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Regulatory Peptides 66 (1996) 203–210

REGULATORY PEPTIDES

# Inhibition of gastrin-stimulated gastric acid secretion by medium-chain triglycerides and long-chain triglycerides in healthy young men

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Received 27 November 1995; revised 7 May 1996; accepted 5 June 1996

**Abstract**

Long-chain triglycerides inhibit gastric acid secretion, but the effect of medium-chain triglycerides in humans is unknown. We compared the effects of intraduodenally perfused saline, medium-chain and long-chain triglycerides on gastrin-stimulated gastric acid secretion and cholecystokinin release. Eight healthy male volunteers participated in this study. Gastrin-stimulated gastric acid output was $9.4 \pm 1.1$ mmol/30 min during saline perfusion. It was suppressed by medium-chain triglycerides by $43 \pm 9\%$ ($P = 0.04$ vs. saline) and by long-chain triglycerides by $74 \pm 6\%$ ($P = 0.0003$ vs. saline). Thus medium-chain triglycerides inhibited gastrin-stimulated gastric acid secretion but less so than long-chain triglycerides. When compared to saline perfusion ($73 \pm 6$ pM × 30 min) integrated plasma cholecystokinin concentrations were significantly elevated by long-chain triglycerides ($96 \pm 5$ pM × 30 min, $P < 0.004$) but not by medium-chain triglycerides perfusion ($65 \pm 7$ pM × 30 min). We also investigated the role of cholecystokinin infusion on gastrin stimulated gastric acid secretion. Higher concentrations ($191.4 \pm 4.5$ pM × 30 min) of CCK than released in the long-chain triglycerides perfusion experiment, did not suppress gastric acid secretion. Thus, circulating cholecystokinin appears not responsible for the inhibition of gastrin-stimulated gastric acid secretion by dietary fat.

*Keywords:* Gastric acid secretion; Cholecystokinin; Long-chain triglyceride; Medium-chain triglyceride; Pancreatic polypeptide

## 1. Introduction

The regulation of gastric acid secretion is important, since gastric acid is involved in the pathogenesis of frequently occurring diseases, like reflux oesophagitis and peptic ulcers. The presence of nutrients in the small intestine inhibits gastric acid secretion in many species, including humans [1–4]. The term 'enterogastrone' has been introduced [5] to describe the undefined intestinal factor(s) responsible for this effect. In humans cholecystokinin (CCK) appears to be involved [6,7], but other enterohormones such as secretin [8], somatostatin [9], pancreatic polypeptide, peptide YY [10], gastric inhibitory polypeptide [11] and neurotensin [12] have also been put forward. We have earlier demonstrated that long-chain triglycerides but not medium-chain triglycerides (MCT) are potent stimuli for the release of CCK and for gallbladder contraction in humans [13]. We question now whether long-chain and medium-chain triglycerides also differ in their effects on gastrin stimulated gastric acid secretion and whether CCK, infused to plasma concentrations somewhat higher than found during perfusion of the duodenum with long-chain triglycerides, was able to inhibit gastrin-stimulated gastric acid secretion.

## 2. Materials and methods

### 2.1. Subjects

Eight healthy male volunteers (20–25 years) participated in the studies. Body mass indexes ranged from 22 to 29 kg/m$^2$. None of the subjects had a history of gastro-intestinal diseases or surgery and none was taking any medication. One volunteer smoked cigarettes. The study protocol was approved by the Medical Ethical Committee of the University Hospital Nijmegen, and written informed consent was obtained from each volunteer.

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*PII* S0167-0115(96)00111-5

### 2.2. Materials

Synthetic non-sulphated gastrin-17 for intravenous infusion was purchased from Cambridge Research Biochemicals (UK). It was dissolved under aseptic conditions in saline containing 2% human serum albumin and stored at −20°C. Highly purified porcine cholecystokinin-33 for intravenous infusion was purchased from Ferring (Malmö, Sweden). Synthetic human $CCK_{33}$ for radioimmunoassay was purchased from Peninsula Laboratories (St. Helens, UK); radioiodinated porcine PP ($^{125}$I-PPP) from Novo Nordisk AS (Bagsvaerd, Denmark). MCT (Ceres-MCT-dietary oil) containing 56% octanoic acid ($C_8$) and 43% decanoic acid ($C_{10}$), was from Bakker (Etten-Leur, The Netherlands). LCT (corn oil), containing 10% palmitic acid ($C_{16:0}$), 27% oleic acid ($C_{18:1}$) and 57% linoleic acid ($C_{18:2}$) was from Genfarma (Maarsen, The Netherlands).

