Supplemental Material

Table SI. Search terms employed in the systematic review

Search 1
(pellets OR spheres OR microsphere OR microspheres OR tablets OR capsules) AND (gastric OR stomach) AND (patients OR volunteers OR subjects OR individuals OR human) AND (emptying OR empty OR emptied) AND pancreatic
Search 2
gastric and (sizes OR size OR diameter) and (microsphere OR microspheres OR pellet OR pellets OR tablet OR tablets) and (meal OR food)
Search 3
gastric and (microsphere OR microspheres OR pellet OR pellets OR tablet OR tablets) and (meal OR food) AND (emptying OR empty OR emptied)
Search 4
(pellet OR pellets OR spheres OR microsphere OR microspheres OR tablets) AND (gastric OR stomach) AND (meal OR food) AND (emptying OR empty OR emptied)
Search 5
(meal or food or liquid or lunch or breakfast) AND (gastric or stomach) AND (emptying or empty or emptied)
Search 6
(pellets or spheres or microsphere or microspheres or tablets OR capsules) AND (gastric or stomach) AND (Size OR diameter) AND (emptying or empty)
Search 7
(meal or food) AND (gastric or stomach) AND (emptying or empty or emptied) and (patients or volunteers or subjects or individuals or human) and pancreatic not diabetes not cancer not leptin not motilin not ghrelin not CCK

Table SII. Temporal relationship of gastric emptying of solid meals and indigestible particles (single size)

Study #	Study Subjects	Study particles	Test Meals and Markers	Outcomes [Comments]	Reference
Healthy subjects, indirect comparison of particles and food emptying					
1	Ten groups of six to eight normal subjects	0.6 – 1.2 mm Pellets	Light (toast, marmalade) or heavy (sausage, bacon, eggs) breakfast followed by ingestion of radiolabelled beads; one group took a self-decided breakfast	Fast pellet emptying, no effect of type of meal, median values of gastric transit time ranging from ? 0.7 to ? 4.5 h (read from their figure 1) [Time metrics fall into the window of emptying of a low fat meal [1]	[2]
2	Six healthy volunteers	Ring-shaped capsules, 1 mm in thickness and 2.0, 4.5, or 7.0 mm in diameter	Rice, boiled salmon, egg, topping, and miso soup; taken together with radio-opaque capsules	Very similar time courses of gastric emptying: with the 2.0, 4.5, and 7.0 mm sizes, 10/20 markers had left the stomach after 97.5, 125.3, and 100.0 min, respectively. Corresponding lag times (time to first marker leaving the stomach) were 52.5, 67.5, and 52.5 min. [Time metrics fall into the window of emptying of a low fat meal[15]; compared to textbook values [3], the lag times comply or are close to that of solid foods (45-60 min) and a light egg substitute test meal (30-45 min), respectively; also, emptying half-times were close to the textbook value for the egg meal (90 min)]	[4]
3	Five healthy volunteers	Tablets 7, 11, and 13 mm in diameter	Radiolabelled tablets taken immediately after light breakfast; the three tablet sizes were studied in each volunteer	Mean gastric emptying times for the 7, 11, and 13 mm tablets were 116, 128, and 171 min. Bolus emptying (all 13 mm experiments)and emptying times > 2 h (tablet size, frequency: 7 mm, 2/5; 11 mm, 3/5; 13 mm, 4/5) were taken to indicate emptying in the interdigestive period. [2/5 subjects emptied 7 mm tablets within < 60 min, indicating pylorus passage from the fed stomach.]	[5]
4	Twelve healthy subjects	Tablets, 3, 4, 5, 6, 7 mm in diameter	Radiolabelled tablets taken immediately after a light, medium or heavy breakfast. Three sizes per breakfast were tested (3, 4, 5 mm or 5, 6, 7 mm).	The nature of the breakfast (light, medium, heavy) had a marked effect on 50 % emptying, whereas there was no effect of size. With 3-5 mm sizes, mean lag times were < 60 min (light breakfast) and ≤ 80 min (heavy breakfast). Respective gastric half-emptying times were 66-114 and 155-212 min, with rather lower values in the 5-7 mm experiments (medium breakfast). The authors concluded that a cut-off size of 2 mm is of little or no relevance to humans. [For the light breakfast, the tablet 50 % emptying times fit into the time course reported in a reference study for emptying of the same type of meal [1]; the lag times are somewhat longer than textbook values for solid foods (45-60 min) and a light egg substitute test meal (30-45 min) [3]	[6, 24]
5	Ten healthy subjects	Tubes (2 mm outer diameter), 2 and 10 mm in length	Radio-opaque tubes taken with a meal consisting of 2 glazed donuts and a soft drink (? 350 ml)	Both types of tube left the stomach together, with and without a meal. The authors considered that most markers left the stomach in the interdigestive phase. [Tubes probably passed the pylorus in a lengthwise alignment, precluding a size comparison; also, the meal was light and probably less solid than meals used in other studies.]	[25]

