The nondigestible fat sucrose polyester does not stimulate gallbladder emptying in humans\textsuperscript{1–3}

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**ABSTRACT**

**Background:** We determined the effect of oral ingestion of sucrose polyester, which was approved as a fat replacer in the United States, on gallbladder motility and on the release of cholecystokinin, the hormone that mediates gallbladder emptying.

**Objective:** Our objective was to measure effects of sucrose polyester on gallbladder emptying and cholecystokinin release.

**Design:** Eight healthy volunteers (3 men and 5 women) drank 60 mL sucrose polyester, digestible fat, or saline solution in a balanced crossover design on 3 separate days.

**Results:** Mean (±SEM) gallbladder emptying, when integrated over time, was low in response to both sucrose polyester (150 ± 214 mL·120 min) and saline solution (−89 ± 123 mL·120 min). In contrast, there was marked emptying in response to digestible fat (1069 ± 253 mL·120 min). Sucrose polyester did not affect plasma cholecystokinin concentrations (29.3 ± 15.0 pmol·120 min/L), whereas digestible fat resulted in a significant increase (89.5 ± 44.8 pmol·120 min/L, \(P = 0.014\)) compared with saline solution (23.0 ± 13.8 pmol·120 min/L).

**Conclusions:** Ingestion of sucrose polyester, in contrast with digestible fat, did not stimulate gallbladder emptying or release of cholecystokinin. *Am J Clin Nutr* 1998;68:1272–5.

**KEY WORDS** Gallbladder motility, sucrose polyester, cholecystokinin, digestible fat, gallstones, obesity, weight loss, very-low-fat diets

**INTRODUCTION**

Gallbladder motility is controlled by the enterohormone cholecystokinin. Digestible fat is a powerful stimulus for plasma cholecystokinin release and subsequent gallbladder emptying (1–5). It has been suggested that gallbladder hypomotility may cause stasis of bile in the gallbladder and may facilitate cholesterol crystallization. These factors may increase the risk of gallstones (6–8). Obese patients who attempt to lose weight with very-low-energy, very-low-fat diets appear to be especially at risk (9–14).

Sucrose polyester is a mixture of hexa-, hepta-, and octaesters of sucrose. It is not hydrolyzed by pancreatic lipases (15) and is not absorbed from the intestine (16, 17). Because it has been approved as a fat replacer in the United States for preparation of chips and snacks, it is important to establish its effects on gallbladder motility. Therefore, we measured gallbladder emptying and cholecystokinin release in plasma in response to sucrose polyester, regular fat, or saline solution in healthy volunteers.

**SUBJECTS AND METHODS**

**Subjects**

Eight healthy volunteers [3 men and 5 women aged 26 ± 3 years with a mean body mass index (in kg/m\(^2\)) of 22 ± 1] participated in the study. 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**

Sucrose polyester containing 10% palmitate (16:0), 6% stearate (18:0), 35% oleate (18:1), and 44% linoleate (18:2) was a gift from Unilever Research, Vlaardingen, Netherlands. Digestible fat (Goldflex) containing 12% palmitate, 9% stearate, 54% oleate, and 23% linoleate was obtained from Van den Bergh Professional BV, Rotterdam, Netherlands. Both the sucrose polyester and digestible fat were liquid at room temperature.

**Experimental design**

Each subject received sucrose polyester, digestible fat, or saline solution in a balanced, multiple crossover design on 3 separate days. The subjects were unaware of which fat they were drinking. After an overnight fast, the volunteers presented themselves at the gastrointestinal research laboratory at 0800. One indwelling, intravenous catheter was placed into the forearm of each subject for the collection of blood samples for the measurement of cholecystokinin. The catheters were kept patent by a...
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Plasma concentrations of cholecystokinin

Plasma cholecystokinin concentrations were measured by a sensitive and specific radioimmunoassay as described previously (20). The antibody used (T204) binds to all biologically active cholecystokinin peptides containing the sulfated tyrosine region with almost equal affinity. On a molar basis, sulfated gastrins cross-reacted <2% in the assay, whereas no cross-reactivity was found with unsulfated gastrins or structurally unrelated peptides. The detection limit of the assay was between 0.5 and 1.0 pmol cholecystokinin/L in plasma. The intraassay precision ranged from 4.6% to 11.5% in the steep part of the standard curve. All samples were measured in the same run.