### 2.3. Experimental design

MCT, LCT or saline was perfused intraduodenally in random order on different days separated by at least 1 week. In a fourth experiment, six of the 8 volunteers were also given intravenous CCK. After an overnight fast, the volunteers presented at the gastro-intestinal research laboratory at 7:30 a.m. A single-lumen polyvinyl perfusion catheter was placed into the proximal duodenum under fluoroscopic control (in the first three experiments) and a polyvinyl gastric drainage tube into the stomach together with a small-bore polyethylene perfusion catheter inserted into one of the three side holes of the gastric drainage tube (in all four experiments). The position of this tube was checked by the water recovery method [14]. Subsequently, the small-bore gastric polyethylene perfusion tube was pulled back about 10 cm, to release it from the drainage tube. The stomach was emptied and subsequently perfused continuously through the small bore polyethylene perfusion tube with a saline solution containing 3 mg/l of phenol red at a rate of 120 ml/15 min. Gastric contents were aspirated continuously during the experiments 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. The catheters were kept patent by a heparin-saline solution. One catheter was used for the collection of blood samples and the other for the infusion of non-sulphated gastrin-17 at a dose of 10 pmol/kg per h. This dose produces plasma gastrin concentrations similar to those found after a meal [15]. 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 2.5 h (Fig. 1). During the final 1.5 h of the experiments either saline (60 ml), or equimolar amounts (60 mmol/60 ml) of MCT or LCT were perfused intraduodenally at a rate of 40 ml/h. In the fourth experiment cholecystokinin was infused intravenously during the final 1.5 h of the experiment in a dose of 1.1 ± 0.2 pmol/kg per h as measured from the tip of the infusion line. No intraduodenal tube was inserted in this experiment. Immediately after the experiments, blood samples were centrifuged for 15 min at 4000 rpm and plasma was stored at −20°C. The volume and pH of each 15-min gastric juice sample was recorded, and the $H^+$ concentration was determined by titration to pH 7.0 with 0.1 M NaOH. Subsequently, gastric samples were filtrated and alkalized with 2.5 M NaOH and the concentration of phenol red was measured spectrophotometrically at 560 nm. Recovery of gastric juice was calculated by the equation: $(V_A \times ABS_A)/(V_P \times ABS_P)$, in which $V_A$ represents the aspirated volume, $ABS_A$ the phenol red absorption of the aspirated volume, $V_P$ the perfused volume and $ABS_P$ the phenol red absorption of the perfused volume, each per 15-min period. The amount of acid secreted (mmol/15 min) was calculated as follows: (acid concentration measured) × $V_A$/recovery.

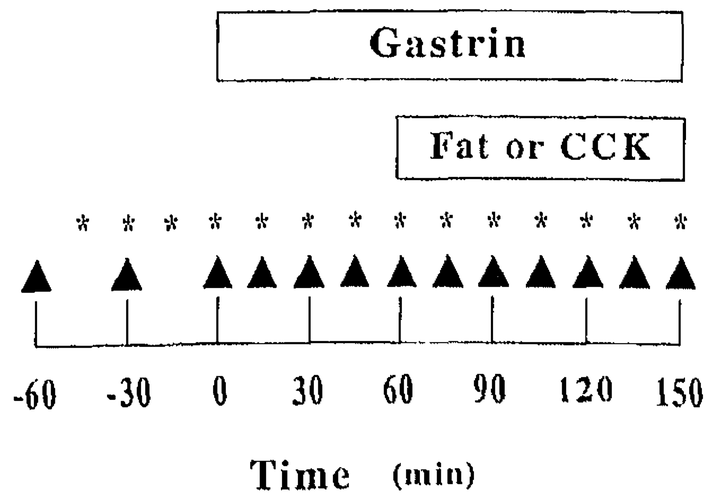


Fig. 1. Design for the three experiments performed in random order in eight subjects and for the fourth experiment in six subjects. In all experiments the stomach was continuously perfused with a saline solution containing 3 mg/l phenol red at a rate of 8 ml/min. Each experiment consisted of the following periods: (a) a basal period of 60 min; (b) an intravenous infusion period of gastrin at a dose of 10 pmol/kg per h for 60 min; and (c) an intraduodenal perfusion/infusion period of equimolar amounts (40 mmol/h) of long-chain triglycerides, medium-chain triglycerides, or saline (60 ml) or intravenous cholecystokinin (1.1 ± 0.2 pmol/kg per h) for 90 min. Blood sampling for the measurement of plasma gastrin and cholecystokinin is indicated by triangles. Gastric juice was collected continuously and sampled at 15-min intervals (*).

