

Sucrose polyester does not inhibit gastric acid secretion or stimulate cholecystokinin release in men¹⁻³

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ABSTRACT Replacement of dietary fat by sucrose polyester reduces fat intake. However, little is known about the effects of sucrose polyester on gastrointestinal function. To investigate the effect on gastric acid secretion and on release of cholecystokinin into plasma, we perfused eight healthy male volunteers intraduodenally with sucrose polyester, digestible fat, or saline on separate days in random order. Intraduodenal perfusion of sucrose polyester did not suppress gastrin-stimulated gastric acid secretion ($-1.8 \pm 6.8\%$) whereas digestible fat suppressed gastric acid secretion by $64 \pm 9\%$ ($P = 0.001$) compared with saline. Sucrose polyester did not affect plasma cholecystokinin concentrations (-12.8 ± 9.3 pmol \cdot 30 min/L) whereas perfusion with digestible fat resulted in a significant increase (31.7 ± 9.3 pmol \cdot 30 min/L, $P = 0.017$) compared with saline. We conclude that sucrose polyester, in contrast with digestible fat, does not inhibit gastrin-stimulated gastric acid secretion or stimulate release of cholecystokinin. *Am J Clin Nutr* 1997;65:761-5.

KEY WORDS Gastric acid secretion, sucrose polyester, cholecystokinin

INTRODUCTION

Lowering dietary fat intake is thought to have beneficial effects on health (1, 2). One way to achieve this goal is to replace dietary fat with a nondigestible fat of comparable texture such as sucrose polyester. Sucrose polyester is a mixture of hexa-, hepta-, and octaesters of sucrose. It is not hydrolyzed by pancreatic lipases so it is not absorbed from the intestine (3). Recently, the sucrose polyester olestra was admitted as a food ingredient in the United States for the preparation of chips and snacks.

Digestible fat and sucrose polyester may differ in their effects on gastrointestinal functions such as gastric emptying, gastric acid secretion, gallbladder motility, or pancreatic exocrine function. Therefore, long-term use of sucrose polyester might conceivably have clinical effects in disorders such as reflux esophagitis (4-7). Ordinary digestible fat is a potent inhibitor of gastric acid secretion (8-10). Decreased suppression of gastric acid secretion by sucrose polyester may affect symptoms in acid-related disorders.

Digestible fat is a powerful stimulus for plasma cholecystokinin (CCK) release and subsequently for gallbladder contraction and pancreatic enzyme secretion (11-17). It has been suggested that the inhibition of gastric acid secretion is also mediated at least in part by CCK (8-10, 18-22).

Stimulation of plasma CCK and pancreaticobiliary secretion by fatty nutrients depends on the presence of the products of fat digestion in the proximal small intestine (23-29). The inhibition of gastric acid secretion by fat might depend on the digestion of fat as well.

We report the effect of digestible fat and the indigestible fat sucrose polyester on gastric acid secretion and on CCK release in men.

SUBJECTS AND METHODS

Subjects

Eight healthy, nonsmoking, male volunteers aged 20-26 y participated in the studies. Body mass indexes (in kg/m²) ranged from 22 to 29. None of the subjects had a history of gastrointestinal diseases or surgery and none was taking any medication. The study protocol was approved by the Medical Ethical Committee of the University Hospital Nijmegen and written informed consent was obtained from each volunteer.

Materials

Synthetic nonsulfated gastrin-17 was purchased from Cambridge Research Biochemicals (Cheshire, United Kingdom). It was dissolved under aseptic conditions in saline containing 2% human serum albumin and stored at -20°C . Synthetic human CCK (CCK₃₃) was purchased from Peninsula Laboratories (St Helens, United Kingdom). Digestible fat (Goldflex), containing 12% palmitate, 9% stearate, 54% oleate, and 23% linoleate was from Van den Bergh Professional BV (Rotterdam, Netherlands). Sucrose polyester containing 10% palmitate, 6% stearate, 35% oleate, and 44% linoleate was a gift from Unilever Research, Vlaardingen, Netherlands.

