary outcomes measured were the differences between changes from baseline for glucose, plasma C-Peptide and insulin after intake of glucose and Zùsto®. The differences between changes from baseline were analyzed by using the Related-Samples Wilcoxon Signed Rank Test. The glycemic index was calculated by expressing each participant's glucose incremental area under the curve (iAUC) for both intake with glucose and Zùsto® according to a previously described formula [19]. Results are reported as mean  $\pm$  standard error of the mean (SEM). The significance of differences was calculated by using the Mann—Whitney-U test. All statistical tests were performed two-sided at the 5% level of significance.

#### 3. Results

All participants completed the study.

Volunteers took either glucose or Zùsto®, and blood samples were taken at different timepoints. The incremental Area Under the Curve (AUC) of glucose as compared to Zùsto® was calculated (Fig. 1). For glucose, the mean iAUC was  $2262 \pm 431$ . For Zùsto®, the mean iAUC was  $353 \pm 77$ .

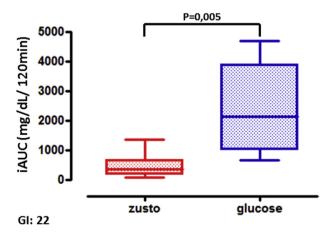


Fig. 1. Incremental Area Under the Curve (iAUC) of glycemia for glucose 25 g (right) as compared to Zùsto® 25 g (left). Box plots with mean and SEM. The GI of Zùsto® is 22.

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