Gastrin, CCK and PP concentrations in plasma were measured by sensitive and specific radioimmunoassays as previously described [16–19].

### 2.4. Data analysis

Results are expressed as mean ± SEM unless stated otherwise.

Basal gastric acid output is defined as the sum of the last two 15-min portions obtained under unstimulated conditions. Gastrin-stimulated gastric acid output is defined as

the sum of the last two 15-min portions obtained during the first hour of gastrin-17 infusion. The percentage of inhibition by saline, MCT, LCT or CCK on gastric acid secretion was calculated as follows:

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

in which $t_{45}+t_{60}$ are the amounts of gastric acid produced during the final 30 min before fat perfusion and $t_{135}+t_{150}$ are those produced during the final 30 min of the fat perfusion period (Fig. 1). Integrated plasma CCK and PP concentrations for the last 30 min of each experimental period are calculated by using the trapezoidal rule as area under the serum concentration vs. time curves.

Statistical analysis was performed by two-way ANOVA and the Student's *t*-test for paired results. All *P*-values are two-tailed.

## 3. Results

### 3.1. Plasma gastrin concentrations

Infusion of gastrin increased plasma gastrin concentrations from basal concentrations of 26 ± 4 to 50 ± 6 pM in the saline experiment, from 20 ± 3 to 46 ± 4 pM in the MCT experiment, from 25 ± 4 to 55 ± 5 pM in the LCT and from 20 ± 3 to 46 ± 4 pM in the CCK-infusion experiment (means ± SEM). Duodenal perfusion of saline, MCT or LCT or intravenous infusion of CCK did not significantly affect these plasma gastrin concentrations.

### 3.2. Plasma cholecystokinin and pancreatic polypeptide concentrations

As shown in Tables 1 and 2, saline perfusion had no effect on plasma CCK. Perfusion of MCT had no effect either. Perfusion of LCT stimulated integrated plasma CCK concentrations by 25% ($P = 0.004$) vs. saline (Table 1). In experiment four, integrated plasma CCK concentrations were more than doubled during cholecystokinin infusion (Table 2). Cholecystokinin infusion resulted in a significant increase in plasma pancreatic polypeptide concentrations (Table 3).

