Selected Conventional and Alternative Sweeteners on Gastrointestinal Hormones

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Sugar consumption is known to be associated with a whole range of adverse health effects, including overweight status and type II diabetes mellitus. Alternative sweeteners have gained interest as substitutes for conventional sweeteners, such as sucrose, glucose, or fructose, to achieve a reduction in sugar intake without loss of the sweet taste. Several human studies have shed light on the differential effects of conventional sweeteners (glucose, fructose, and sucrose) and alternative sweeteners on metabolic parameters such as gastrointestinal (GI) hormone secretion, gastric emptying rates, energy intake, glycemic control, blood lipids, and uric acid.

Keywords: glucose ; fructose ; sucrose ; sucralose ; D-allulose ; sweeteners ; metabolic effects ; gastrointestinal hormones

1. Introduction

Sugar consumption, particularly that of sucrose (commonly known as table sugar) and glucose–fructose syrups predominantly present in sugar-sweetened beverages (SSBs), has demonstrated a significant increase among both children and adults in recent decades [1][2]. Across Europe, SSBs rank as the second most substantial source of added sugar, following sweet products such as confectionery and sweets [3][4]. In 2015, the World Health Organization (WHO) issued a guideline, both for adults and children, recommending the reduction of sugar intake to less than 10% of total energy intake (TEI) and preferably less than 5% of TEI [5].

In this context, alternative sweeteners have gained interest as substitutes for conventional sweeteners, such as sucrose, glucose, or fructose, to achieve a reduction in sugar intake without loss of the sweet taste. Alternative sweeteners can be categorized into three groups and are discussed: artificial low-calorie sweeteners (LCS), natural low-calorie bulk sweeteners, and rare sugars.

Just recently, the WHO has released a new guideline on the use of LCS (a category which includes acesulfame K, aspartame, advantame, cyclamate, neotame, saccharin, sucralose, stevia, and stevia derivatives), and cautions against their use as a direct substitution for sugar [6]. Noteworthily, natural low-calorie bulk sweeteners such as erythritol or xylitol, as well as rare sugars such as D-allulose, are not discussed in this new guideline.

Several human studies have shed light on the differential effects of conventional sweeteners (glucose, fructose, and sucrose) and alternative sweeteners on metabolic parameters such as gastrointestinal (GI) hormone secretion, gastric emptying rates, energy intake, glycemic control, blood lipids, and uric acid. These investigations offer valuable insights into their unique metabolic effects.

Previous comprehensive and narrative reviews focused on specific outcomes (e.g, glycemic control, weight, or energy intake), were only covering specific sweetener groups, and/or did not include recent publications—especially those on erythritol, xylitol, or D-allulose [7][8][9][10][11][12].

2. Effects on Gastrointestinal Hormones

2.1. Sucrose, Glucose, and Fructose

Sucrose has been shown to induce the secretion of GI hormones in several acute human studies. Ma et al. [13] reported that intragastric administration of 50 g of sucrose in 500 mL saline led to increased plasma concentrations of glucagon-like peptide-1 (GLP-1) and gastric inhibitory polypeptide (GIP), compared to sucralose or saline solutions in healthy normal-weight participants. Additionally, Yunker et al. [14] investigated the effects of oral consumption of 75 g sucrose in 300 mL

water versus sucralose or water, finding that sucrose resulted in an increase in plasma GLP-1, but not peptide tyrosine tyrosine (PYY), and a decreased in ghrelin, compared to sucralose or water, in participants with a body mass index (BMI) of 19.2–40.3 kg/m^2 [14]. Tai et al. [15] reported that, when compared to water, oral consumption of 100 g of sucrose in 300 mL water led to a reduction in plasma ghrelin concentrations in healthy normal-weight participants. Furthermore, Maersk et al. [16] compared the acute intake of a sucrose beverage (500 mL of regular cola containing 53 g sucrose) to isocaloric milk, an aspartame-sweetened diet cola, and water in participants with overweight status and obesity, observing a reduction in ghrelin and an increase in GLP-1 and GIP concentrations after sucrose.

Steinert et al. [17] examined the effects of intragastric administration of 50 g glucose and 25 g fructose, compared to 62 mg sucralose, 169 mg aspartame, 220 mg acesulfame K (dissolved in 250 mL water), and water alone in healthy, normal-weight individuals. The authors found an increase in GLP-1 and PYY concentrations after glucose, compared to all other substances. Similar results were observed for ghrelin concentrations, with a decrease in ghrelin after glucose but no change after administration of the other substances [17]. Meyer-Gerspach et al. [18], on the other hand, observed an increase in GLP-1 after intragastric administration of both glucose (50 g in 250 mL water) and fructose (25 g in 250 mL water), compared to acesulfame K (220 mg in 250 mL water), and water (only for the glucose). There was no difference in GLP-1 release between glucose and fructose. Moreover, they found that both glucose and fructose induced a significant secretion of cholecystokinin (CCK), as compared to acesulfame K and water. There was no difference in CCK release between glucose and fructose. For ghrelin, their findings show a stronger decrease after glucose compared to that for fructose, with no change after acesulfame K or water.

