A review of the physiology of the canine digestive tract related to the development of *in vitro* systems

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Abstract

Food and nutrition studies in animals and human beings often meet with technical difficulties and sometimes with ethical questions. An alternative to research in living animals is the dynamic multicompartmental *in vitro* model for the gastrointestinal tract described by Minekus *et al.* (1995) and Havenaar & Minekus (1996). The dynamic conditions that are simulated in this model are peristaltic movements, transit times, pH responses, secretion of enzymes and electrolytes and absorption of nutrients and water. To obtain data for an *in vitro* model of the dog gastrointestinal tract, the literature was surveyed for physiological responses to different types of dog food. These included: values of enzyme activities, electrolyte concentrations, gastric emptying and intestinal transit times, pH values, secretion and composition of bile and absorption rates in different parts of the dog gastrointestinal tract. The review focuses on research carried out on healthy, adult dogs of 10–20 kg and on parameters related to the oral cavity, stomach and small intestine. This literature research gives sufficient data on the physiology of the canine digestive tract for the development of an *in vitro* dynamic model that adequately simulates the functions of the stomach and small intestine of the dog.

Introduction

In vivo studies on the physiology of food in the gastrointestinal tract (GIT) both in living animals and men meet with serious technical difficulties and sometimes ethical questions. Therefore much attention has been given recent years to the development of *in vitro* models which mimic metabolic processes of the GIT. Such models can lead to information on and prediction of food digestion in the GIT. An interesting *in vitro* model of the stomach and small intestine has been described in literature (Minekus *et al.* 1995; Havenaar & Minekus, 1996; Minekus & Havenaar 1996). The model is a multicompartmental laboratory system which is made of glass and silicon and which simulates the kinetics in the successive parts of the GIT of humans, calves and pigs (Fig. 1*a*, *b*). Parameters, such as peristaltic movements, transit time, pH and secretion are included in this model. In this model different aspects can be studied, such

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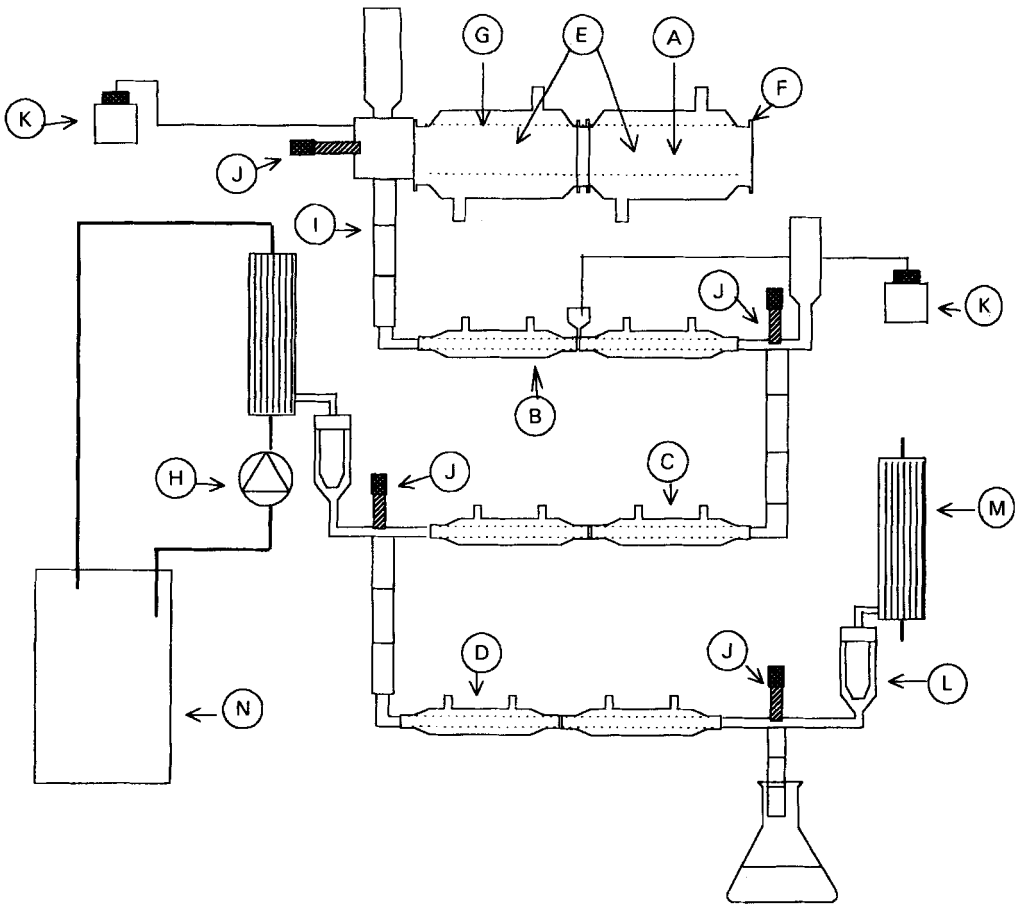