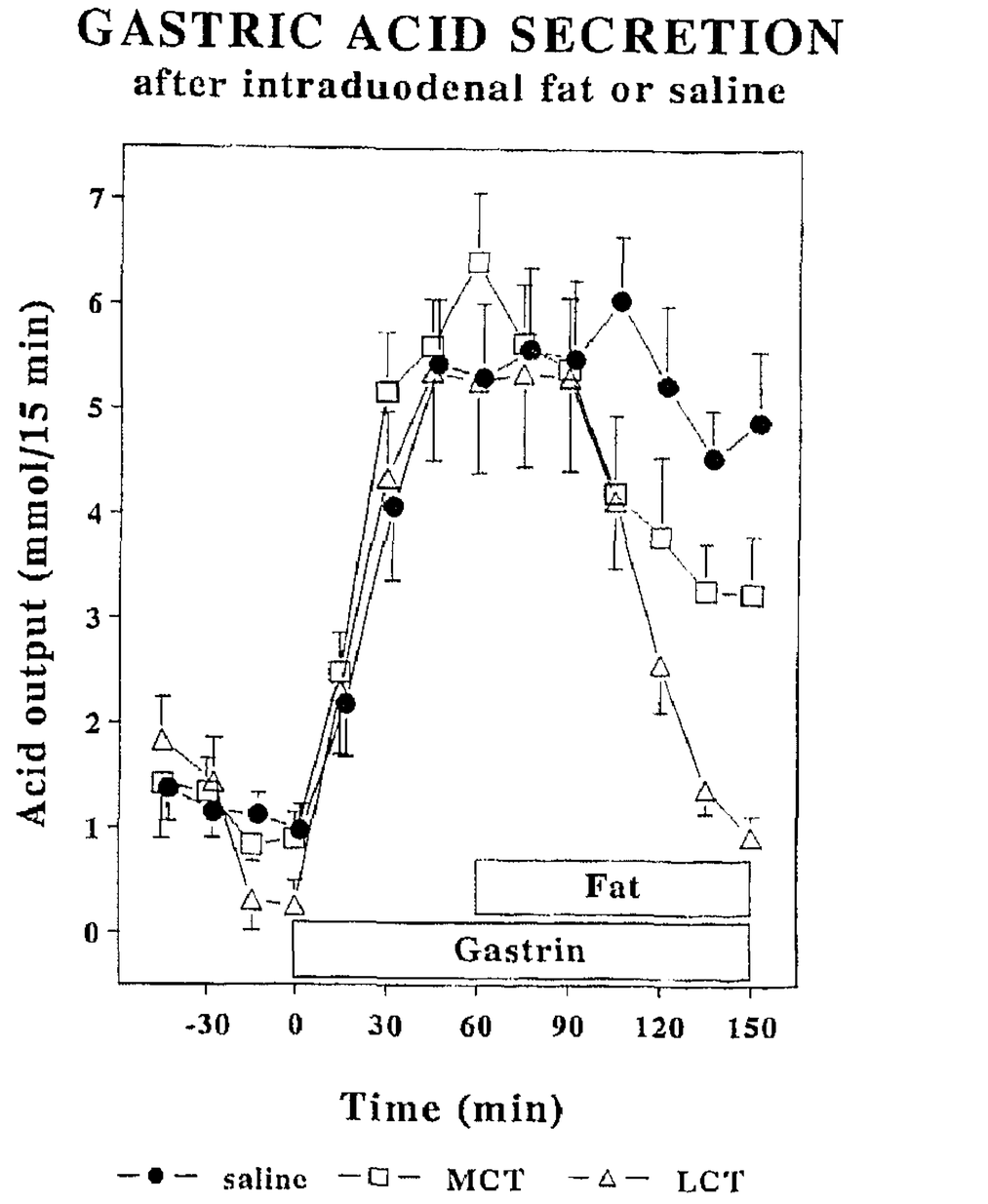


Fig. 2. Mean gastric acid output ± SEM in eight volunteers under basal conditions and during intravenous infusion of gastrin (10 pmol/kg per h), subsequently combined with intraduodenal administered long-chain triglycerides (40 mmol/h; △), medium-chain triglycerides (40 mmol/h; □) or saline (60 ml; ●).

### 3.3. Gastric acid secretion

Infusion of gastrin markedly stimulated basal gastric acid output (Tables 4 and 5). Intraduodenal perfusion of MCT suppressed gastrin stimulated gastric acid secretion by 43% compared to saline; LCT resulted in a more marked suppression of 74% (Table 4 and Fig. 2). In the CCK-infusion experiment, absolute levels of acid output were somewhat lower before CCK infusion than before

Table 1
Effect of LCT and MCT on plasma cholecystokinin concentrations

| Treatment | Plasma cholecystokinin | | | |
|---|---|---|---|---|
| | Basal (pM × 30 min) | Gastrin (pM × 30 min) | Gastrin + Fat or Saline (pM × 30 min) | Change (pM × 30 min) |
| Saline | 84.2 ± 5.5 | 71.8 ± 6.1 | 73.1 ± 6.1 | 1.3 ± 5.3 |
| MCT | 80.4 ± 4.1 | 70.9 ± 6.1 | 64.6 ± 6.8 | −4.8 ± 4.2 |
| LCT | 92.4 ± 4.4 | 76.7 ± 4.8 | 95.7 ± 5.2 | 19.0 ± 4.1 [a,b] |

Mean integrated plasma cholecystokinin concentrations ± SEM before intravenous gastrin infusion (basal), during intravenous gastrin infusion, and during intraduodenal perfusion of long-chain triglycerides (LCT), medium-chain triglycerides (MCT) or saline in combination with intravenous gastrin infusion in eight subjects. Changes are the effect of fat perfusion during gastrin infusion relative to gastrin infusion alone.
[a] Compared to saline, $P = 0.0039$.
[b] Compared to MCT, $P = 0.0042$.