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² Funded by a PhD fellowship to MIMM from the Faculty of Medical Sciences, Nijmegen.

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Received March 7, 1996.

Accepted for publication November 7, 1996.

Experimental design

Over 1 mo each subject underwent three experiments in random order on different days separated by ≥ 1 wk. After an overnight fast, the volunteers arrived at the gastrointestinal research laboratory at 0800. A single-lumen polyvinyl perfusion catheter for the administration of fats or saline was placed into the proximal duodenum under fluoroscopic control. A polyvinyl gastric drainage tube was placed into the stomach together with a small-bore polyethylene perfusion catheter inserted into one of the three side holes of the gastric drainage tube. The position of this tube was checked by the water recovery method (30); subsequently, the small-bore catheter was pulled back ≈ 10 cm to release it from the drainage tube. The stomach was emptied and then perfused with a saline solution containing 3 mg phenol red/L at a rate of 120 mL/15 min. Gastric contents were aspirated continuously during the experiments by using a suction pump that provided intermittent negative pressure. The gastric aspirates were collected in 15-min portions and kept on ice.

Indwelling intravenous catheters were placed into the left and right forearm of each subject. The catheters were kept patent with a saline solution. One catheter was used for the collection of blood samples and the other for the infusion of nonsulfated gastrin-17 at a dose of $10 \text{ pmol} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. This dose produces plasma gastrin concentrations similar to those found after a meal (31). Blood samples were taken every 30 min during the 1-h basal period and every 15 min during the subsequent gastrin-infusion period. Blood samples were collected into ice-chilled 10-mL glass tubes containing 15 mg EDTA.

Four 15-min gastric samples were collected under unstimulated conditions. Subsequently, the intravenous gastrin-17 infusion was started and continued for 3 h. After 1 h of gastrin infusion, 30 mL of either saline, sucrose polyester (containing 92.9 mmol fatty acids), or digestible fat (containing 93.4 mmol fatty acids) was perfused intraduodenally at a rate of 20 mL/h for 90 min. This was followed by a 30-min period during which no fat was perfused.

Immediately after the experiments the blood samples were centrifuged for 15 min at 4000 rpm, $2560 \times g$, at room temperature and plasma was stored at -20°C . The volume and pH of each 15-min gastric juice sample was recorded, and the hydrogen ion concentration was determined by titration to pH 7.0 with 0.1 mol NaOH/L. Then the gastric samples were centrifuged for 1 min at $12\,000 \times g$ and the supernate was alkalinized with 2.5 mol NaOH/L, after which the concentration of phenol red was measured spectrophotometrically at 560 nm. Recovery of gastric juice was calculated by the following equation:

$$(V_A \times \text{ABS}_A) / (V_P \times \text{ABS}_P) \quad (1)$$

where V_A represents the volume of aspirated gastric juice, ABS_A the phenol red absorption of the aspirated gastric juice, V_P the volume of phenol red solution perfused into the stomach, and ABS_P the phenol red absorption of the perfused solution, each per 15-min period. The amount of acid secreted (mmol/15 min) was calculated as follows:

$$(\text{Acid concentration measured} \times V_A) / \text{recovery} \quad (2)$$

Plasma gastrin and CCK concentrations were measured by sensitive and specific radioimmunoassays as described previously (32–35).

Data analysis

Results are expressed as means \pm SEMs unless stated otherwise. Basal gastric acid output was defined as the sum of the last two 15-min portions obtained under unstimulated conditions [$t = -15 \text{ min} (t_{-15}) + t_0$]. Gastrin-stimulated gastric acid output was defined as the sum of the last two 15-min portions obtained during the first hour of gastrin-17 infusion ($t_{45} + t_{60}$). The percentage inhibition of gastric acid secretion by saline, sucrose polyester, or digestible fat was calculated as follows:

$$\frac{(t_{45} + t_{60}) - (t_{135} + t_{150})}{t_{45} + t_{60}} \times 100\% \quad (3)$$

where $t_{45} + t_{60}$ represents the final 30 min before fat perfusion and $t_{135} + t_{150}$ the gastric acid secretion over the final 30 min of the fat-perfusion period. Integrated plasma CCK concentrations for the last 30 min of each experimental period were calculated as area under the plasma concentration-versus-time curves by using the trapezoidal rule. Statistical analysis was performed by two-way analysis of variance (ANOVA) for repeated measurements and the two-tailed t test for paired results. SPSS 5.0 (SPSS, Benelux BV, Gorinchem, Netherlands) was used for statistical analysis.