Study		Study particles	Test Meals and Markers	Outcomes	Refe-rence
#	Subjects			[Comments]	
6	Fifty-seven healthy volunteers	Floating and non-floating delivery systems with a diameter of at least 4.8, 7.5, and 9.9 mm (swelling over time)	Administration of radiolabelled systems 15 min after a standard breakfast; keeping upright or supine position	Units were either floating on the gastric content or sinking down; on the average, non-floating units emptied size-dependently, with gastric residency times of 87-213 min (upright position) or 113-195 min (supine position). The authors mooted an individually variable cut-off size for emptying from the fed stomach, sometimes much higher than 2-5 mm. [For non-floating units, the end of gastric residency fell into the emptying period for a light breakfast [1]; the results refute a fixed limit of 2 mm for pyloric transfer in the fed state. The authors [11] cite scintigraphic images indicating completion of digestion after ? 3 h, so that a number systems obviously emptied in the interdigestive phase]	[26, 27]
Healthy subjects, direct comparison of particle and food emptying					
7	Twenty healthy volunteers	3 mm Cubes	100 Radio-opaque cubes, taken in three equal portions before, during, and after a meal of meat (including radiolabelled rabbit liver), vegetables, fries, yoghurt and fruit, lasting 30 min	Cubes and meal showed superimposed time courses of gastric emptying for 150 min (evident from figure). [Argues against a 2 mm size limit for particles passing the pylorus in the fed state, and against an optimal size of 1.4 mm]	[28]
8	Twelve healthy subjects	2 x 5 mm Pieces of tubing	Radio-opaque pieces swallowed along with a meal (pasta, beef, salad, olive oil, bread); gastric emptying determined by ultrasonography	Gastric emptying of indigestible solids and digestible solids occurred simultaneously, with as light temporal advantage of the food at 120 min (87 versus 73 %, read from their figure 2) [Argues against a fixed sphere size, e.g. 1.4 mm, for optimal synchronization between food and particle emptying]	[29]
9	Nine healthy subjects	Pancreatin microspheres, 2 mm diameter	Radiolabelled microspheres taken after the first bite of a radiolabelled pancake meal	Pancake emptied faster than but overlapping with the 2 mm spheres (opposite to findings in patients) [Confirms the sequential emptying – fatty food faster than spheres – seen in other volunteer studies [13, 14]]	[9]
10	Eight healthy volunteers	5 x 7 mm Tablets	Radiolabelled meal (scrambled egg on a piece of toast) of 5 min duration, radiolabelled tablets taken immediately thereafter	Deduced from the pattern of contractions, 4/8 subjects emptied all 5 labelled tablets in the fed state, 2/8 did so with 4/5 tablets; two subjects emptied only one or none of the tablets in the fed state. The authors concluded that 5x7-mm tablets can empty from the fed stomach, prior to the onset of interdigestive activity. [60 % of the tablets had emptied after a mean of 98 min; refutes a fixed limit of 2 mm for pyloric transfer in the fed state and consistent with passage being more variable with increasing particle size]	[10]

