Clinical Nutrition ESPEN 23 (2018) 103–106

Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: http://www.clinicalnutritionespen.com

Original article

Zùsto: A new sweetening agent with low glycemic index

Joeri Jan Pen [a, 1], Galina Khorosheva [a, 1], Ursule Van de Velde [a], Corinne Debroye [a], André Huyghebaert [b], Raoul Rottiers [c], Bart Keymeulen [a, *]

[a] Diabeteskliniek UZ Brussel, Vrije Universiteit Brussel (VUB), Brussels, Belgium
[b] Food Safety and Quality, Faculty Bioscience Engineering, Ghent University (UGent), Ghent, Belgium
[c] Dienst Endocrinologie, UZ Gent, Universiteit Gent (UGent), Ghent, Belgium

ARTICLE INFO

Article history:
Received 23 March 2017
Accepted 28 November 2017

Keywords:
Glycemia
Glycemic index
Zùsto®

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® 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®, 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® is composed of non-digestible, water soluble fibers and sweeteners. 10 healthy, female non-obese volunteers received glucose and Zùsto®, 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®; a GI of 22 for Zùsto® was calculated. Furthermore, Zùsto® 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® was perceived as sweet by all volunteers, with no particular aftertaste.

Conclusion: Zùsto® 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.

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 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®, is tested for its GI, as compared to glucose. Glycemia, C-peptide release and

* Corresponding author.
E-mail address: Bart.Keymeulen@uzbrussel.be (B. Keymeulen).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.clnesp.2017.11.009

insulinemia after ingestion are assessed. Moreover, the sweet taste of Zùsto® 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 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.

Table 1
Subject characteristics (n = 10).

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

All data are expressed as mean (SD).

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 ± 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 ± 431. For Zùsto®, the mean iAUC was 353 ± 77.

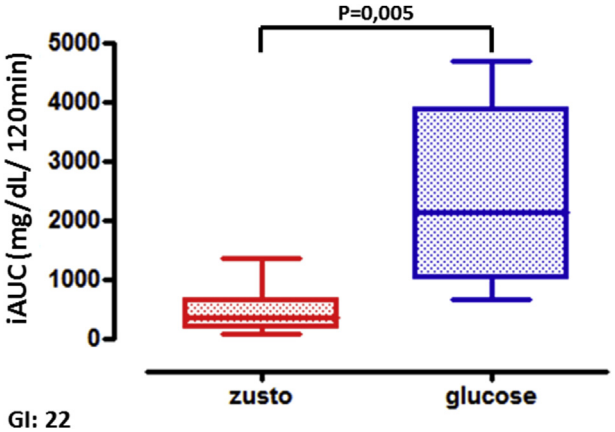

Fig. 1. Incremental Area Under the Curve (iAUC) of glycemia for glucose 25 g (right) as compared to Zùsto® 25 g (left). Box plots with mean and SEM. The GI of Zùsto® is 22.

An expected 360% increase of glycemia after ingestion with glucose was measured, but this increase was minor with Zùsto® (plus 40%). After 60', glycemia after glucose had fallen again to a level not significantly different from that with Zùsto® (Fig. 2, upper panel). Plasma C-peptide was elevated after glucose during 180 min the last timepoint measured (Fig. 2, middle panel). This was also the case with insulin secretion after intake (Fig. 2, lower panel). In contrast, no significant increase of plasma C-peptide and insulin levels were measured after intake of Zùsto®. Moreover, at 180', plasma glucose was slightly lower after intake of glucose (6 mg/dl) than after intake of Zùsto® (Fig. 1, upper panel), presumably reflecting the strong stimulus of insulin secretion after intake of glucose.

All volunteers tended to designate Zùsto® as sweet. No volunteer remarked an added taste or aftertaste.

