Effects of Palatinose and Sucrose Intake on Glucose Metabolism and Incretin Secretion in Subjects With Type 2 Diabetes

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Excessive sugar intake is associated with higher risk of insulin resistance and type 2 diabetes (T2D) (1). Recently, we reported that Palatinose (isomaltulose), a 1,6-linked glucose-fructose dimer that is completely digested and absorbed in the small intestine (2), improved glucose homeostasis and prevented fatty liver compared with 1,2-linked sucrose. Palatinose intake reduced postprandial glucose-dependent insulinotropic peptide (GIP) and insulin release in mice (3). Postprandial insulin secretion and glycemic excursions are regulated by the stimulation of incretin hormones. These intestinal peptides are glucagon-like peptide 1 (GLP-1) and GIP (4).

We compared the effects of sucrose versus Palatinose intake on glucose metabolism, insulin and glucagon secretions, and endogenous responses of incretins in T2D participants. In a randomized within-subject crossover study with ≥7 days washout period, 10 overnight-fasted T2D subjects (2 women and 8 men, aged 61 ± 4.6 years, BMI 32.1 ± 4.06 kg/m^2) received 50 g of Palatinose (BENEO GmbH, Mannheim, Germany) or sucrose (Südzucker, Mannheim, Germany) dissolved in 300 mL of tap water. Active GLP-1 and total GIP were measured using commercially available ELISA kits (EMD Millipore Corp., Billerica, MA). Insulin and glucagon concentrations were assessed by ELISA kits (Mercodia, Uppsala, Sweden).

In comparison with sucrose intake, peak glucose concentrations were significantly 2.5 mmol/L (20%) lower with Palatinose ingestion ($P < 0.01$) (Fig. 1*A*). Accordingly, insulin secretion was 55% lower after Palatinose ingestion compared with sucrose intake (Fig. 1*B*). We observed an initial small increase in glucagon concentrations during the first 15 min and followed by a sharp reduction until 180 min. There were no significant differences in plasma glucagon levels between sucrose and Palatinose loading (Fig. 1*C*).

Following sucrose intake, plasma concentrations of GIP peaked at 15 min with 2.8-fold increase ($P < 0.001$). Responses of GIP to Palatinose were dramatically smaller and delayed peaking after 60 min with 1.5-fold increase ($P < 0.001$) (Fig. 1*D*). Consequently, the incremental area under the curve (iAUC), which was calculated by trapezoid rule, of GIP was substantially reduced by 40% ($P < 0.001$) following Palatinose intake compared with sucrose intake (Fig. 1*E*).

After sucrose intake, GLP-1 concentrations briefly increased to a maximum and then rapidly declined to nearly baseline values within 60 min postload. Conversely, GLP-1 concentrations after Palatinose ingestion decreased slightly but remained significantly higher than sucrose. Accordingly, GLP-1$_{iAUC}$ was remarkably and significantly 6.3-fold ($P < 0.05$) higher after Palatinose administration in comparison to that following sucrose administration (Fig. 1*F* and *G*).

We show the beneficial effects of Palatinose on glucose metabolism and reduced insulin secretion without influence on glucagon levels in T2D subjects. Both disaccharides elicited almost opposing profiles of GIP and GLP-1, which is well explained by the slow cleavage of the 1,6-disaccharide bond in Palatinose as compared with the 1,2-disaccharide bond in sucrose by intestinal glucosidases (5). Therefore, Palatinose bypasses the upper intestinal K cells producing GIP and reaches the more distally located L cells producing GLP-1. As glucose and fructose are known to be completely resorbed, the differences in intestinal hormone responses must explain the much more favorable metabolic profile after Palatinose intake. Thus, Palatinose possesses a favorable profile for diabetes nutrition by lowering postprandial endogenous GIP levels, increasing GLP-1