Study		Study particles	Test Meals and Markers	Outcomes	Refe-rence
#	Subjects			[Comments]	
11	Eight healthy volunteers	Particles of diameters of 0.8-1.1 mm	Radiolabelled meal (scrambled egg on a piece of toast) of 5 min duration, capsules with radiolabelled pellets taken immediately thereafter	Pellet exit from the stomach occurred at similar rates as the meal in 2/8 subjects, but was delayed in 6/8, in one of them extremely [Even very small particle sizes do not guarantee emptying synchronously with meal.]	[11]
12	Twelve healthy subjects	Tubes (2 mm outer diameter), of 10 mm length	Radio-opaque tubes taken with a meal consisting of 2 glazed donuts and a soft drink, (? 350 ml) followed by two radiolabelled scrambled eggs	50 % of the tubes had left the stomach at ? 200 min, the value for the food label was ? 160 min (read from their figure 7). The authors considered that most markers left the stomach in the interdigestive phase. [Longitudinal alignment will be time consuming, enhancing any difference between meal and tube emptying time]	[12]
13	Nine healthy subjects	Spheres with a volume of 30 mm^3 (diameter ? 3.85 mm)	Intake of radio-opaque spheres and a radiolabelled meal (bread, egg white, ground meat, butter, and skim milk) within 10 min	Food clearly emptied faster than the spheres. [The indicated sphere volume (30 mm^3) corresponds to a diameter of 3.85 mm, with about 10 % having left the stomach at 10 hours (read from figure). This is consistent with the view that sizes of about 3.0 - 3.6 mm do not easily pass through the pylorus.]	[13]
14	Twenty healthy subjects	2 x 5 mm Cylinders	Radio-opaque cylinders given "together with" meal of pasta, beef hamburger, bread, olive oil; gastric emptying monitored using ultrasonography	Cylinders and meal emptied together (linear correlation), indistinguishable for the first 90 or 120 min (read from their figure 1), later with some delay of the particles. [same comment as entry above]	[14]
15	Five healthy volunteers	Pancreatin microspheres, 2 mm diameter	Radio-opaque microspheres taken with liquid (oily) test meal; gastric emptying followed by recovery of ingested xylose in blood	Gastric microsphere emptying started two hours after ingestion of the liquid test meal. [Relevance to solid food is questionable, as liquid meals empty faster than solid ones and indigestible particles are known to clear the stomach only after a lag time even when administered with a liquid [21]]	[16]
Patients with pancreatic disease					
16	Eight patients (chronic pancreatitis)	Pancreatin microspheres, diameter 2 mm	Radiolabelled microspheres taken after the first bite of a radiolabelled pancake meal	2 mm Spheres emptied faster than the pancake (opposite to finding in healthy subjects) [Casts doubt on relevance of results in healthy subjects. Further, as the transition from undisturbed to compromised pancreatic function will be gradual rather than abrupt, the temporal relationship between food and particle emptying is also likely to reverse gradually.]	[9]
17	Seven patients (chronic pancreatitis)	Pancreatin granules, 1.0-1.5 mm	Radiolabelled liver pate, rye bread, and yoghurt, ingested with radiolabelled particles in 10 min	Granules and liver pate emptied simultaneously. [Granules obviously falling short of any limiting size]	[17]
18	Twelve patients (cystic fibrosis)	Pancreatin pellets, mean diameter < 1.2 mm	Pancake and baked beans; capsules with radiolabelled pellets taken immediately before radiolabelled meal	Food emptied faster in 6, pellets in 5 patients; about equal rates were measured in 1 patient. [Individual traits, rather than pellet size (if appropriate), determine the temporal relationship between pellet and food emptying.]	[18]

Table SIII. Size dependence of gastric emptying of indigestible particles of different sizes, taken with a solid meal

Study #	Study Subjects	Study particles	Test meals	Outcomes [Comments]	Reference
Healthy subjects					
19	Twelve healthy subjects	Caffeine (0.7 mm diameter) and acetaminophen (3.6 mm diameter) tablets	Tablets taken A) 15 min after the first portion of a viscous caloric meal; B) after a fatty meal (muffin, fried egg, ham, cheese, hash brown); first appearance of drug in plasma was used as a surrogate for gastric emptying	0.7 mm pellets were emptied faster than 3.6 mm pellets with both types of meal, appearance of the latter coinciding with phase II fasted state activity. [Suggests that a diameter of 3.6 mm restricts pyloric transit in the fed state; the method allowed no quantitative evaluation of the temporal relation between emptying of food and the smaller pellets]	[19]
20	Ten patients (exocrine pancreatic insufficiency)	Pancreatin micropellets, 1.0-1.2 and 1.8-2.0 mm diameters	Liquid meal, composed of various lipids, enabling a cholesteryl-^{14}C-Octanoate breath test, plus a roll with jam	Faster accumulation of exhaled ^{14}C for the smaller size micropellets in 3 of 10 patients, with less obvious differences in the remaining patients (no statistical significance) [Corroborates the view that individual responses are heterogeneous, precluding definition of a fixed size limit; relevance to solid food is questionable due to a mostly liquid meal (spheres emulgated in lipids)]	[20]
21	Twenty-six healthy subjects in various experiments	Spheres, 1.0, 1.6, 2.4 and 3.2 mm in diameter	Radiolabelled spheres given "with the meal": radiolabelled chicken liver with steak (low calorie) or the same plus potatoes, salad and ice cream (high calorie)	1.0 mm Spheres emptied faster than 2.4 and 3.2 mm spheres. 50 % retention times (mean of all tests) of 1.0, 1.6, 2.4, and 3.2 mm spheres were 101, 152, 203, and 152 min, respectively; that of chicken liver was 134 min. There was no difference between higher- and lower-calorie meals. Compared to chicken liver, 1.6 mm spheres emptied in parallel in 2/4 volunteers, much faster in one and much slower in the last one (no emptying for 150 min, when 60 % of the liver label had left the stomach). Extrapolation, based on emptying data of all sphere sizes, suggested that 1.4 mm spheres would have emptied at the same rate as chicken liver (cf. Figure 3). [Three experiments using 1.6 mm spheres with a large meal were performed. Average 50% emptying times were 120 min, > 210 min, and ? 200 min (all read from figures); tabulated and used for analyses in the paper were values obtained by linear interpolation of the individual time courses, which were 107, 171, and 156 min, respectively. The results are consistent with a sphere size effect, but not with a fixed 2 mm limit for pyloric transit; results at 1.6 mm are difficult to reconcile with the extrapolation that a diameter of 1.4 mm is suited to secure the meal-synchronized pyloric transit of indigestible spheres.]	[21]
22	Total of 14 normal subjects	Pancreatin microspheres, 1 and 2 mm in diameter	Capsules with radiolabelled pellets taken just before the meal; dose dependence study: spaghetti meal with sauce, ground beef, bread and jam; study on effect of oil: same vs. spaghetti ground beef, and olive oil; food (oil) emptying estimated by reference to previous work	Dose-dependent emptying of spheres, with no difference between the two sizes; no significant effect of sphere size on gastric emptying, both kinds of sphere lagging behind oil in the first hour (comparison with previous data from the same laboratory). This may be explained by sphere aggregation in the oil phase observed in vitro [13]. [Any differences between sphere sizes of 1 and 2 mm tend to blur with fatty meals]	[8]