Data analysis

All measurements were performed in duplicate and the means of these measurements were used for further analysis. Gallbladder volume was expressed in milliliters or as percentage of the mean basal gallbladder volume. Integrated plasma cholecystokinin concentrations were determined by calculating the area under the plasma concentration–time curve after subtracting the basal value. Integrated gallbladder response was determined by calculating the area under the gallbladder emptying–time curve. This curve was obtained by subtracting gallbladder volumes measured at each time point after ingestion of the meal from mean basal gallbladder volume. Integrated plasma cholecystokinin and gallbladder responses were calculated for a period of 120 min.

Results are expressed as means ± SEMs. Statistical analysis of the gallbladder volume responses was performed by two-way analysis of variance with subject and treatment as factors (21). If analysis of variance indicated a significant treatment effect, it was followed by Student’s t test for paired results to determine which treatments were significantly different from each other (22). The nonparametric Friedman two-way analysis of variance was applied for statistical analysis of plasma cholecystokinin responses because these data were not normally distributed. This was followed by Wilcoxon’s signed-rank test when analysis of variance indicated a significant treatment effect. Differences with a two-tailed P value < 0.05 were considered significant.

Baseline gallbladder volumes were 21 ± 2 mL before consumption of digestible fat, 22 ± 2 mL before consumption of sucrose polyester, and 20 ± 2 mL before consumption of saline solution. Saline solution did not affect gallbladder volume (Figure 1) but ingestion of 60 mL digestible fat induced a highly significant reduction (P < 0.0001; Figure 1). The smallest gallbladder volume (42 ± 10% of baseline) was measured 105 min after the digestible fat meal (Figure 1). Ingestion of 60 mL sucrose polyester did not decrease gallbladder volume (Figure 1).

There was a marked difference in gallbladder response integrated over time between digestible fat (1069 ± 253 mL · 120 min) and sucrose polyester (−150 ± 214 mL · 120 min; P < 0.001) and between digestible fat and saline solution (−89 ± 12 mL · 120 min; P < 0.002), but the difference in response between saline solution and sucrose polyester was not significant.

Plasma cholecystokinin

The mean (±SEM) fasting plasma cholecystokinin concentration was 3.4 ± 0.4 pmol/L before each of the 3 treatments. Neither ingestion of sucrose polyester nor ingestion of saline solution induced significant changes in plasma cholecystokinin concentrations (Figure 2). Ingestion of digestible fat induced an increase in plasma cholecystokinin concentration to a peak value of 4.6 ± 0.8 pmol/L 60 min after the meal (Figure 2). Integrated plasma responses after ingestion of sucrose polyester (−9.3 ± 15.0 pmol · 120 min/L) and saline solution (−3.0 ± 13.8 pmol · 120 min/L) were significantly smaller than the response after ingestion of digestible fat (89.5 ± 44.8 pmol · 120 min/L; P < 0.03 compared with digestible fat).