Figure 1*a*: Schematic view of TIM(*T*NO gastro*i*ntestinal *m*odel (Minekus *et al.* 1995) (*a*) gastric compartment; (*b*) duodenal compartment; (*c*) jejunal compartment; (*d*) ileal compartment; (*e*) basic unit; (*f*) glass jacket; (*g*) flexible wall; (*h*) rotary pump; (*i*) peristaltic valve pump; (*j*) pH electrodes; (*k*) secretion pump (valveless metering pump); (*l*) prefilter; (*m*) hollow fibre device; (*n*) water bath.

as digestion of food components (Minekus, 1996), survival of bacteria (Marteau *et al.* 1997), availability for absorption of minerals (Larsson *et al.* 1997) and pharmacokinetics.

This dynamic model enables simulating of the physical conditions that occur in the GIT of a dog. It can thus be used to study the hydrolyses of food components into nutrients as part of the digestive processes. For such a dynamic *in vitro* model to function it is of significance that the *in vivo* conditions regarding the physiology of the canine GIT are properly simulated.

The objective of this review is to make an inventory of the published data on diet and canine GIT in order to obtain a standard which can be used for the design and interpretations of *in vitro* studies from the model as described above. The review focusses on research carried out on healthy, adult dogs of 10–20 kg, and on those parameters which are of special importance for the setup of the dynamic *in vitro* model simulating the stomach and small intestine. Although the large intestine is important for further (microbial) breakdown of food components, data on the large intestine are not included.

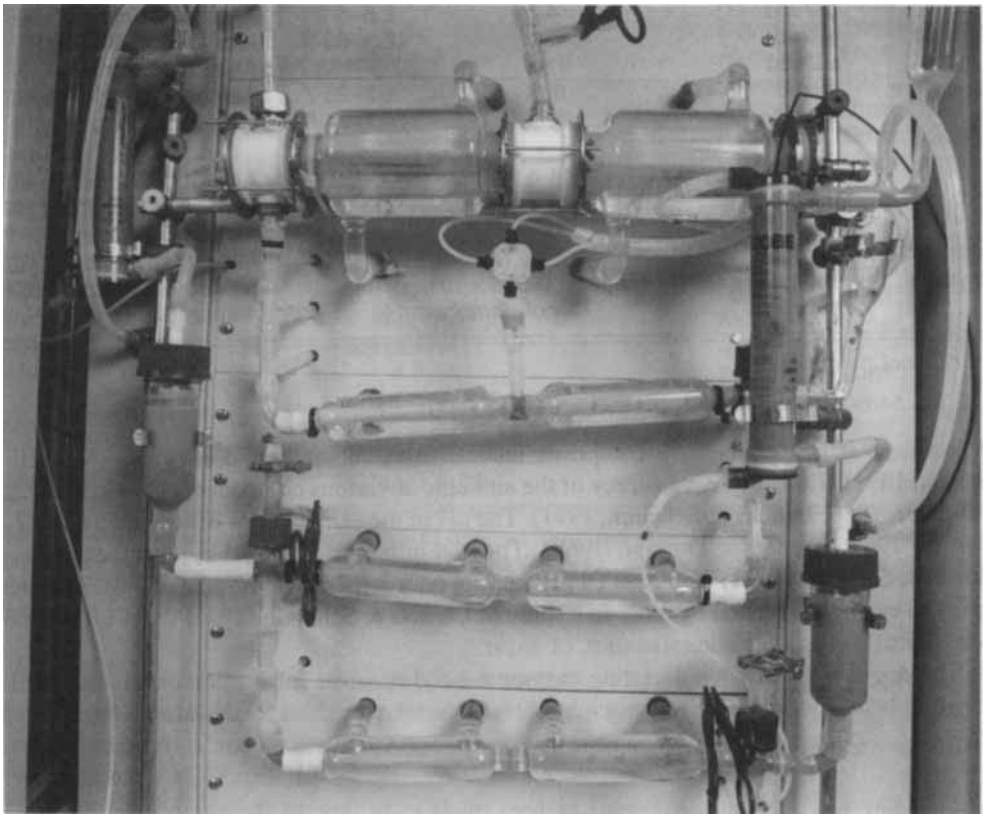

Figure 1*b*: Photograph of TIM

Physiological data

Physiological data of the mouth, stomach, small intestine, pancreas and gall bladder are discussed in response to different types of dog food.