Study		Study particles	Test meals	Outcomes	Refe-rence
#	Subjects			[Comments]	
Healthy subjects					
23	Ten healthy volunteers	Tablets, 3 and 10 mm in diameter	Mixture of minced beef and mashed potato (shepherd's pie); timing of radiolabelled tablets not indicated; food empyting followed by radiolabel and electrical impedance tomography	In nearly all instances, tablets emptied after the food had emptied completely. The authors suggested that the sphincter pylori had opened to allow tablet emptying. [Suggests that 3 mm is a diameter restricting pyloric transit in the fed state; counterintuitively, 3 mm tablets were even slower to leave the stomach than 10 mm tablets.]	[22]
24	Twelve healthy volunteers	Caffeine (0.7 mm diameter) and acetaminophen (3.6 mm diameter) tablets	similar to line # 19, but no fatty meal	0.7 mm pellets were emptied faster than 3.6 mm pellets, appearance of the latter coinciding with phase II fasted state activity. [Suggests that a diameter of 3.6 mm restricts pyloric transit in the fed state; the method allowed no quantitative evaluation of the temporal relation between emptying of food and the smaller pellets]	[23]
25	Twenty healthy subjects	3 mm Cubes; 1.5 and 3 mm cubes in a condition-finding experiment	Radio-opaque cubes taken with a radiolabelled omelette from 2 eggs and 150 ml of a soft drink	Both kinds of cube emptied more slowly than food, 3 mm cubes being only slightly slower than 1.5 mm ones; the respective retained gastric contents for food,1.5 and 3,0 mm cubes (%-%-%, min) were: 60-90-90, 60; 28-72-61, 120; 7-54-49, 180; all read from their figure 1). [The authors emphasized their previous observation that emptying of the cubes was unrelated to gastric phase III of the migrating motor complex.]	[30]
26	Ten healthy volunteers	Cubes of 1.5 or 3.0 mm side lengths; cylindrical particles of a 7 mm diameter (height not given)	Standard breakfast; radio-opaque particles taken "with the meal"; combined with antral manometry	All 1.5 and 3.0 mm cubes were emptied within 4.5 h. In all subjects, the smaller particles (1.5 mm) showed a slight, insignificant tendency to exit the stomach more rapidly than the larger (3 mm) particles. There was no evidence of antral phase III activity before all cubes had been emptied from the stomach. Exit of the 7 mm particles was slower, but at least a portion (30 %) emptied within 1 hour. [Refutes a fixed limit of 2 mm for pyloric transfer in the fed state]	[33]
Patients with pancreatic disease					
27	Seven patients (cystic fibrosis)	Pancreatin microspheres, 1.2 and 2.0 mm diameters	Radiolabelled microspheres taken at the start and after a spaghetti meal that was preceded by milk with or without oleic acid; radiolabelled olive oil used to follow oil emptying	? 40 % of the oil had left the stomach within 60 min but only < 15 % of either type of sphere. From 150-300 min, pancreatin (both preparations) and oil emptying was synchronous. Aggregate formation in the oil phase, observed in vitro, may explain the delay. [Any differences between sphere sizes of 1 and 2 mm tend to blur with fatty meals.]	[7]