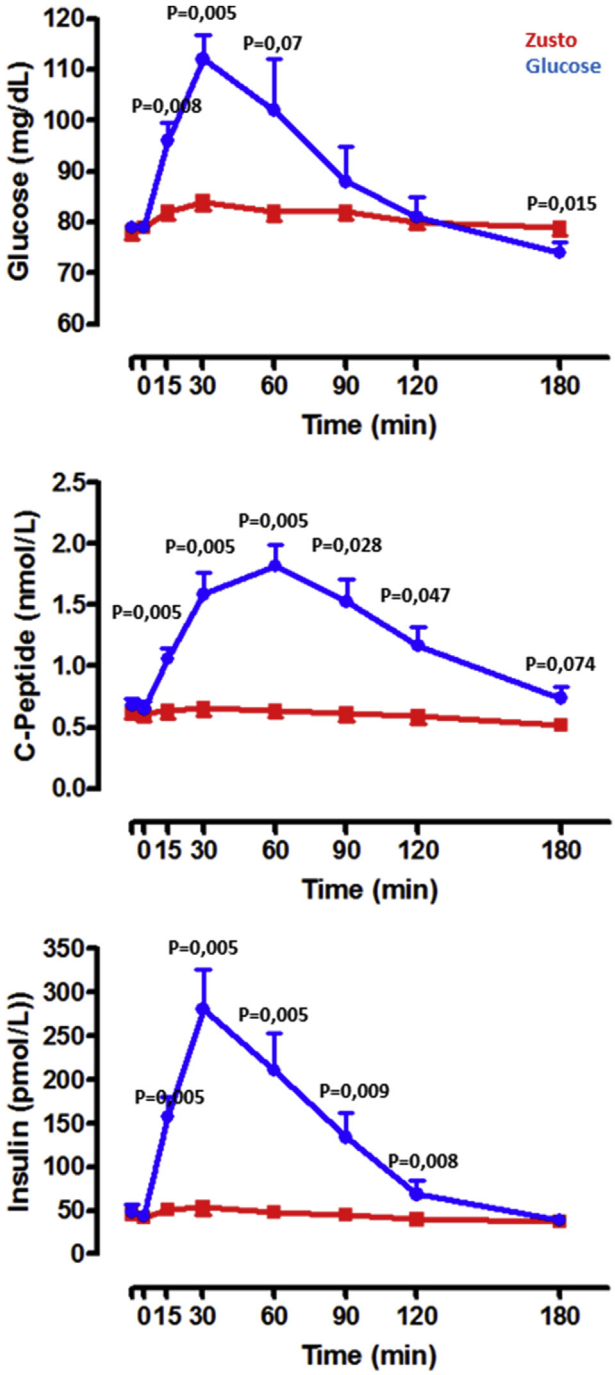

Fig. 2. Glycemia (upper panel), plasma C-peptide (middle panel) and insulin (lower panel) at different time points after intake of glucose 25 g (blue line) as compared to Zùsto® 25 g (red line).

4. Discussion

This study shows that a novel sweetening agent, Zùsto®, can be used as a replacement for fast sugars, as it has a low GI. Its taste is perceived as sweet and it has no effect on postprandial glycemia, C-peptide release and insulinemia, unlike fast sugars.

The fact that postprandial glycemia is not altered by Zùsto®, is important because both the GI as the glycemia itself are thought of having an effect on a patient's overall health, as well as their well-being. Moreover, insulinemia is not altered, which is the case with the standard drink glucose as well as food with a higher GI. Hyperinsulinemia has been correlated with a higher prevalence of increased appetite and weight gain, (pre)diabetes, cardiovascular disease and even cancer (see Introduction), although none of these associations have been studied in this small pilot trial. By consequence, Zùsto®'s non-metabolic disturbance is of significant importance, as the absence of hyperinsulinemia after ingestion suggests that the appetite, and by consequence weight gain, will not be increased. These hypotheses need to be suggested in a larger trial.

The GI is typically low to 0 in sweetening agents, as they are artificially designed to replace fast sugars. Biochemically, they are multiple times as sweet as normal fast sugars. The problem with many sweetening agents is that their overall taste is not universally appreciated by all patients. Stevioside, saccharin and aspartame are sweeteners with a GI of 0 [20], but the first two are perceived as having a bitter aftertaste by many patients, and are not even tolerated in a small fraction of them [5,6,21], while aspartame is unstable at high temperatures [22,23]. This is not the case with Zùsto®, although the sample size is small. Another advantage of Zùsto® is that one dose is composed of only 25 g of carbohydrates, as compared to classical food (bread, potatoes). While Zùsto® was indeed perceived as sweet by all participants, it should be noted that this was not an endpoint of the study.

In conclusion, Zùsto® is a novel sweetening agent that can be used as an alternative to fast sugars, both in diabetic and other patients.

Acknowledgements

The UZ Brussel investigators declare no conflict of interest. RR declares no conflict of interest. AH has been consulted during the development of the formula but has no financial interest.