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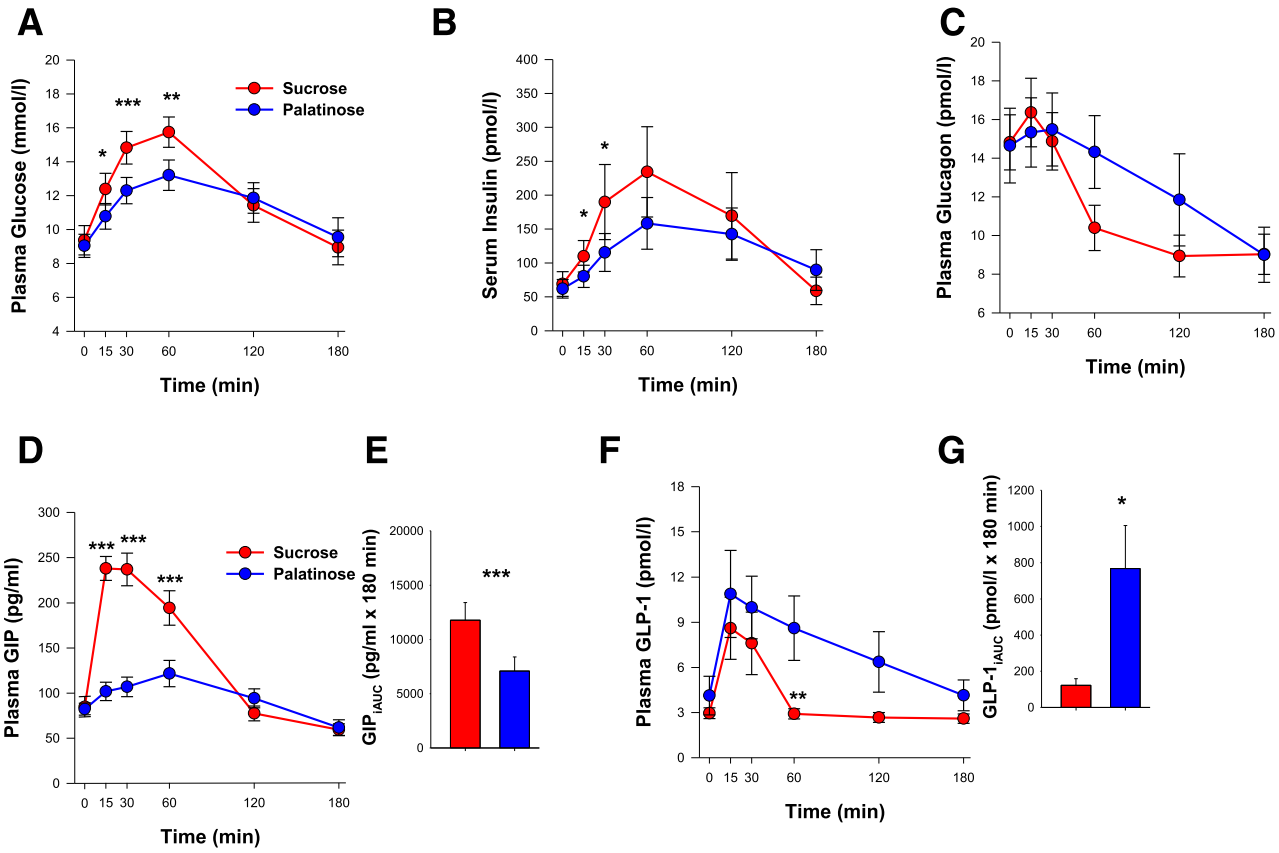

Figure 1—Effects of oral Palatinose (blue circles) and sucrose (red circles) intake on blood glucose (*A*), serum insulin (*B*), and plasma glucagon (*C*) concentrations in T2D subjects. Plasma concentrations and iAUCs for GIP (*D* and *E*) and GLP-1 (*F* and *G*) after oral intake of sucrose (red circles and bars) and Palatinose (blue circles and bars). Values are mean ± SEM. $*P < 0.05$, $**P < 0.01$, and $***P < 0.001$ compared with Palatinose.

concentrations, and saving insulin secretion, which ultimately results in better management of blood glucose in T2D.

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