RESULTS

Plasma gastrin concentrations

Infusion of gastrin increased plasma gastrin concentrations from a basal concentration of 23 ± 3 to 55 ± 5 pmol/L in the saline experiment, from 23 ± 2 to 54 ± 3 pmol/L in the sucrose polyester experiment, and from 26 ± 4 to 51 ± 3 pmol/L in the digestible-fat experiment. Subsequent duodenal perfusion of sucrose polyester or digestible fat during gastrin infusion did not further affect plasma gastrin concentrations.

Gastric acid secretion

The initial infusion of gastrin raised gastric acid output in all experiments to a similar extent (Figure 1). Subsequent intraduodenal perfusion of sucrose polyester did not suppress acid secretion in contrast with digestible fat, which suppressed gastrin-stimulated gastric acid secretion by $64.2 \pm 8.8\%$ ($P = 0.001$, Table 1) relative to saline.

Plasma cholecystokinin concentrations

Perfusion of sucrose polyester had no significant effect on plasma CCK (Figure 2). Perfusion of digestible fat resulted in significantly ($P = 0.017$) higher integrated plasma CCK concentrations than did saline (Table 2).

DISCUSSION

This study showed that the nondigestible fat sucrose polyester cannot inhibit gastrin-stimulated gastric acid secretion or stimulate the release of CCK. In contrast, digestible fat significantly inhibited gastric acid secretion and augmented CCK release. The key difference between sucrose polyester and

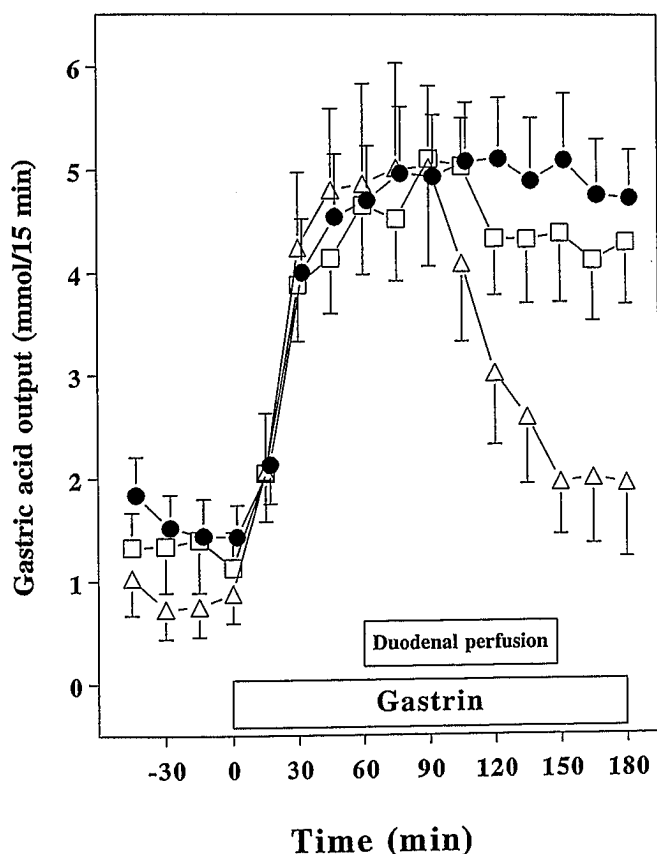


FIGURE 1. Mean (\pm SEM) gastric acid output in eight volunteers under basal conditions and during intravenous infusion of gastrin ($10 \text{ pmol} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$), subsequently combined with an intraduodenal perfusion of digestible fat (62 mmol/h ; Δ), sucrose polyester (62 mmol/h ; \square), or saline (20 mL/h ; \bullet).