Table SIV. Marketed pancreatin preparations

Product	Dosage form	Enzyme activities	Particle size
Cotazym 20.000 / GER	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 20.000 Ph. Eur. U** Amylase: ≥ 14.500 Ph. Eur. U Protease: ≥ 850 Ph. Eur. U	1.4 - 2.4 mm
Cotazym 30.000 / GER	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 30.000 Ph. Eur. U** Amylase: ≥ 21.750 Ph. Eur. U Protease: ≥ 1.275 Ph. Eur. U	1.4 - 2.4 mm
Cotazym 40.000 / GER	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 40.000 Ph. Eur. U** Amylase: ≥ 25.000 Ph. Eur. U Protease: ≥ 1.500 Ph. Eur. U	1.4 - 2.4 mm
CREON 3.000/15.000/ 9.500 / USA	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 3.000 USP U** Amylase: 15.000 USP U Protease: 9.500 USP U	0.7 - 1. 6 mm
CREON 6.000/30.000/ 19.000 / USA	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 6.000 USP U** Amylase: 30.000 USP U Protease: 19.000 USP U	0.7 - 1. 6 mm
CREON 12.000/60.000/38.000 / USA	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 12.000 USP U** Amylase: 60.000 USP U Protease: 38.000	0.7 - 1. 6 mm
CREON 24.000/120.000/ 76.000 / USA	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 24.000 USP U** Amylase:120.000 USP U Protease: 76.000 USP U	0.7 - 1. 6 mm
CREON 36.000/180.000/ 114.000 / USA	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 36.000 USP U** Amylase: 180.000 USP U Protease: 114.000 USP U	0.7 - 1. 6 mm
CREON 12.000 / F	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 12.000 Ph. Eur. U** Amylase: 8.000 Ph. Eur. U Protease: 6.000 Ph. Eur. U	0.7 - 1. 6 mm
CREON 25.000 / F	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 25.000 Ph. Eur. U** Amylase: 18.000 Ph. Eur. U Protease: 1.000 Ph. Eur. U	0.7 - 1. 6 mm
CREON GRAN 5.000 / F, Creon Micro 60,12 mg gastro-resistant granules / UK, Kreon für Kinder (for children) / GER	Granulate, enteric coated micropellets	**per Dose:** **Lipase: 5.000 Ph. Eur. U/BP U** Amylase: 3.600 Ph. Eur. U/BP U Protease: 200 Ph. Eur. U/BP U	0.7 -1.0 mm
Creon 10.000 / UK, Kreon 10.000 / GER	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 10.000 Ph. Eur. U/BP U** Amylase: 8.000 Ph. Eur. U/BP U Protease: 600 Ph. Eur. U/BP U	0.7 - 1. 6 mm
Creon 20.000 / UK, Kreon 20.000 / GER	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 20.000 Ph. Eur. U**/BP U Amylase: 16.000 Ph. Eur. U/BP U Protease: 1.200 Ph. Eur. U/BP U	0.7 - 1. 6 mm
Creon 25.000 / UK, Kreon 25.000 / GER	Delayed-release capsule, containing enteric coated micropellets	**Lipase: ≥ 25.000 Ph. Eur. U**/BP U Amylase: ≥ 18.000 Ph. Eur. U/BP U Protease: ≥ 1.000 Ph. Eur. U/BP U	0.7 - 1. 6 mm
Creon 35.000 / UK, Kreon 35.000 / GER	Delayed-release capsule, containing enteric coated micropellets	**Lipase: ≥ 35.000 Ph. Eur. U**//BP U Amylase: ≥ 25.200 Ph. Eur. U/BP U Protease: ≥ 1.400 Ph. Eur. U/BP U	0.7 - 1. 6 mm
Creon 40.000 / UK	Delayed-release capsule, containing enteric coated micropellets	**Lipase: ≥ 40.000 BP U** Amylase: ≥ 25.000 BP U Protease: ≥ 1.600 BP U	0.7 - 1. 6 mm
EUROBIOL 2.500 / F	Enteric coated microtablets	**per Dose:** **Lipase: 2.500 Ph. Eur. U** Amylase: 2.250 Ph. Eur. U Protease: 125 Ph. Eur. U	2 mm

