Effect of oral versus gastric delivery on gastric emptying of corn oil emulsions

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Kaplan, Joel M., William Siemers, and Harvey J. Grill. Effect of oral versus gastric delivery on gastric emptying of corn oil emulsions. Am. J. Physiol. 273 (Regulatory Integrative Comp. Physiol. 42): R1263–R1270, 1997.—Several studies have shown that fluids delivered to the stomach tend to empty more rapidly than when ingested by mouth. To better characterize the “delivery route effect” for corn oil, rats received intragastric or intraoral infusions matched for concentration and for the rate and duration of stimulus delivery. We showed, first, that more than twice as much oil emptied by the end of 12-min intragastric versus intraoral infusions but that the emptying curves remained roughly parallel for 1 h after infusion offset. Remaining experiments therefore focused on stimulus parameters of relevance to emptying control during stomach fill. Emptying during intraoral infusions approximately doubled with doublings of oil concentration (25–50%), infusion duration (6–12 and 12–24 min), and infusion rate (0.5–1.0 ml/min). Emptying during intraoral infusions, by contrast, was entirely unaffected by these manipulations. Unlike oil emptying, glucose emptying did not vary as a function of delivery route. The nutrient specificity of the delivery route effect cannot be explained in terms of energy density, as the effect was obtained for oil but not for glucose when their energy densities were equated (50% glucose, 25% corn oil). In discussion, we suggest that the oral influence on corn oil emptying during stomach fill is a gating factor that enables the expression of inhibition derived from postgastric nutrient stimulation.

cephalic phase response; glucose; intraoral infusion; intragastric infusion; lingual lipase; feedback control

There is evidence placing gastric emptying among a number of visceral and endocrine functions influenced by the route (oral versus gastric) of nutrient delivery (review in Ref. 23). Fluids delivered directly to the stomach tend to empty more rapidly than when ingested by mouth (7, 18; see also Refs. 21, 22). This “delivery route effect” reafirms a contribution of oral stimulation in digestive physiology (20) and is relevant to studies of satiation where the researcher attempts to deliver nutritive fluids to the intestine in a manner that simulates gastric emptying during normal ingestion.

An adequate characterization of the delivery route effect will entail identification of which mechanisms of gastric emptying control are influenced by oral versus gastric delivery and provide inferences about the integration of relevant oral and postoral signals. In the present study, we provide a parametric analysis of the effects of delivery route on corn oil emptying, focusing on emptying control mechanisms that operate during versus after a load has been delivered and that control the amount emptied as functions of nutrient concentration and stimulus delivery parameters. The goal of the study is to provide functional data that offer clues about the physiological underpinnings of the delivery route effect.

One obstacle to an effective parametric analysis of the delivery route effect is the inherent difficulty in delivering a given stimulus, on different occasions, to the mouth and to the stomach at the same rates and for the same durations. This problem was overcome in the present study, where we infused the test fluids intragastrically via a gastric fistula or intraorally via an indwelling oral cannula. We developed the intraoral infusion paradigm as a model for normal fluid ingestion (e.g., Refs. 3, 9–12, 25) in the rat. For the present application, it is important to note that, despite the arbitrary nature of fluid presentation, the oral stimulatory and motor aspects of “intraoral intake” are comparable to those of spout licking in the rat. Ingestion of intraoral infusions is taste sensitive (4, 5) and, like spout licking, involves the coordination of intraoral transport (via rhythmic orolingual movements emitted at the licking frequency) and swallowing actions (9, 10, 26, 27). The special advantage of the intraoral infusion method for the present analysis lies in bringing the parameters of oral and gastric fluid delivery into explicit register. Our assessment of the role of the oral factor in gastric emptying control, therefore, is not subject to the behavioral variability (e.g., in ingestion rate and pausing during ingestion) of standard fluid ingestion tests and can be anchored to the progress and termination of the period of gastric fill.