Table 2
Cholecystokinin concentrations after intravenous cholecystokinin infusion

| Treatment | Plasma cholecystokinin | | | |
|---|---|---|---|---|
| | Basal (pM × 30 min) | Gastrin (pM × 30 min) | Gastrin + CCK or Saline (pM × 30 min) | Change (pM × 30 min) |
| Saline | 86.0 ± 7.3 | 74.9 ± 7.7 | 84.8 ± 8.1 | 9.9 ± 3.6 |
| CCK | 81.3 ± 6.2 | 82.6 ± 12.8 | 191.4 ± 4.5 | 108.8 ± 10.5 |

Mean integrated plasma cholecystokinin concentrations ± SEM before intravenous gastrin infusion (basal), during intravenous gastrin infusion, and during intravenous infusion of saline or cholecystokinin in six subjects. Intravenous gastrin infusion was continued during saline or CCK infusion. Changes are the effect of CCK infusion combined with gastrin infusion relative to gastrin infusion alone.

saline (Fig. 3; $t = 30$ to $t = 60$ min). However, gastric acid secretion was not inhibited by CCK relative to control (Table 5 and Fig. 3; 120–150 min vs. 30–60 min).

## 4. Discussion

Our first objective was to determine whether long-chain and medium-chain triglycerides have different effects on gastrin-stimulated gastric acid secretion, since we have earlier demonstrated that long-chain triglycerides but not medium-chain triglycerides are potent stimuli for the release of CCK and for gallbladder contraction in humans [13]. We have found that intraduodenal perfusion of fat mainly composed of long-chain triglycerides as well as fat composed of medium-chain triglycerides suppressed gastrin-stimulated gastric acid secretion in humans, MCT being less potent than LCT.

Our finding that fat composed of medium-chain triglycerides did not evoke an increase in the release of cholecystokinin, in contrast to fat mainly composed of long-chain triglycerides agrees with previous studies [13,20,21].

Our second objective was to examine the role of CCK in the inhibition of gastrin-stimulated gastric acid secretion. We showed in the present study that circulating CCK plays no role in MCT-induced inhibition of gastrin-stimulated gastric acid secretion and also that infusion of CCK did not inhibit gastrin-stimulated gastric acid secretion.

Our results suggest that the chain-length of the constituent fatty acids is not only important for the release of CCK, but also for the enterogastrone effect of fat.

The situation in humans is in contrast to what has been found in rats. In rats medium-chain triglycerides evoke a greater CCK-release than triglycerides with longer chain lengths as measured by the same radioimmunoassay [22]. The reason for this discrepancy is not obvious, but it suggests important species differences with respect to plasma CCK release [23].

In previous studies it was found that isocaloric amounts of fat, protein, and carbohydrates similarly inhibit gastric emptying [24,25]. The different inhibitory effect of medium-chain triglycerides and long-chain triglycerides on gastric acid secretion might also be explained by differences in caloric load between the long-chain and medium-chain triglycerides. So far, the effect of caloric load of different nutrients on gastric acid secretion has only been studied in calves [26] where it was found that energy contents did not affect gastric acid secretion. Whether the effect of nutrients on gastric acid secretion in humans is dependent on the molar or caloric load of fats remains to be established. In the present study, we have chosen to compare medium-chain and long-chain triglycerides on a molar base, since previous studies suggest that the CCK stimulating capacity of nutrients is related to the molar amounts of fatty acids released by hydrolysis [27–29].

We have tested the enterogastrone effect of fat on gastrin-stimulated rather than on meal-stimulated gastric acid secretion to avoid difficulties encountered in the sampling of gastric juice after a meal. For the same reason we have administered fat intraduodenally. Despite the use of gastrin instead of food and the duodenal instead of oral administration of fat, we believe that our findings are of

Table 3
Pancreatic polypeptide concentrations after intravenous cholecystokinin infusion

| Treatment | Plasma pancreatic polypeptide | | | |
|---|---|---|---|---|
| | Basal (pM × 30 min) | Gastrin (pM × 30 min) | Gastrin + CCK or Saline (pM × 30 min) | Change (pM × 30 min) |
| Saline | 465 ± 21 | 434 ± 24 | 470 ± 47 | 36 ± 43 |
| CCK | 455 ± 26 | 444 ± 61 | 759 ± 159 | 315 ± 136 * |

Mean integrated plasma pancreatic polypeptide concentrations ± SEM before intravenous gastrin infusion (basal), during intravenous gastrin infusion, and during intravenous infusion of saline or cholecystokinin in six subjects. Intravenous gastrin infusion was continued during saline or CCK infusion. Changes are the effect of CCK infusion combined with gastrin infusion relative to gastrin infusion alone.