FIGURE 1. Mean (±SEM) gallbladder volumes in 8 healthy volunteers after ingestion of 60 mL digestible fat (▲), 60 mL sucrose polyester (◇), or 60 mL saline solution (●).
only corn oil that had been predigested with bile and pancreatic release with a fatty meal and that addition of pancreatic enzymes diminished gallbladder emptying rates and cholecystokinin (30) who showed that patients with pancreatic insufficiency have significant gallbladder emptying during fasting. It agrees with the findings of Masclee et al (29) and Jansen et al (26, 27). Furthermore, it was shown that intraduodenal administration of sucrose polyester failed to stimulate the release of cholecystokinin in healthy volunteers. This absence of a stimulating effect on gallbladder emptying is in sharp contrast with the potent stimulatory effect of digestible fat on gallbladder motility as observed in the present study and numerous other studies (2, 23, 24). Sucrose polyester probably failed to induce gallbladder emptying because it did not stimulate cholecystokinin release; cholecystokinin is the major stimulant for gallbladder emptying after a meal (3–5). Infusion of cholecystokinin to plasma concentrations in the range observed here in response to ingestion of digestible fat induced comparable decreases in gallbladder volume (3, 25). It is unlikely that differences in gastric emptying accounted for the absence of cholecystokinin stimulation or gallbladder emptying because gastric emptying of sucrose polyester has been shown to be as fast or faster than that of digestible fat (26, 27). Furthermore, it was shown that intraduodenal administration of sucrose polyester also failed to stimulate the release of cholecystokinin (28).

Thus, fatty acids that remain esterified, like the fatty acids in sucrose polyester, do not stimulate the release of plasma cholecystokinin and do not induce gallbladder emptying. This finding supports the hypothesis that lipolysis of lipid nutrients is important for intestinal stimulation of plasma cholecystokinin release. It agrees with the findings of Masclee et al (29) and Jansen et al (30) who showed that patients with pancreatic insufficiency have diminished gallbladder emptying rates and cholecystokinin release with a fatty meal and that addition of pancreatic enzymes to the meal normalized the impaired responses. The finding that only corn oil that had been predigested with bile and pancreatic juice induced plasma cholecystokinin secretion and a reduction of gallbladder volume in patients with untreated celiac disease (31, 32) also supports this hypothesis. Furthermore, the lipase inhibitor orlistat reduced the release of cholecystokinin in humans (33, 34). This again supports the hypothesis that it is not fat itself but the products of fat digestion that stimulate the release of cholecystokinin and affect gastrointestinal function.

Kelly and Hunter (35) reported a 22% reduction in gallbladder volume in response to sucrose polyester, whereas the reduction in response to fat was 45%. Sucrose polyester still affected fasting gallbladder volume, whereas in our study sucrose polyester did not affect the gallbladder. However, in their study sucrose polyester was included in a test milk. Proteins or amino acids in the milk might have stimulated the release of cholecystokinin and induced a decrease in gallbladder volume (23, 36, 37).

Our results showed that sucrose polyester did not reduce gallbladder volume. However, because other components within a meal also affect gallbladder motility and because sucrose polyester will probably not be ingested without other components, it is likely that the gallbladder will still be stimulated. However, it is not clear to what extent ordinary digestible fat can be replaced by sucrose polyester while conserving gallbladder emptying. It has been suggested that 10 g fat is enough to produce normal gallbladder emptying (13).

The absence of gallbladder emptying might conceivably have clinical implications. It has been suggested that reduced gallbladder emptying may increase the risk of gallstone formation. Impaired gallbladder emptying has been shown in patients receiving long-term parenteral nutrition and it has been associated with an increased incidence of gallstone formation (38, 39). Gallstone formation in these patients was shown to be prevented by daily infusions of cholecystokinin (40), suggesting that gallbladder motility is involved in the development of gallstones. Obese persons attempting to lose weight with very-low-energy, low-fat diets also have an increased risk of stone formation (10–12). Again, it has been suggested that this might be due, in part, to reduced gallbladder motility (13, 14) because low fat and low energy intakes have been shown to be related to low gallbladder motility (13, 23, 41).

Proteins or amino acids also stimulate the release of cholecystokinin and induce gallbladder contraction (23, 36, 37). Therefore, a normal meal in which fat has been replaced by sucrose polyester may still stimulate the release of cholecystokinin and induce gallbladder emptying.

In conclusion, this study showed that in strong contrast with digestible fat, sucrose polyester did not reduce gallbladder volume or stimulate the release of cholecystokinin in plasma. This may impair gallbladder motility, but other components of a meal also can induce gallbladder emptying and therefore we cannot conclude whether the risk of gallstone formation with a diet with sucrose polyester will be affected.

REFERENCES
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