In addition, other acute studies compared the conventional sweeteners sucrose, glucose, and fructose against each other. Wölnerhanssen et al. [19] observed that an intragastric administration of 75 g of glucose or 25 g of fructose in 300 mL water resulted in an increase in GLP-1 and GIP concentrations, but significantly higher GLP-1 and GIP concentrations after 75 g glucose compared to 25 g fructose. Also, Kong et al.'s study revealed that oral fructose (75 g in 300 mL water) stimulated GLP-1 less than did 75 g glucose [20]. Yau et al. [21] found that sucrose (36 g), glucose (39.6 g), fructose (36 g), and a combination of glucose (19.8 g) with fructose (18 g) (all in 600 mL water) similarly stimulated GLP-1 release in healthy participants (mean BMI 25.5 ± 3.8 kg/m^2). GIP secretion was induced after sucrose, glucose, and a combination of glucose and fructose, but not after fructose alone. Additionally, lower GIP concentrations were found after sucrose compared to the combination of glucose and fructose. The highest GIP concentrations were found after glucose. Each of the four substances lead to a similar decrease in ghrelin [21]. Furthermore, Yunker et al. [22] compared the effects of 75 g sucrose and 75 g glucose in 300 mL water in healthy participants (mean BMI 27.0 ± 5.0 kg/m^2), finding that sucrose led to smaller increases in GLP-1 and PYY, compared to glucose, while the decrease in acyl-ghrelin concentrations did not differ between sucrose and glucose [22]. Finally, Matikainen et al. [23] found no change in fasting GLP-1, GIP, and PYY and during an OGTT (GLP-1 and GIP only) before and after a 12-week administration of oral fructose (75 g in 330 mL, 3×/day) in participants with overweight status and obesity. Moreover, there were no changes in GLP-1, GIP, or PYY during a mixed-meal test.

Collectively, these findings suggest that acute intake of sucrose, glucose, and fructose can stimulate the secretion of GI hormones and suppress the secretion of the hunger hormone ghrelin. Chronic intake of fructose appears to have no effect on the secretion of gastrointestinal hormones in response to an OGTT.

2.2. Sucralose

Several studies have consistently demonstrated that varying doses of acute sucralose administration (oral, intragastric, or intraduodenal) have had no effect on GI hormones, such as GLP-1, PYY, GIP, or ghrelin [13][14][17][24][25][26][27][28]. However, some studies have reported higher concentrations of GLP-1 during an oral glucose tolerance test (OGTT) when sucralose was given as a preload compared to water [29][30].

A recent study showed that a daily sucralose intake (2 sachets containing 102 mg + 5.898 g glucose as bulking agent, 3×/day) over a two-week period did not lead to changes in GLP-1 concentrations during an OGTT in participants with a BMI between 18–28 kg/m^2 [31]. In contrast, Lertrit et al. [32] observed an increase in GLP-1 concentrations during an OGTT after consumption of 200 mg/d of sucralose for 4 weeks in healthy participants (BMI: 18.5–27.0 kg/m^2).

Acute intake of sucralose in isolation has no effect on GI hormone release. When it is given as a preload before an OGTT or when it is given chronically, some studies find an increase in GLP-1 release.

2.3. Xylitol and Erythritol

Researchers' recent research has repeatedly demonstrated that acute intragastric or oral administration of varying doses of xylitol (7 to 50 g in 300 mL water) leads to an increase in GLP-1, CCK, and PYY secretion, with no effect on GIP [33][34][35].

Similar results have been observed for erythritol. Acute intragastric or oral administration of varying doses (10 to 75 g in 300 mL water) of erythritol induced the secretion of GLP-1, CCK, and PYY, but not GIP [34][35][36][37][38]. Teysseire et al. [39] found a decrease in plasma ghrelin concentrations in response to an intragastric administration of 50 g of erythritol in 300 mL water, compared to D-allulose and water, in healthy, normal-weight individuals. Sorrentino et al. [40] observed a similar effect following oral consumption of 50.8 g of erythritol in 250 mL water, compared to aspartame in a similar participant population.

In summary, both xylitol and erythritol similarly stimulate the secretion of GLP-1, CCK, and PYY, and have no effect on GIP, irrespective of the dose and administration route. Additionally, erythritol reduces ghrelin secretion. Currently, there is a lack of human studies investigating the effects of xylitol consumption on ghrelin concentrations.

2.4. D-Allulose

To date, and to the best of our knowledge, there has been only one relevant human trial, and it studied the acute effects of 25 g D-allulose in 300 mL water on GI hormones, and found an increase in GLP-1, PYY, and CCK, compared to water, with no effect on ghrelin concentrations found in healthy, normal-weight participants [38][39].

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