regular fats is that the fatty acids in sucrose polyester cannot be split off by pancreatic lipases (36–38). This might be the reason for the absence of plasma CCK secretion and suppression of gastric acid secretion in response to sucrose polyester. CCK may be involved in the suppression of gastric acid secretion by intraduodenal fat (18–22), although we showed that suppression of acid secretion can be reached by medium-chain triacylglycerols without concomitant CCK release (39). The increase of plasma CCK in response to digestible fat was

TABLE 1

Gastric acid output in the stomach before gastrin infusion (basal), during gastrin infusion, and during intraduodenal perfusion of sucrose polyester (SPE), digestible fat, or saline in eight volunteers; intravenous gastrin infusion was continued during the intraduodenal perfusion of fat¹

Treatment	Gastric acid output			
	Basal	Gastrin	Gastrin + saline or fat	Change ²
	<i>mmol/30 min</i>	<i>mmol/30 min</i>	<i>mmol/30 min</i>	<i>%</i>
Saline	3.1 ± 0.7	9.1 ± 1.3	9.6 ± 1.1	9.7 ± 8.3
SPE	2.7 ± 1.0	8.6 ± 1.3	8.2 ± 1.3	-1.8 ± 6.8
Digestible fat	1.6 ± 0.7	8.6 ± 1.6	3.0 ± 0.9	-64.2 ± 8.8^3

¹ $\bar{x} \pm \text{SEM}$.

² The effect of fat perfusion relative to gastrin infusion alone.

³ Significantly different from other treatments, $P \leq 0.001$.

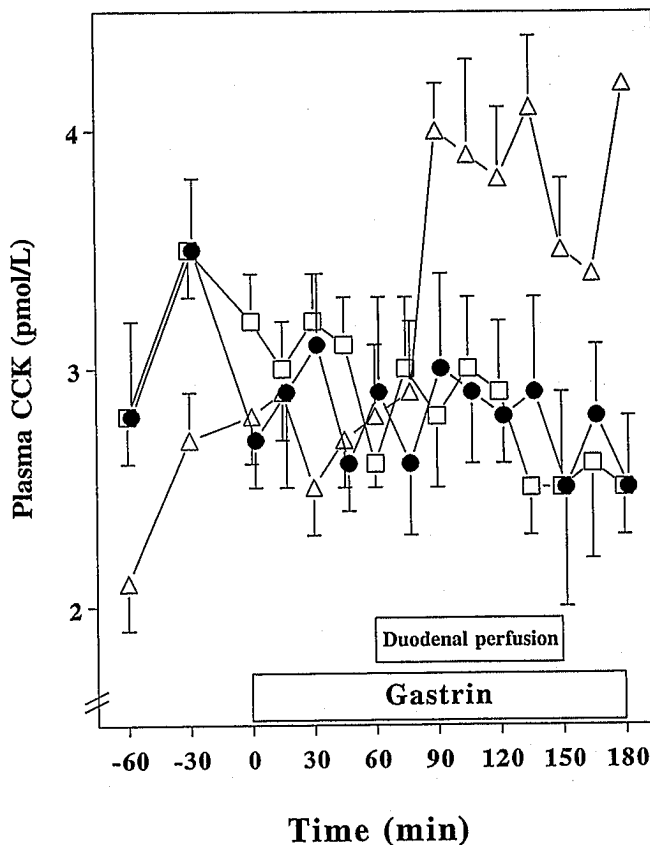


FIGURE 2. Mean (\pm SEM) plasma cholecystokinin (CCK) concentrations in eight volunteers under basal conditions and during intravenous infusion of gastrin ($10 \text{ pmol} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$), subsequently combined with an intraduodenal perfusion of digestible fat (62 mmol/h ; Δ), sucrose polyester (62 mmol/h ; \square), or saline (20 mL/h ; \bullet).

probably of physiologic significance because we have found that plasma CCK increments during fat perfusion in the same range as in the present study stimulated gallbladder contraction (14, 40) and delayed gastric emptying (41, 42).