Previous work with rats receiving intragastric infusions of glucose (13) revealed differences in gastric emptying control during versus after the stomach fill period. After fill, solute emptying was stable over time and not affected by changes in stimulus concentration. During gastric fill, solute emptying rate was considerably higher than after termination of fluid delivery and varied broadly with stimulus concentration. This distinction prompted us to ask whether the delivery route effect is expressed in both phases of emptying control. We describe (expt 1) an effect of delivery route that, interestingly, was entirely restricted to the fill period. Remaining experiments therefore focused on parameters that influence emptying during stomach fill. In our previous work (13), glucose emptying during fill varied with stimulus concentration (as noted) and also with the rate and duration of fluid delivery. The same stimulus parameters were manipulated here (expts 2–4) to determine their general influence on during-fill emptying of corn oil and, in particular, whether such effects vary as a function of route of fluid delivery.
We also addressed the nutrient specificity of the delivery route effect. Ramirez found a delivery route effect for gastric emptying of corn oil (21, 22) but little or no such effect for glucose (23, 24). We attempted (expt 4) to replicate this finding using matched intraoral and intragastric infusions and to determine whether between-stimulus differences can be reconciled with respect to caloric density.

**GENERAL METHODS**

**Subjects**

A total of 20 adult male Sprague-Dawley rats (Charles River, Kingston, NY) weighing 350–400 g at the time of surgery were used. Rats were housed individually in hanging cages with food (Purina Rat Chow no. 5001) and water available ad libitum. Tests were run during the light phase of a 12:12-h light-dark cycle, with individual rats tested at the same time each day.

**Surgery**

Rats were deprived of food 17–24 h, deeply anesthetized with a ketamine and xylazine (87 and 13 mg/kg) mixture, and implanted with a stainless steel gastric fistula and two intraoral cannulas. An oral cannula was positioned just anterior to the first maxillary molar on each side, and they were led intramuscularly to the top of the head, where they were fixed to the skull with jeweler’s screws and dental acrylic (see Ref. 5 for details). During the same surgical procedure, a gastric cannula was implanted in the ventral forestomach according to the procedure of Weinberg and Powley (28).

**Apparatus**

Rats were tested in rectangular Plexiglas chambers. A syringe infusion pump (Harvard Apparatus Pump 44) was used for both intraoral and intragastric infusions. Infusions were gated to the rat by a manual three-way valve mounted on the syringe. The intraoral infusion line was led from the valve to a fluid commutator mounted in the top of the cage and from there to the rat. Intragastic infusions were delivered through Tygon tubing that was led to the rat though an opening at the base of the testing chamber’s front panel.

**Procedure**

One hour before an intraoral or intragastric infusion, the cannula screw was removed and the stomach was gently rinsed with 5-ml flushes of isotonic saline until effluent was clear. The screw was replaced, and the rat was placed in a holding cage. Rats were placed in the test chamber 5 min before testing.

Intraoral and intragastric infusions. For each daily test session, rats received a single intraoral or intragastric infusion of corn oil emulsion or glucose, delivered at 1.0 ml/min (expts 1, 2, 4) or 0.5 ml/min (expt 3). Corn oil was emulsified using 4 g/l of phosphatidyl choline. Before an infusion, the distal end of the Tygon tubing was press fitted into a hollowed screw assembly. Five minutes before intragastric infusion onset, the tube was filled with the fluid stimulus and the assembly was screwed into the open gastric fistula. When the intragastric infusion was terminated, the tube was clamped at the mouth of the fistula and cut ~1.5 cm from the clamp. Five minutes before an intraoral infusion, the tube assembly was screwed into the open gastric fistula, as above. Here, the tube was clamped and cut before the beginning of the test.

Withdrawal of gastric contents. Immediately, or at a scheduled time after infusion offset, gastric contents were drawn into a 20-ml syringe inserted into the cut end of the Tygon tube. After the primary withdrawal, two 10-ml flushes of distilled water were introduced and then aspirated to collect any infusate that may remain in the stomach. Note that any solute that remains in the stomach, despite the evacuation and subsequent water flushes, would result in an overestimate of the amount emptied. We expect, however, that such measurement error would not vary systematically as a function of delivery route or other experimental variables. Our analysis and discussion of results, therefore, is focused on differences in amounts emptied across experimental conditions, rather than on absolute amounts emptied.

Analysis of gastric samples. CORN OIL. The withdrawn fluid (along with any oil return from two 10-ml water rinses) was placed in a test tube, and concentrated HCl was added to facilitate separation of organic and aqueous portions. After separation, the aqueous fraction was drained through a separation funnel. The weight of the recovered oil was subtracted from the amount of oil infused to yield an estimate of the amount (g) of corn oil emptied.