Mouth

The first step in the digestion of food is the secretion of saliva during mastication. Amount and composition of the saliva are dependent on the type of food (especially the water content) ingested. Enzyme activity levels are usually not influenced by the rate of secretion. The dog produces saliva from the parotid gland (0·14–1·40 ml/min; mean 0·55) and from the submaxillary gland (0·20–3·84 ml/min; mean 1·31) (Chauncey *et al.* 1963). Saliva consists of *c.*

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Table 1. Amounts of electrolytes and amylase in saliva of dogs

Constituent	Source of saliva	Mean, (mmol/l)	Range	Reference
Calcium	mixed	n.m.*	1·45–3·3	Altman & Dittmer (1968)
	mixed	1·85	1·0–2·75	Larmas & Scheinin (1971)
	parotid	4·3	2·5–5·2	Altman & Dittmer (1968)
Chloride	mixed	n.m	16·3–69·3	Altman & Dittmer (1968)
	parotid	81·9	37·5–103·7	Altman & Dittmer (1968)
Potassium	mixed	n.m.	12·3–23·7	Altman & Dittmer (1968)
	mixed	20·2	14·1–24·8	Larmas & Scheinin (1971)
	parotid	11·4	4·3–12·6	Altman & Dittmer (1968)
Sodium	mixed	74·1	42·0–99·8	Larmas & Scheinin (1971)
	parotid	108	48·8–132·9	Altman & Dittmer (1968)
Bicarbonate	parotid	55	34·7–69·1	Altman & Dittmer (1968)
Amylase	submaxillary	$< 0{\cdot}010 \times 10^2$ mg/ml		Altman & Dittmer (1968)
	parotid	not demonstrable		Altman & Dittmer (1968)

* n.m. = not mentioned

99 % water, the remaining 1 % comprises mucus, inorganic salts and enzymes (Maskell & Johnson, 1993). Table 1 gives a survey of the amounts of various components of saliva (Altman & Dittmer, 1968; Larmas & Scheinin, 1971). The pH of the saliva varies between 7·34 and 7·80 (Gurtler, 1967; Altman & Dittmer, 1968). These results are comparable with the results of Larmas & Scheinin (1971) who found a pH varying between 7·2 and 8·1 (mean 7·7). The pH of the saliva can be influenced by food. In a study of Larmas & Scheinin (1971) the pH felt rapidly about 0·5 pH units after administration of sugar.

The dog lacks the starch digesting enzyme α-amylase in its saliva; this lack is reflected in the eating behaviour of dogs, which tend to bolt all but the toughest foods (Maskell & Johnson, 1993).

Stomach

Digestion in the stomach is determined by physical and chemical properties of ingested food and by the concentrations of electrolytes and activity of enzymes. Gastric emptying and pH are of major importance because they play a role in the activity of enzymes. Also the contact time of the food with the enzymes is determined by these factors.

Electrolytes and enzymes

The concentrations of electrolytes in gastric juice (Table 2) reported in the literature vary widely. The major enzymes present in the lumen of the stomach are lipase and pepsin.

Dog gastric lipase is a 49 kDa glycoprotein containing 13 % carbohydrate which is formed by a single polypeptide chain of 377–379 amino acid residues, acting on both long and short chain triglycerides. At pH 4 this lipase is 13 times more active on long-chain than on short-chain triacylglycerols (Carrière *et al.* 1991). The lipase is irreversibly inactivated below pH 1·5, its activity also decreases significantly above pH 6·0, and it is completely inactivated at pH 7·0. At pH values below 6·0, which normally prevail in the duodenum after ingestion of a liquid meal, a gastric lipase activity of *c.* 90 % is recovered (Carrière *et al.* 1993).

Table 2. Electrolyte composition of gastric juice in dogs

Constituent	Mean ± S.D. (range) (mmol/l	Reference
Bicarbonate	5·0 ± 0·7	Alexander, 1965*
	33	Davenport, 1961†
Potassium	28·0 ± 3·7	Alexander, 1965
	7·0	Davenport, 1961
	7·2	Altman & Dittmer, 1968
	15·2 (10·3–22·0)	Altman & Dittmer, 1968‡
Sodium	58·0 ± 9·1	Alexander, 1965
	155	Davenport, 1961
	22	Altman and Dittmer, 1968
	64 (46·3–79·0)	Altman and Dittmer, 1968‡
Chloride	149·0 ± 5·3	Alexander, 1965
	133	Davenport, 1961
	172·9	Altman & Dittmer, 1968
	123 (98–143)	Altman & Dittmer, 1968‡
Calcium	4·0	Davenport, 1961
	0·5–1·7	Altman & Dittmer, 1968
Phosphate	12·0 ± 2·7	Alexander, 1965
	0·25 mg/100 ml	Altman & Dittmer, 1968
Magnesium	0·5 mg/100 ml	Altman and Dittmer, 1968