* $P = 0.048$.

Table 4
Effect of LCT and MCT on gastrin-stimulated gastric acid secretion

| Treatment | Gastric acid output | | | |
|---|---|---|---|---|
| | Basal (mmol/30 min) | Gastrin (mmol/30 min) | Gastrin + Fat or Saline (mmol/30 min) | Change (%) |
| Saline | 2.1 ± 1.24 | 10.8 ± 3.7 | 9.4 ± 3.1 | 9.4 ± 6.5 |
| MCT | 1.7 ± 1.1 | 12.0 ± 2.9 | 6.5 ± 2.6 | −43.0 ± 9.1 [a] |
| LCT | 2.6 ± 1.5 | 10.6 ± 4.8 | 2.3 ± 0.9 | −74.3 ± 6.2 [b,c] |

Mean gastric acid output ± SEM before gastrin infusion (basal), during gastrin 17-I infusion and during (A) intraduodenal perfusion of long-chain triglycerides (LCT), medium-chain triglycerides (MCT) or saline in eight subjects. Intravenous gastrin infusion was continued during the intraduodenal perfusion of fat or saline. Changes are the effect of fat perfusion during gastrin infusion relative to gastrin infusion alone.
[a] Compared to saline, $P = 0.0426$.
[b] Compared to saline, $P = 0.0003$.
[c] Compared to MCT, $P = 0.0499$.

physiological relevance. Firstly, infusion of gastrin resulted in plasma gastrin concentrations in the same range as observed after a meal [15]. Secondly, gastrins are the major factor responsible for postprandial gastric acid secretion [30]. Thirdly, gastrin-17 is the major molecular form of gastrins released in response to a meal [31], whereas non-sulphated gastrin-17 is equipotent to sulphated gastrin-17 in stimulating gastric acid secretion [32], and finally, we have perfused fat into the duodenum at a rate that was comparable to the gastric emptying rate of fat after a meal [33].

The mechanisms through which nutrients inhibit gastric acid secretion when they enter the small intestine, the so called enterogastrone effect, are not clear. Several possibilities have been suggested [7,9–12,34]. Of old, one of the most important enterogastrone candidates is CCK [7]. In previous studies, infusion of high, probably supraphysiological, doses of CCK inhibited gastric acid secretion [35]. Recent studies with CCK receptor antagonists also support an inhibitory effect of endogenous CCK on gastric acid secretion, since specific type A CCK-receptor antagonists augmented basal as well as stimulated gastric acid output [36–41]. However, in the present study infusion of CCK did not inhibit gastric acid secretion, and medium chain triglycerides were able to inhibit gastric acid secretion without concomitant release of CCK. Therefore, MCT-induced inhibition of gastric acid secretion acts via another mechanism. It might be that CCK has an additive effect in case of LCT-induced inhibition of gastric acid secretion. We have investigated this possibility in two subjects by combining intraduodenal perfusion of MCT with intravenous infusion of CCK. However, the inhibition of gastrin-stimulated gastric acid secretion in these 2 subjects was comparable to the effect found during intraduodenal perfusion of MCT without CCK infusion (data not shown). Therefore the present findings suggest that circulating CCK is not responsible for the enterogastrone effect of MCT, since MCT did not stimulate CCK release into the circulation. Furthermore, it is not likely that the more potent inhibitory effect of LCT on gastrin stimulated gastric acid secretion when compared to MCT is a result of the ability of LCT to release CCK.

Absence of suppression of gastric acid secretion by CCK-33 infusion in the present study agrees with the observation that intravenous infusion of CCK-8, inducing plasma CCK increments within the physiological range, did not significantly alter gastrin stimulated gastric acid secretion [42]. Absence of acid suppression by CCK in our study was not related to lack of biological activity of CCK, since CCK infusion markedly stimulated the release of pancreatic polypeptide [43–45].

Although our data are in contrast with a role of CCK as an enterogastrone, it can not be excluded that CCK acts locally as a neurotransmitter or neuromodulator to inhibit gastric acid secretion, since specific cholecystokinin receptor antagonists augment gastric acid secretion in previous experiments [36–41].