GLUCOSE. A 50-µl aliquot was taken from the withdrawn fluid. The aliquot was diluted 50× (12.5% glucose) or 200× (50% glucose), and its glucose concentration was measured using a Beckman Glucose Analyzer II. From the measured concentration, the volume withdrawn from the stomach, and the known amount of glucose infused, an estimate of the amount (g) of glucose emptied was calculated.

For all experiments, when session data could not be obtained or evaluated (e.g., due to pump problems or solid food recovered in the gastric sample), the rat was restested under the same condition the following day.

Habituation training. Over a period of 5–10 days, beginning 10 days after surgery, rats were habituated to the testing chamber, handling and gastric rinsing, and the withdrawal procedure. They then received a series of intraoral infusions with the stimulus (corn oil emulsion or glucose) they would receive in the subsequent experimental phase. They were tested once daily until intraoral intake exceeded 12 ml.

Experiment 1. Seven rats received four intraoral and four intragastric infusions of 50% corn oil emulsion. All infusions were 12 min in duration and delivered at 1.0 ml/min. Gastric contents were withdrawn at different times (0, 12, 24, 60 min) after infusion offset, with the order of sampling time counterbalanced across rats. Infusion route (intraoral vs. intragastric) was varied in an ABBA pattern for a total of eight conditions. Results were analyzed via two-way (oral vs. gastric delivery × withdrawal time) repeated-measures analysis of variance (ANOVA).

Experiment 2. Intraoral and intragastric infusions of 50% corn oil emulsion were delivered at 1.0 ml/min and matched for infusion duration and the interval between infusion onset and withdrawal of the gastric sample. Six rats (including 3 from expt 1) received three intraoral and three intragastric infusions. Three infusion durations: sample time (D:S) combinations were run. In the first condition (designated 6:6), the infusion lasted 6 min and the gastric sample was taken immediately after infusion offset. In the second (12:12), the gastric withdrawal began immediately after a 12-min infusion. In the third condition (6:12), the gastric sample was obtained 6 min after the offset of a 6-min infusion (i.e., 12 min after infusion onset). The three conditions were presented in a counterbalanced design, across which the mode of infusion (intraoral vs. intragastric) was varied in an ABBA pattern.

The overall effects of delivery route (oral vs. gastric infusion) and D:S condition on amount (g) of corn oil solute...
emptying were evaluated by a two-way repeated-measures ANOVA. Post hoc tests were run on D:S pairs within each delivery route set to explicate the two-factor interaction obtained. One comparison of interest was between amounts emptied for the 6:12 and 12:12 conditions. For both conditions, the gastric sample was withdrawn at the same time after infusion onset, but for the 12:12 condition, twice as much corn oil was infused over twice the infusion duration than for the 6:12 condition. If the rate of emptying is independent of the amount infused, the amount in the stomach, and how long the stomach is filling, then there should be no difference in amount emptied between these two conditions. We also compared amounts emptied for the 6:6 and 12:12 conditions to determine whether emptying rate differs between the two 6-min segments of a 12-min infusion.

Experiment 3. Four rats received two intragastric and two intraoral infusions of 50% corn oil delivered at 0.5 ml/min, one-half the infusion rate of expt 2. Intraoral and intragastric infusions were delivered for 12 or 24 min, with the gastric sample withdrawn in each case immediately after infusion offset (12:12, 24:24). The effects of delivery route (oral vs. gastric infusion) and infusion duration on corn oil emptying were evaluated by a two-way repeated-measures ANOVA.

Selected comparisons were made between results of expt 3 and expt 2. 1) The effect of infusion rate was evaluated by comparing the 12:12 conditions of this experiment (0.5 ml/min) and expt 2 (1.0 ml/min) in a two-way mixed-design ANOVA, with delivery route as the within-subjects factor and infusion rate as the between-subjects factor. The two-factor interaction obtained indicated that the effect of infusion rate was evaluated separately (t-test) for the intraoral and intragastric delivery conditions. 2) The previous analyses (see results: Experiment 2) revealed effects of infusion duration and infusion rate, but only for gastric delivery conditions. An additional ANOVA assessed whether emptying varies as a product of infusion duration and infusion rate, where halving the value of one parameter can be offset by doubling the other. This analysis aligns, for the gastric delivery conditions, the 12:12 and 24:24 infusion conditions of this experiment, respectively, with the 6:6 and 12:12 conditions of expt 2. For the paired conditions, the same amount of oil was infused, but with different infusion rate and duration weightings. The two-way mixed-design ANOVA treats infusion duration (12,24 vs. 6,12) as a within-subjects factor and how rate infusion and duration are varied to deliver a given amount of corn oil (i.e., twice rate × one-half duration vs. one-half rate × twice duration) as a between-subjects factor.