RR, AH and BK concepted and designed the study. GK, UVDV and CD executed the study. JP, AH, RR and BK interpreted the results.

This academic study was performed thanks to a grant provided by SDC (Sweet D'Light Creations NV) Belgium.

References

[1] Campbell MD, Gonzalez JT, Rumbold PLS, Walker M, Shaw JA, Stevenson EJ, et al. Comparison of appetite responses to high- and low-glycemic index postexercise meals under matched insulinemia and fiber in type 1 diabetes. Am J Clin Nutr [Internet] 2015 Mar;101(3):478–86 [cited 2015 Oct 28] Available from: http://www.ncbi.nlm.nih.gov/pubmed/25733632.

[2] Farvid MS, Homayouni F, Shokoohi M, Fallah A, Farvid MS. Glycemic index, glycemic load and their association with glycemic control among patients with type 2 diabetes. Eur J Clin Nutr [Internet] 2014 Apr;68(4):459–63 [cited 2015 Oct 28] Available from: http://www.ncbi.nlm.nih.gov/pubmed/24549029.

[3] Stenvers DJ, Schouten LJ, Jurgens J, Endert E, Kalsbeek A, Fliers E, et al. Breakfast replacement with a low-glycaemic response liquid formula in patients with type 2 diabetes: a randomised clinical trial. Br J Nutr [Internet] 2014 Aug 28;112(4):504–12 [cited 2015 Oct 28] Available from: http://www.ncbi.nlm.nih.gov/pubmed/25091284.

[4] Maurício SF, da Silva JB, Bering T, Correia MITD. Relationship between nutritional status and the Glasgow Prognostic Score in patients with colorectal cancer. Nutrition [Internet] 2013 Apr;29(4):625–9 [cited 2014 Oct 13] Available from: http://www.ncbi.nlm.nih.gov/pubmed/23298973.

[5] Brunner S, Holub I, Theis S, Gostner A, Melcher R, Wolf P, et al. Metabolic effects of replacing sucrose by isomaltulose in subjects with type 2 diabetes: a randomized double-blind trial. Diabetes Care [Internet] 2012 Jun;35(6):1249–51 [cited 2015 Oct 28] Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3357231&tool=pmcentrez&rendertype=abstract.

[6] Maki KC, Phillips AK. Dietary substitutions for refined carbohydrate that show promise for reducing risk of type 2 diabetes in men and women. J Nutr [Internet] 2015 Jan;145(1):159S–63S [cited 2015 Oct 28] Available from: http://www.ncbi.nlm.nih.gov/pubmed/25527674.

[7] Bhupathiraju SN, Tobias DK, Malik VS, Pan A, Hruby A, Manson JE, et al. Glycemic index, glycemic load, and risk of type 2 diabetes: results from 3 large US cohorts and an updated meta-analysis. Am J Clin Nutr [Internet] 2014 Jul;100(1):218–32 [cited 2015 Sep 14] Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4144100&tool=pmcentrez&rendertype=abstract.

[8] Livesey G, Taylor R, Livesey H, Liu S. Is there a dose-response relation of dietary glycemic load to risk of type 2 diabetes? Meta-analysis of prospective cohort studies. Am J Clin Nutr [Internet] 2013 Mar;97(3):584–96 [cited 2015 Oct 28] Available from: http://www.ncbi.nlm.nih.gov/pubmed/23364021.

[9] Greenwood DC, Threapleton DE, Evans CEL, Cleghorn CL, Nykjaer C, Woodhead C, et al. Glycemic index, glycemic load, carbohydrates, and type 2 diabetes: systematic review and dose-response meta-analysis of prospective studies. Diabetes Care [Internet] 2013 Nov 21;36(12):4166–71 [cited 2015 Oct 5] Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3836142&tool=pmcentrez&rendertype=abstract.

[10] Choi Y, Giovannucci E, Lee JE. Glycaemic index and glycaemic load in relation to risk of diabetes-related cancers: a meta-analysis. Br J Nutr [Internet] 2012 Dec 14;108(11):1934–47 [cited 2015 Oct 28] Available from: http://www.ncbi.nlm.nih.gov/pubmed/23167978.

[11] Philippou E, Constantinou M. The influence of glycemic index on cognitive functioning: a systematic review of the evidence. Adv Nutr [Internet] 2014 Mar;5(2):119–30 [cited 2015 Oct 23] Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3951795&tool=pmcentrez&rendertype=abstract.