Product	Dosage form	Enzyme activities	Particle size
EUROBIOL 12.500 / F	Delayed-release Capsule, containing thin coated microtablets	**Lipase: 12.500 Ph. Eur. U** Amylase: 11.250 Ph. Eur. U Protease: 625 Ph. Eur. U	2 mm
EUROBIOL 25.000 / F	Delayed-release Capsule, containing thin coated microtablets	**Lipase: 25.000 Ph. Eur. U** Amylase: 22.500 Ph. Eur. U Protease: 1.250 Ph. Eur. U	2 mm
EUROBIOL 40.000 / F	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 40.000 Ph. Eur. U** Amylase: 25.000 Ph. Eur. U Protease: 1.500 Ph. Eur. U	1.4 - 2.4 mm
Mezym f / GER	Enteric coated tablet	**Lipase: 10.000 Ph. Eur. U** Amylase: ≥ 7.500 Ph. Eur. U Protease: ≥ 375 Ph. Eur. U	10.3 x 4.0 mm
Nutrizym 22 / UK	Delayed-release capsule, containing enteric coated microtablets	**Lipase: ≥ 22.000 BP U** Amylase: ≥ 19.800 BP U Protease: ≥ 1.100 BP U	2.2 - 2.5 mm
Ozym 20.000 / GER	Delayed-release Capsule, containing thin coated microtablets	**Lipase: 20.000 Ph. Eur. U** Amylase: ≥ 15.000 Ph. Eur. U Protease: ≥ 900 Ph. Eur. U	2 mm
Ozym 40.000 / GER	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 40.000 Ph. Eur. U** Amylase: ≥ 25.000 **Ph. Eur. U** Protease: ≥ 1.500 **Ph. Eur. U**	1.4 - 2.4 mm
Pancrease HL / UK	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 25.000 BP U** Amylase: 22.500 BP U Protease: 1.250 BP U	2.2 - 2.5 mm
PANCREAZE 2.600 / USA	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 2.600 USP U** Amylase: 10.850 USP U Protease: 6.200 USP U	2 mm
PANCREAZE 4.200 / USA	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 4.200 USP U** Amylase: 24.600 USP U Protease: 14.200 USP U	2 mm
PANCREAZE 10.500 / USA	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 10.500 USP U** Amylase: 61.500 USP U Protease: 35.500 USP U	2 mm
PANCREAZE 16.800 / USA	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 16.800 USP U** Amylase: 98.400 USP U Protease: 56.800 USP U	2 mm
PANCREAZE 21.000 / USA	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 21.000 USP U** Amylase: 83.900 USP U Protease: 54.700 USP U	2 mm
Pancrex Granules / UK	Granules	**Lipase: 5.000 BP U** Amylase: 4.000 BP U Protease: 300 BP U	n.a.
Pancrex V Capsules / UK	Powder-filled capsules, uncoated	**Lipase: 8.000 BP U** Amylase: 9.000 BP U Protease: 430 BP U	n.a.
Pancrex V Tablets / UK	Enteric coated tablet	**Lipase: 1.900 BP U** Amylase: 1.700 BP U Protease: 910 BP U	n.a.
Pancrex V forte Tablets / UK	Enteric coated tablet	**Lipase: 5.600 BP U** Amylase: 5.000 BP U Protease: 330 BP U	n.a.
Pangrol 10.000 / GER	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 10.000 Ph. Eur. U** Amylase: ≥ 9.000 Ph. Eur. U Protease: ≥ 500 Ph. Eur. U	2 mm