Experiment 4. Six rats received a series of 12-min intraoral and intragastric infusions (1.0 ml/min) of glucose (12.5 and 50%) and corn oil (25 and 50%). (Energy density was matched for 1 across-nutrient stimulus pair (50% glucose and 25% corn oil).) Gastric contents were withdrawn immediately after the offset of each infusion. Rats received one intraoral infusion and one intragastric infusion of each of the four stimuli. Four rats first received the four glucose infusions and then the four corn oil infusions; the other two rats were tested in reverse order. The two infusions of a given stimulus were presented consecutively, with one-half of the rats first receiving the intraoral infusion and the other one-half tested in reverse order. Testing order for the higher and lower concentrations of each fluid was also counterbalanced across rats. Results were analyzed for glucose and corn oil via respective two-way (oral vs. gastric delivery × concentration) ANOVAs.

RESULTS

Experiment 1

Figure 1 shows the amount (g) of corn oil emptied for samples withdrawn at various times up to 1 h after offset of 12-min intraoral and intragastric infusions. Two-way ANOVA revealed a significant effect of delivery route (intraoral vs. intragastric) [F(1,6) = 33.69, P < 0.001] and sample time [F(3,18) = 6.61, P < 0.003]. The roughly parallel appearance of the emptying curves for intraoral and intragastric conditions is underscored by the lack of a significant two-factor interaction [F(3,18) = 1.08, NS]. (The modest apparent reduction in the intraoral/intragastric difference over the first 3 sample times was not statistically reliable.) These results indicate that the delivery route effect is fully expressed by the end of the 12-min infusions.

Experiment 2

A two-way ANOVA (see General Methods) revealed significant effects of delivery route (intraoral vs. intragastric) [F(1,5) = 31.85, P = 0.002] and D:S condition [F(2,10) = 33.64, P < 0.001] (see Fig. 2). Most interesting was the significant interaction [F(2,10) = 11.43, P < 0.003] between the two factors. Starkly different emptying profiles for intraoral and intragastric infusion conditions underlie this interaction. The distinction is characterized by post hoc tests for D:S condition pairs within each delivery route set, as follows.

Intraoral infusion. No significant difference was obtained for any comparison among the intraoral infusion conditions (Fig. 2, solid bars). All measurable emptying for a 12-min infusion, therefore, occurs within the first 6 min of intraoral intake. An estimate of ~0.5 g emptied was obtained for all three conditions, which, for the 12-min infusion (12:12), represents 12.5% of the oil infused. As noted in General Methods, some unknown portion of the emptying estimate may be ascribed to
corn oil that remains in the stomach despite syringe aspiration and collection of any oil return from two 10-ml water rinses. It should be granted, however, that such estimation error should not vary systematically with the experimental treatment.

Intragastric infusion. There was no significant increase in amount emptied from the 6:6 to 6:12 conditions. This result indicates that emptying rate slowed dramatically once the 6-min infusion was terminated to a level within the measurement error of the gastric sample taken 6 min later. By contrast, the amount of oil emptied after a 6-min infusion increased dramatically if the infusion was sustained throughout the 12-min sample interval (6:12 vs. 12:12 comparison: P < 0.01). A similar increase in amount emptied, an approximate doubling, was obtained from the 6:6 to the 12:12 conditions (P < 0.02). These results show that emptying of intragastrically infused 50% corn oil varied directly with infusion duration.