Recent studies suggest that hydrolysis of triacylglycerols, resulting in the release of fatty acids and monoacylglycerols, is an important prerequisite for appropriate stimulation of plasma CCK (23–29). Plasma CCK secretion and gallbladder empty-

TABLE 2

Integrated plasma cholecystokinin concentrations before intravenous gastrin infusion (basal), during intravenous gastrin infusion, and during additional intraduodenal perfusion of sucrose polyester (SPE), digestible fat, or saline in eight volunteers; intravenous gastrin infusion was continued during the intraduodenal perfusion of fat¹

Treatment	Plasma cholecystokinin			
	Basal	Gastrin	Gastrin + saline or fat	Change ²
	<i>pmol · 30 min/L</i>			
Saline	91.5 ± 4.7	83.9 ± 7.3	79.3 ± 8.9	-4.6 ± 7.0
SPE	100.5 ± 5.3	89.5 ± 5.0	76.8 ± 8.0	-12.8 ± 9.3
Digestible fat	81.9 ± 3.9	81.4 ± 6.3	113.1 ± 6.4	31.7 ± 9.3^3

¹ $\bar{x} \pm \text{SEM}$.

² The effect of fat perfusion relative to gastrin infusion alone.

³ Significantly different from other treatments, $P \leq 0.02$.

ing in response to a meal were reduced in patients with pancreatic insufficiency (23, 24), whereas addition of pancreatic enzymes to the meal normalized the impaired responses. In contrast with undigested corn oil, corn oil that had been pre-digested with bile and pancreatic juice induced plasma CCK secretion and gallbladder contraction in patients with untreated celiac disease (25, 26). Furthermore, it was shown that the lipase inhibitor orlistat inhibited biliary and pancreatic output and increased postprandial gastric acidity (27, 28). Animal data also point to the necessity of digestion of fat for gastric acid secretion or pancreatic enzyme release (29, 43, 44). In humans it was shown that oleic acid inhibited gastric acid secretion whereas oleyl alcohol did not (45), indicating that the free carboxyl group of the fatty acid molecule has an important role in the inhibition of gastric acid secretion. Because the carboxyl groups of the fatty acids in sucrose polyester remain esterified, the results of the present study supply further evidence that the products of fat digestion play an important role in the intestinal phase of plasma CCK secretion and gastric acid suppression in humans.

The finding that sucrose polyester does not inhibit gastric acid secretion and does not release CCK into the plasma may have clinical implications. On the one hand, gastric acid may play a role in the pathogenesis of gastroesophageal reflux disease (46, 47). Both increased basal and food-stimulated acid secretion likely contribute to longer duration of esophageal acid exposure (5-7, 48). Increased aggressiveness of refluxed material owing to a lower gastric pH may potentiate the noxious effects of refluxed gastric material and possibly of refluxed bile (5, 6, 47-49).

On the other hand, substitution of ordinary fat by sucrose polyester may also affect other factors that are supposed to be involved in gastroesophageal reflux disease, including gastric emptying (50) and esophageal sphincter pressure (51-54). However, contradictory results have been published on the effects of sucrose polyester on gastric emptying (55, 56) and on the role of gastric emptying in reflux esophagitis (50). Fat has been shown to decrease esophageal sphincter pressure (57), which may result in gastroesophageal reflux (58). CCK, which is released by fat but not by sucrose polyester, may be the mediator of this lower esophageal sphincter relaxation (59, 60). The effect of sucrose polyester on the lower esophageal sphincter has not been studied yet as far as we know, but it has been shown that sucrose polyester decreases postprandial gastroesophageal reflux episodes and esophageal acid exposure (61).

The overall effect of sucrose polyester on gastroesophageal reflux disease is therefore unpredictable and further studies are needed to investigate the role of sucrose polyester on gastroesophageal reflux symptoms. We conclude that intraduodenal sucrose polyester, in contrast with regular fat, does not suppress the stimulated gastric acid secretion and does not stimulate plasma CCK release, probably because sucrose polyester is not digested, and therefore, no fatty acids or monoacylglycerols are released. ■

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