Product	Dosage form	Enzyme activities	Particle size
Pangrol 20.000 / GER	Enteric coated tablet	**Lipase: 20.000 Ph. Eur. U** Amylase: ≥ 12.000 Ph. Eur. U Protease: ≥ 900 Ph. Eur. U	11.3 x 4.7 mm
Pangrol 25.000 / GER	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 25.000 Ph. Eur. U** Amylase: ≥ 22.500 Ph. Eur. U Protease: ≥ 1.250 Ph. Eur. U	2 mm
Pangrol 40.000 / GER	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 40.000 Ph. Eur. U** Amylase: ≥ 25.000 Ph. Eur. U Protease: ≥ 1.500 Ph. Eur. U	1.4 - 2.4 mm
Pankreatan 10.000 / GER	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 10.000 Ph. Eur. U** Amylase: ≥ 7.500 Ph. Eur. U Protease: ≥ 450 Ph. Eur. U	2 mm
Pankreatan 20.000 Ph.Eur.-Einheiten / GER	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 20.000 Ph. Eur. U** Amylase: ≥ 15.000 Ph. Eur. U Protease: ≥ 900 Ph. Eur. U	2 mm
Pankreatan 25.000 / GER	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 25.000 P**h. Eur. U Amylase: ≥ 18.750 Ph. Eur. U Protease: ≥ 1.125 Ph. Eur. U	2 mm
Pankreatan 36.000 / GER	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 36.000 Ph. Eur. U** Amylase: ≥ 22.000 Ph. Eur. U Protease: ≥ 1.200 Ph. Eur. U	2 mm
Pankreatin 40.000 Nordmark / GER	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 40.000 Ph. Eur. U** Amylase: ≥ 25.000 Ph. Eur. U Protease: ≥ 1.500 Ph. Eur. U	1.4 - 2.4 mm
Pankreatin Mikro-ratiopharm 20.000 / GER	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 20.000 Ph. Eur. U** Amylase: ≥ 15.000 Ph. Eur. U Protease: ≥ 900 Ph. Eur. U	2 mm
Pankreatin Stada 20.000 / GER	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 20.000 Ph. Eur. U** Amylase: ≥ 15.000 Ph. Eur. U Protease: ≥ 900 Ph. Eur. U	2 mm
Pankreatin Stada 20.000 Aliud / GER	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 20.000 Ph. Eur. U** Amylase: ≥ 15.000 Ph. Eur. U Protease: ≥ 900 Ph. Eur. U	2 mm
Pankreatin 10.000 Laves Mikro / GER	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 10.000 Ph. Eur. U** Amylase: ≥ 7.500 Ph. Eur. U Protease: ≥ 425 Ph. Eur. U	2 mm
Pankreatin 20.000 Laves Mikro / GER	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 20.000 Ph. Eur. U** Amylase: ≥ 15.000 Ph. Eur. U Protease: ≥ 900 Ph. Eur. U	2 mm
Panzytrat ok / GER	Enteric coated microtablets	orange / green, per measuring Spoon **Lipase: 20.000 / 5.200 Ph. Eur. U** Amylase: ≥ 18.000 / 4.680 Ph. Eur. U Protease: ≥ 10.000 / 2600 Ph. Eur. U	2 mm
Panzytrat 10.000 / GER	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 10.000 Ph. Eur. U** Amylase: ≥ 9.000 Ph. Eur. U Protease: ≥ 500 Ph. Eur. U	2 mm
Panzytrat 25.000 / GER	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 25.000** Ph. Eur. U Amylase: ≥ 15.000 Ph. Eur. U Protease: ≥ 800 Ph. Eur. U	2 mm
Panzytrat 40.000 / GER	Delayed-release capsule, containing enteric coated micropellets	**Lipase: 40.000** Ph. Eur. U Amylase: ≥ 25.000 Ph. Eur. U Protease: ≥ 1.500 Ph. Eur. U	1.4 - 2.4 mm

Product	Dosage form	Enzyme activities	Particle size
PERTZYE 8.000 / USA	Delayed-release capsule, containing bicarbonate-buffered enteric coated micropellets	**Lipase: 8.000 USP U** Amylase: 30.250 USP U Protease: 28.750 USP U	0.8 - 2.2 mm
PERTZYE 16.000 / USA	Delayed-release capsule, containing bicarbonate-buffered enteric coated micropellets	**Lipase: 16.000 USP U** Amylase: 60.500 USP U Protease: 57.500 USP U	0.8 - 2.2 mm
VIOKACE 10.440 / USA	Tablet, non enteric coated	**Lipase: 10.440 USP U** Amylase: 39.150 USP U Protease: 39.150 USP U	n.a.
VIOKACE 20.880 / USA	Tablet, non enteric coated	**Lipase: 20.880 USP U** Amylase: 78.300 USP U Protease: 78.300 USP U	n.a.
ZENPEP 3.000 / USA	Delayed-release capsule, containing enteric coated beads	**Lipase: 3.000 USP U** Amylase: 14.000 USP U Protease: 10.000 USP U	1.8 - 1.9 mm
ZENPEP 5.000 / USA	Delayed-release capsule, containing enteric coated beads	**Lipase: 5.000 USP U** Amylase: 24.000 USP U Protease: 17.000 USP U	1.8. - 1.9 mm
ZENPEP 10.000 / USA	Delayed-release capsule, containing enteric coated beads	**Lipase: 10.000 USP U** Amylase: 42.000 USP U Protease: 32.000 USP U	2.2 - 2.5 mm
ZENPEP 15.000 / USA	Delayed-release capsule, containing enteric coated microtablets	**Lipase: 15.000 USP U** Amylase: 63.000 USP U Protease: 47.000 USP U	2.2 - 2.5 mm
ZENPEP 20.000 / USA	Delayed-release capsule, containing enteric coated beads	**Lipase: 20.000 USP U** Amylase: 84.000 USP U Protease: 63.000 USP U	2.2 - 2.5 mm
ZENPEP 25.000 / USA	Delayed-release capsule, containing enteric coated beads	**Lipase: 25.000 USP U** Amylase: 105.000 USP U Protease: 79.000 USP U	2.2 - 2.5 mm
ZENPEP 40.000 / USA	Delayed-release capsule, containing enteric coated beads	**Lipase: 40.000 USP U** Amylase: 168.000 USP U Protease: 126.000 USP U	2.2 - 2.5 mm