[12] Rouhani MH, Salehi-Abargouei A, Azadbakht L. Effect of glycemic index and glycemic load on energy intake in children. Nutrition [Internet] 2013 Sep;29(9):1100–5 [cited 2015 Oct 28] Available from: http://www.ncbi.nlm.nih.gov/pubmed/23746381.

[13] Horan MK, McGowan CA, Gibney ER, Donnelly JM, McAuliffe FM. Maternal low glycaemic index diet, fat intake and postprandial glucose influences neonatal adiposity–secondary analysis from the ROLO study. Nutr J [Internet] 2014 Jan;13:78 [cited 2015 Oct 28] Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4124499&tool=pmcentrez&rendertype=abstract.

[14] Walsh JM, Mahony RM, Canty G, Foley ME, McAuliffe FM. Identification of those most likely to benefit from a low-glycaemic index dietary intervention in pregnancy. Br J Nutr [Internet] 2014 Aug 28;112(4):583–9 [cited 2015 Oct 28] Available from: http://www.ncbi.nlm.nih.gov/pubmed/24896237.

[15] Bhupathiraju SN, Pan A, Malik VS, Manson JE, Willett WC, van Dam RM, et al. Caffeinated and caffeine-free beverages and risk of type 2 diabetes. Am J Clin Nutr [Internet] 2013 Jan;97(1):155–66 [cited 2015 Sep 29] Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3522135&tool=pmcentrez&rendertype=abstract.

[16] Bray GA. Energy and fructose from beverages sweetened with sugar or high-fructose corn syrup pose a health risk for some people. Adv Nutr [Internet] 2013 Mar;4(2):220–5 [cited 2015 Oct 28] Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3649102&tool=pmcentrez&rendertype=abstract.

[17] de Koning L, Malik VS, Rimm EB, Willett WC, Hu FB. Sugar-sweetened and artificially sweetened beverage consumption and risk of type 2 diabetes in men. Am J Clin Nutr [Internet] 2011 Jun;93(6):1321–7 [cited 2015 Oct 28] Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3095502&tool=pmcentrez&rendertype=abstract.

[18] Imamura F, O'Connor L, Ye Z, Mursu J, Hayashino Y, Bhupathiraju SN, et al. Consumption of sugar sweetened beverages, artificially sweetened beverages, and fruit juice and incidence of type 2 diabetes: systematic review, meta-analysis, and estimation of population attributable fraction. BMJ [Internet] 2015 Jan;351:h3576 [cited 2015 Jul 23] Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4510779&tool=pmcentrez&rendertype=abstract.

[19] Wolever TMS. Effect of blood sampling schedule and method of calculating the area under the curve on validity and precision of glycaemic index values. Br J Nutr [Internet] 2004 Mar;91(2):295–301 [cited 2015 Oct 30] Available from: http://www.ncbi.nlm.nih.gov/pubmed/14756916.

[20] Bryant CE, Wasse LK, Astbury N, Nandra G, McLaughlin JT. Non-nutritive sweeteners: no class effect on the glycaemic or appetite responses to ingested glucose. Eur J Clin Nutr [Internet] 2014 May;68(5):629–31 [cited 2015 Nov 18] Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4012981&tool=pmcentrez&rendertype=abstract.

[21] Chranioti C, Chanioti S, Tzia C. Comparison of spray, freeze and oven drying as a means of reducing bitter aftertaste of steviol glycosides (derived from Stevia rebaudiana Bertoni plant)–Evaluation of the final products. Food Chem [Internet] 2016 Jan 1;190:1151–8 [cited 2015 Oct 21] Available from: http://www.ncbi.nlm.nih.gov/pubmed/26213089.

[22] Sanyude S, Locock RA, Pagliaro LA. Stability of aspartame in water: organic solvent mixtures with different dielectric constants. J Pharm Sci [Internet] 1991 Jul;80(7):674–6 [cited 2015 Nov 18] Available from: http://www.ncbi.nlm.nih.gov/pubmed/1941567.

[23] Bell LN, Labuza TP. Aspartame degradation as a function of “water activity”. Adv Exp Med Biol [Internet] 1991 Jan;302:337–49 [cited 2015 Nov 18] Available from: http://www.ncbi.nlm.nih.gov/pubmed/1746339.