Experiment 3

The overall effects of intraoral versus intragastric infusion and infusion duration on emptying of corn oil delivered at 0.5 ml/min were evaluated by a two-way ANOVA. A significant main effect was obtained for delivery route [F(1,3) = 53.40, P = 0.005]. There was no overall effect of infusion duration [F(1,3) = 3.51, P = 0.158]. A two-factor interaction, however, was obtained [F(1,3) = 17.41, P < 0.05]. The nature of the interaction is clear from inspection of Fig. 3 and from the corresponding post hoc t-tests. There was no significant difference in oil emptying for the intragastral infusion conditions (t = 0.55, NS), but a significant increase (a doubling) in amount emptied attended the doubling of intragastric infusion rate (t = 5.73, P < 0.001).

Given the significant effects of infusion rate (above) and of infusion duration (expts 2 and 3) for intragastrically delivered corn oil, we asked whether the effect of halving the value of one parameter is offset by a doubling of the other. The 12- and 24-min intragastric infusions of expt 3 (Fig. 3, left and right solid bars) were compared, respectively, with the 6- and 12-min intragastric conditions of expt 2 (Fig. 2, left and right solid bars), where the same amounts of oil were delivered but at one-half the rate and for twice the duration. The corresponding two-way ANOVA (see General Methods) revealed a significant effect of doubling the amount infused via infusion duration doubling (6 to 12 min, 12 to 24 min) [F(1,8) = 23.65, P < 0.001], in agreement with the separate analyses of the experiments. There was no effect, however, of how a given amount of corn oil was delivered (twice rate × one-half duration vs. one-half rate × twice duration) [F(1,8) = 1.81, NS] and no two-factor interaction [F(1,8) = 0.02, NS]. The latter results are consistent with the suggestion that the more oil emptied during 24-min intragastric infusions than during intraoral infusions of the same duration (P < 0.005).

A significant effect of infusion rate was obtained when the 12-min infusion conditions of this and the previous experiment (0.5 and 1.0 ml/min, respectively) were compared [F(1,8) = 22.95, P < 0.001]. The two-way ANOVA also revealed a significant effect of delivery route [F(1,8) = 55.27, P < 0.001] and a significant rate × delivery route interaction [F(1,8) = 23.36, P < 0.001]. The nature of the interaction is clear from inspection of the relevant portions of Fig. 2 (right) and Fig. 3 (left) and from the corresponding post hoc t-tests. There was no significant difference in oil emptying for the intraoral infusion conditions (t = 0.55, NS), but a significant increase (a doubling) in amount emptied attended the doubling of intragastric infusion rate (t = 5.73, P < 0.001).

![Graph showing mean oil emptied during different infusion durations](http://ajpregu.physiology.org/Downloaded/from)
emptying of intragastrically infused corn oil varies as the simple product of infusion rate and duration.

Experiment 4

For glucose (Fig. 4), there was no main delivery route effect \([F(1,5) = 0.05, \text{NS}]\) and no two-factor interaction \([F(1,5) = 0.06, \text{NS}]\). Glucose emptied approximately doubled when glucose concentration was increased from 12.5 and 50\% (see Fig. 4, left and right), yielding a significant main effect for concentration \([F(1,5) = 9.79, P = 0.026]\).

For corn oil (Fig. 5), we obtained significant main effects of delivery route \([F(1,5) = 50.72, P < 0.001]\) and concentration \([F(1,5) = 15.33, P = 0.011]\), as well as a significant two-factor interaction \([F(1,5) = 11.23, P = 0.02]\). The increase (a doubling) in amount of oil emptied as intragastrically infused oil concentration doubled from 25 to 50\% was significant \((P < 0.01; \text{Fig. } 4, \text{ solid bars})\). There was, however, no suggestion that oil concentration influenced emptying when oil was delivered by intraoral infusion (Fig. 5, open bars).

Table 1 summarizes the corn oil infusion conditions for the four experiments and lists the mean (±SE) gastric volumes recovered for each condition.

**DISCUSSION**

The contrasts between the emptying profiles for intraorally and intragastrically infused corn oil were dramatic. A delivery route effect for corn oil was expected on the basis of previous work (e.g., Refs. 21–23). However, the increase in oil emptying shown here for intragastric infusion conditions, where substantial amounts of corn oil were infused (e.g., 12-min infusions of 50\% corn oil), are the largest (2- to 4-fold) yet reported. The size and reliability of the effect recommend the matched intraoral/intra gastric infusion paradigm for further analyses of the oral contribution to gastric emptying control.