Our finding that circulating CCK does not inhibit gastrin-stimulated gastric acid secretion, does not exclude that other peptides might be involved in the inhibition of

Table 5
Effect of CCK infusion on gastrin-stimulated gastric acid secretion

| Treatment | Gastric acid output | | | |
|---|---|---|---|---|
| | Basal (mmol/30 min) | Gastrin (mmol/30 min) | Gastrin + CCK or saline (mmol/30 min) | Change (%) |
| Saline | 2.5 ± 0.9 | 10.8 ± 0.6 | 8.9 ± 0.5 | −16.7 ± 4.3 |
| CCK | 2.8 ± 0.9 | 8.6 ± 1.5 | 6.9 ± I.1 | −17.9 ± 6.7 |

Mean gastric acid output ± SEM before gastrin infusion (basal), during gastrin 17-I infusion and during intravenous infusion of cholecystokinin (CCK) or saline in six subjects. Intravenous gastrin infusion was continued during the intravenous infusion of cholecystokinin or saline. Changes are the effect of CCK infusion combined with gastrin infusion relative to gastrin infusion alone.

Table 4
Effect of LCT and MCT on gastrin-stimulated gastric acid secretion

| Treatment | Gastric acid output | | | |
|---|---|---|---|---|
| | Basal (mmol/30 min) | Gastrin (mmol/30 min) | Gastrin + Fat or Saline (mmol/30 min) | Change (%) |
| Saline | 2.1 ± 1.24 | 10.8 ± 3.7 | 9.4 ± 3.1 | 9.4 ± 6.5 |
| MCT | 1.7 ± 1.1 | 12.0 ± 2.9 | 6.5 ± 2.6 | −43.0 ± 9.1 [a] |
| LCT | 2.6 ± 1.5 | 10.6 ± 4.8 | 2.3 ± 0.9 | −74.3 ± 6.2 [b,c] |

Mean gastric acid output ± SEM before gastrin infusion (basal), during gastrin 17-I infusion and during (A) intraduodenal perfusion of long-chain triglycerides (LCT), medium-chain triglycerides (MCT) or saline in eight subjects. Intravenous gastrin infusion was continued during the intraduodenal perfusion of fat or saline. Changes are the effect of fat perfusion during gastrin infusion relative to gastrin infusion alone.
[a] Compared to saline, $P = 0.0426$.
[b] Compared to saline, $P = 0.0003$.
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| Saline | 2.5 ± 0.9 | 10.8 ± 0.6 | 8.9 ± 0.5 | −16.7 ± 4.3 |
| CCK | 2.8 ± 0.9 | 8.6 ± 1.5 | 6.9 ± 1.1 | −17.9 ± 6.7 |

Mean gastric acid output ± SEM before gastrin infusion (basal), during gastrin 17-I infusion and during intravenous infusion of cholecystokinin (CCK) or saline in six subjects. Intravenous gastrin infusion was continued during the intravenous infusion of cholecystokinin or saline. Changes are the effect of CCK infusion combined with gastrin infusion relative to gastrin infusion alone.