Conversions [32] (Eur. Pharm : BP : USP): Lipase, 1:1: ?1; Amylase, 1:1: ?4.15; Protease, 1:1: ? 62.5
F, France; GER, Germany; UK, United Kingdom; USA, United States
Pharm. Eur., European Pharmacopoeia; BP, British Pharmacopoeia;USP, United States Pharmacopeia

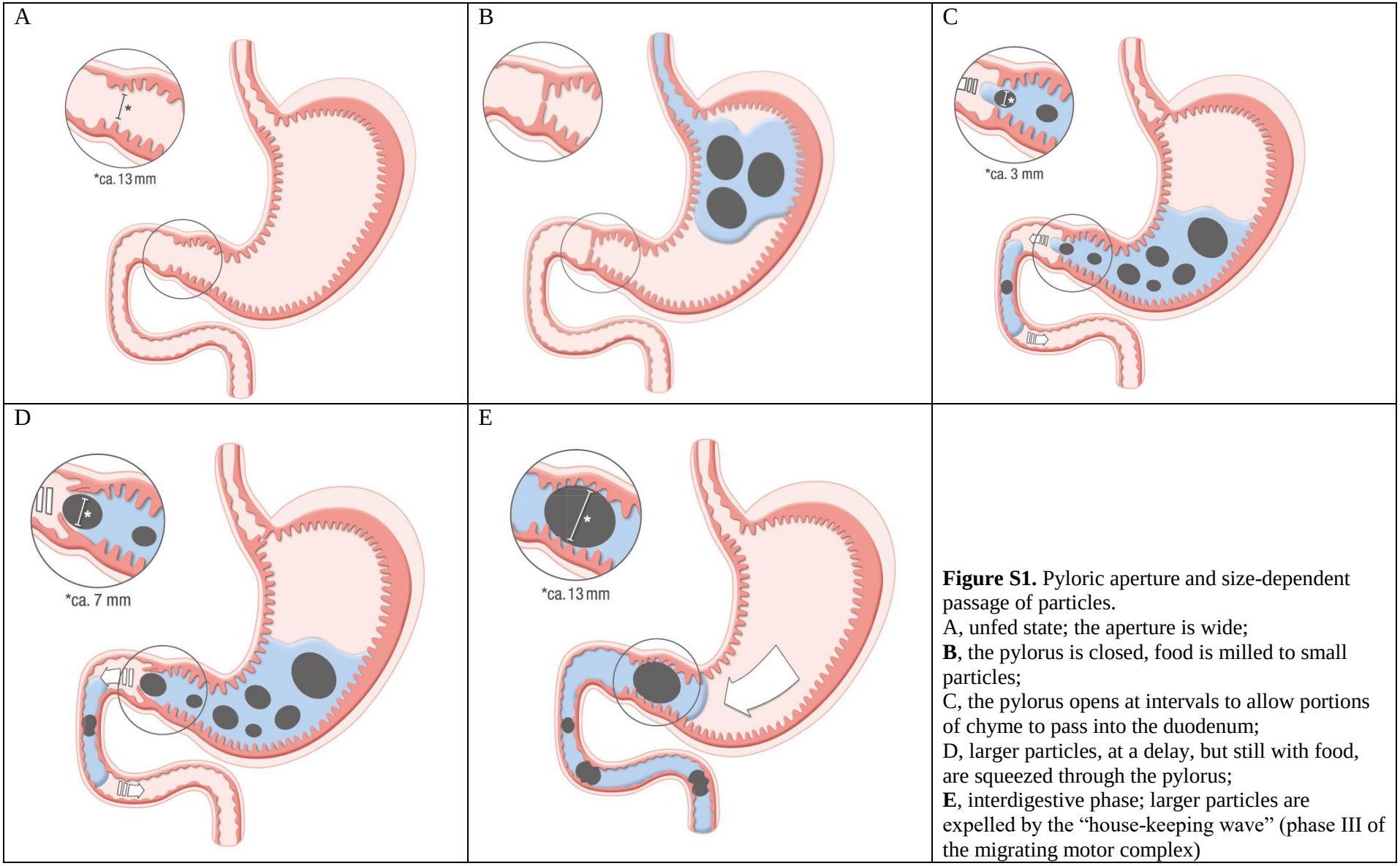

Figure S1. Pyloric aperture and size-dependent passage of particles.
A, unfed state; the aperture is wide;
B, the pylorus is closed, food is milled to small particles;
C, the pylorus opens at intervals to allow portions of chyme to pass into the duodenum;
D, larger particles, at a delay, but still with food, are squeezed through the pylorus;
E, interdigestive phase; larger particles are expelled by the "house-keeping wave" (phase III of the migrating motor complex)

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