The delivery route effect was not uniformly expressed across experimental conditions. Experiment 1 revealed an effect during, but not in the 60 min after termination of, corn oil infusion. The delivery route effect, therefore, did not outlast the treatment. This finding focused the remaining experiments on variables that affect gastric emptying during fill and their interaction with route of corn oil delivery. In each experiment, the interaction took the same form. During intragastric fill, the amount of oil emptied was influenced broadly by each treatment (concentration, infusion duration, and infusion rate: expts 2-4), whereas no treatment affected emptying when the oil was orally ingested.

Results of expt 2 showed that the delivery route effect was not uniformly expressed within the time frame of a 12-min infusion. For intraoral infusions, all measurable emptying occurred by the end of the first 6-min segment (compare 6:6 and 12:12 conditions, Fig. 2). For intragastric infusions, in contrast, twice as much corn oil emptied during the 12-min infusion than the 6-min infusion, indicating that the rate of emptying
was stable throughout the 12-min-infusion interval. Little emptied, however, in the 6 min after the termination of 6-min intragastric infusions. This dramatic decline in the emptying rate was reminiscent of the decline after termination of the 12-min intragastric infusions of expt 1. It appears, therefore, that, in contrast to the temporal profile for emptying of orally delivered corn oil, emptying rate for intragastric delivered oil slows not as a function of time per se but in relation to the termination of the infusion, regardless of its duration.

Experiments 2-4 explored, in different ways, the effect of varying the amount of corn oil delivered on the amount of corn oil emptied during intragastric and intraoral infusions. The rate of infusion and corn oil concentration were held constant in expt 2 (50% corn oil × 1.0 ml/min) and in expt 3 (50% corn oil × 0.5 ml/min), as infusion duration was varied. Experiments 2 and 3 were compared to evaluate the effect of doubling infusion rate (0.5–1.0 ml/min) while holding concentration and infusion duration constant (50% corn oil × 12 min). Finally, corn oil concentration was doubled from 25 to 50% in expt 4, with infusion rate and duration held constant (1.0 ml/min × 12 min). The results were consistent across experiments. In no case was the amount emptied during intraoral infusions influenced by the treatment, whereas oil emptied during intragastric infusions approximately doubled with doubling of concentration, infusion duration, or infusion rate.

We frame our interpretation of the qualitative contrasts between intraoral and intragastric emptying profiles in relation to the “feedback control model.” It is widely held that gastric emptying is subject to feedback regulatory control (1, 15–17) based on nutrient stimulation of postgastric receptors. In accordance with the model, solute emptying rate is held within a relatively narrow range, independent of the amount of nutrient delivered and of the gastric content (volume or concentration) at any given time. The model accounts for two common observations. First, relatively stable solute emptying rates are obtained across tests where the nutrient concentration of the test stimulus is varied (e.g., 1, 2, 8, 13, 14, 17). The model also accounts for the second typical finding (1, 2, 13–16) that, after loads have been delivered, nutrients tend to empty from the stomach at a relatively stable rate, not exponentially slowing as would be expected if the diminishing volume or content of the stomach were controlling variables (see Ref. 16). If, however, the independence of emptying rate and gastric content is to be held as a general property of feedback regulatory control, then we would expect emptying also to be little influenced by the increase in stomach volume or content during ingestion.

The corn oil emptying profile associated with oral delivery conforms to all expectations we derive from the feedback model. The invariance of oil solute emptied with changes in stimulus concentration is a hallmark of feedback regulatory control. The invariance of oil emptying with increases in infusion duration and rate (and, more generally, in amount delivered) further suggests that the principle of feedback regulatory control can be extended to the period of stomach fill.

The pattern of gastric emptying during intragastric infusions provides no evidence of feedback regulatory control. A case might have been made for an imperfect compensatory response had the amount of corn oil emptied less than doubled when any stimulus parameter value was doubled. However, with doubling of each of the three parameters that codetermine the amount of corn oil delivered to the stomach, an approximate doubling of oil solute emptying was obtained. There was, therefore, no detectable compensation, via reduced emptying, for the increases in the amount of nutrient delivered to the intestine.