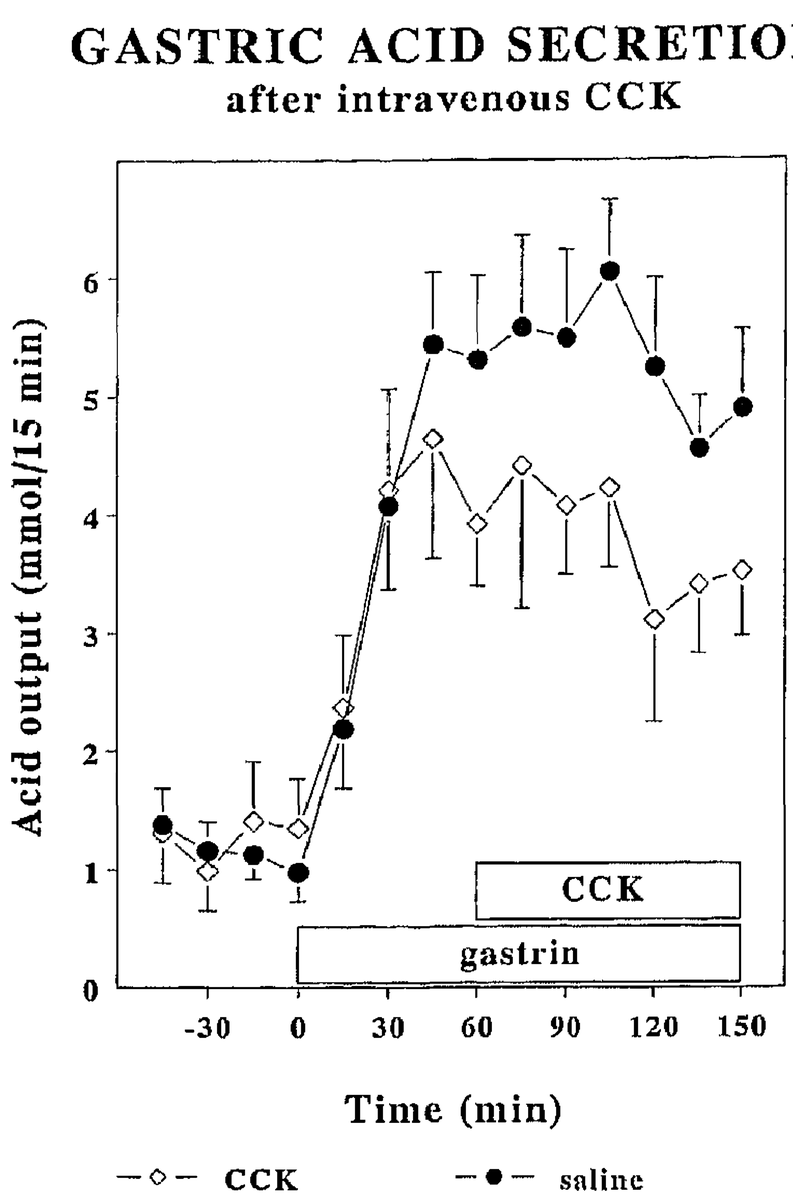


Fig. 3. Mean gastric acid output ± SEM in six volunteers under basal conditions and during intravenous infusion of gastrin (10 pmol/kg per h), subsequently combined with intraduodenal administered saline (60 ml; ●) or intravenously administered cholecystokinin (1.1 ± 0.2 pmol/kg per h; ◇).

gastrin-stimulated gastric acid secretion by long-chain and medium-chain triglycerides. Possible candidates include neurotensin, peptide YY, somatostatin, secretin, and gastric inhibitory peptide. Neurotensin is a hormone that might inhibit gastric acid secretion. It is released in response to fat in the intestine and requires vagal integrity for full activity [46]. However, it has been shown that the concentrations of neurotensin released by fat are insufficient to account for the inhibition of gastric acid secretion caused by fat ingestion [12].

Somatostatin is established as an important inhibitor of several gastro-intestinal functions, including gastric acid secretion [47–53]. It is well known that fat is a stimulant for somatostatin release [54] but whether medium-chain triglycerides are also able to stimulate the release of somatostatin is presently unknown. Secretin has also been shown to be an inhibitor of gastric acid secretion in dogs [8,55], as well as in humans [56] although it seems less potent in humans [57].

The only hormone besides CCK and PP which is known to be released differently by long-chain and medium-chain triglycerides is gastric inhibitory polypeptide. Gastric inhibitory peptide is released more potently by long-chain than by medium-chain triglycerides in dogs [58] whereas in humans it was found to be released by long-chain triglycerides but not by medium-chain triglycerides [59]. In dogs gastric inhibitory peptide seems to be an important enterogastrone [60], but in humans its inhibitory potency is relatively weak [60,61] and it cannot fully account for the inhibition of gastric acid secretion by fat. The best candidate to explain the enterogastrone effect of fat is PYY. Circulating concentrations of peptide YY released after fat ingestion have been shown to be nearly sufficient to account for acid inhibition in dog [62] and man [63]. In addition, it has been shown in rats that PYY can inhibit pentagastrin stimulated gastric acid secretion [64]. But, whether MCT has different effects on PYY release than LCT remains to be established. However, it is more likely to suggest that no single peptide accounts for the full enterogastrone effects of fat in the intestine but that combinations of peptides exert a cumulative inhibitory effect as shown in humans for secretin and PYY [65].

In conclusion, the present study demonstrated that the enterogastrone effect of fat is dependent on the chain-length of fatty acids, and that the enterogastrone effect of MCT is not explained by the release of CCK into the circulation. Furthermore, exogenous CCK in physiological concentrations did not inhibit gastrin stimulated gastric acid secretion. Our findings thus cast doubt on the enterogastrone role of CCK, especially regarding dietary fat.

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