Although the during-fill emptying profile associated with intragastric oil infusion is not consistent with the feedback model, it is not unprecedented. A parallel can be drawn between the intragastric oil infusion results and those reported in our study of emptying during intragastric glucose infusion (13). Similar to the intragastric corn oil profile here, glucose emptying in that study varied substantially as a function of the rate of fluid delivery, infusion duration, and the nutrient concentration of the infusate. Glucose emptying rate was much higher during than after infusion, regardless of infusion duration. A similar result was reported here in the dramatic slowing of gastric emptying in the 6 min after a 6-min corn oil infusion and in the phase of slow corn oil emptying that began promptly after termination of 12-min intragastric infusions (expt 1). Thus qualitatively similar results were obtained with intragastric corn oil and intragastric glucose delivery. The feedback model fails to provide an adequate account for either during-fill emptying profile. However, emptying after intragastric infusions of either nutrient appears entirely consistent with the principle of feedback regulation. The linearity of the post-intragastric fill emptying curve (stability in emptying rate) for each nutrient is a basic finding addressed by the feedback model. The second basic finding, stability in solute emptying rate with adjustment of nutrient concentration, was obtained for glucose in the post-intragastric fill period (13), although not explored here for corn oil. Our conclusions about resistance to feedback inhibition, therefore, apply specifically and perhaps exclusively to the intragastric fill interval.

Despite the comparable emptying profiles for intragastrically delivered corn oil and glucose, a prominent delivery route effect was obtained for corn oil, but not for glucose. For glucose, the same amounts emptied under the matched intragastric and intraoral infusion conditions for each concentration tested (Fig. 5). The contrast in the emptying profiles for the two nutrients cannot be explained in terms of energy density, as the delivery route effect was obtained for oil but not for glucose when the energy density of the two nutritive fluids was roughly equated (50% glucose, 25% corn oil) in expt 4. The delivery route effect, we conclude, is nutrient specific. A consistent during/after-fill emptying pattern is seen with intragastric and intraoral delivery of glucose and with intragastric corn oil deliv-
The oral delivery of corn oil, in particular, evokes a different pattern of emptying as the stomach is filling. The basis for the nutrient specificity of the delivery route effect is not clear. Perhaps a factor related to digestive processing underlies the delivery route effect for corn oil. One concern is the role of lingual lipase for the hydrolysis of triglycerides in the stomach (6, 18). If hydrolysis attributed to oral lipases were eliminated when the mouth is bypassed, then feedback inhibition could be diminished due to weaker stimulation of the relevant postgastric receptors. A tentative argument against enzymatic mediation of the oral effect on oil emptying, however, can be offered. First, given the action of postoral lipases (19) and gastric acid, it is unlikely that triglyceride hydrolysis was completely disrupted during gastric oil infusion. Sufficient time should have been available for partial breakdown and, thereby, for significant stimulation of receptors relevant to feedback inhibition. Yet no evidence of feedback inhibition was obtained during intragastric corn oil infusion. Second, if ineffective oil breakdown were a factor in the rapid gastric emptying during fill, then emptying rate should be higher for some time after intragastric than after intraoral infusion. Yet no such carryover of the delivery route effect into the post-fill period was obtained (Fig. 1). The termination of the 12-min intragastric infusion marked an abrupt transition from a period of apparent resistance to feedback inhibition to a prolonged interval, over which the emptying curve was linear, where one infers that effective regulatory control applies. These considerations lead us to suggest a neural integrative, rather than enzymatic, underpinning of the delivery route effect.

The unambiguous contrast between the emptying profiles associated with oral and gastric delivery of corn oil constrains our thinking about how relevant oral and postgastric feedback signals might be integrated with respect to emptying control during fill. Any simple (e.g., additive, multiplicative, or synergistic) combination of two inhibitory influences might reasonably be ruled out. Postpyloric feedback, when effective, is clearly inhibitory (16, 17). It would appear inappropriate, however, to label as inhibitory the signals associated with oral ingestion of corn oil. It appears, rather, that the oral influence on corn oil emptying is a gating factor that enables the expression of inhibition derived from other, presumably postgastric, sources. During intragastric corn oil infusions, the feedback mechanism, despite potentially high levels of stimulation of the relevant postgastric receptors, exerted no recognizable influence on gastric emptying under the conditions tested. When enabled during oral ingestion, the feedback mechanism accounts well for the pattern of gastric emptying. The oral ingestion-related effect for corn oil, therefore, appears permissive in nature.

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REFERENCES