*The dogs were killed 4–6 h after a meal of canned food and concentrations were measured
† The values were calculated from analyses of samples of juice being secreted at different rates in response to graded doses of histamine
‡ sham feeding stimulation

The basal secretion rate of lipase is 606 ± 40 units/h (1 unit equals 1 μmol of butyric acid released from tributyrin per minute). Lipase is secreted in both the proximal and antral area of the canine stomach (Carrière *et al.* 1992). The activity of lipase in the gastric juice varies from 0·9 to 3900 units/ml (Engel, 1946).

For pepsin the amount present after sham feeding ranged between 41 and 164 units/ml (mean 81). The factors responsible for the variability between the individual dogs are unknown (Villareal *et al.* 1955). The amount of pepsin secreted can be influenced by hormones, such as adrenocorticotropic hormone (ACTH) which causes an increase in activity (Villareal *et al.* 1955). Pepsin has an optimum activity at a pH of 2·0 maintained by gastric secretion of hydrochloric acid; its proteolytic activity decreases when chyme leaves the stomach, since it is irreversibly inactivated at neutral pH.

Acid secretion and pH

Gastric secretion is influenced by the amount of protein in a meal and by the volume of the meal (Carpentier *et al.* 1988). Some hormones will indirectly effect the acidity of the stomach contents. ACTH increases hydrochloric acid production (Villareal *et al.* 1955), and secretin decreases production through suppression of the release of gastrin (Jin *et al.* 1994*b*). The nervous system also plays a role in the secretion of hydrochloric acid as shown by Lawson *et al.* (1994): gastric acid secretion is doubled when a calcitonin gene-related peptide antagonist is infused.

Gastric pH can be measured by different methods: directly in samples taken from the stomach (Banta *et al.* 1979; Carrière *et al.* 1993) or by radiotelemetry (Youngberg *et al.* 1985).

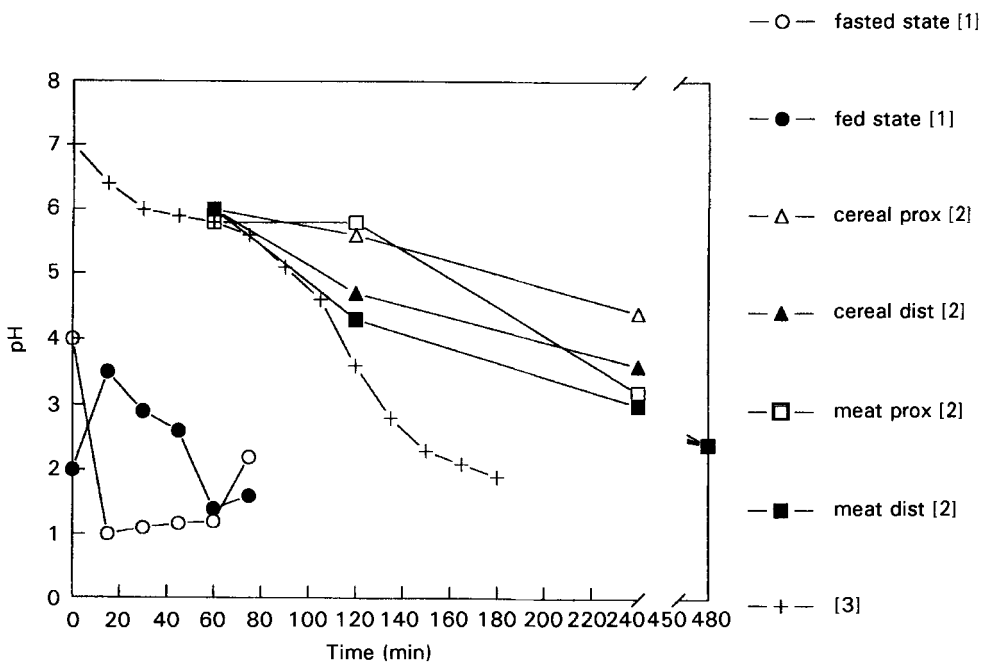

Figure 2. Changes in pH with time of gastric contents; [1], Youngberg *et al.* (1985), [2], Banta *et al.* (1979), [3], Carrière *et al.* (1993). Prox., proximal stomach; dist., distal stomach.

When measured in time a gastric pH curve can be mimicked (Fig. 2). In the fasting state gastric pH fluctuates little with time, whereas postprandially there are wave-like patterns (Youngberg *et al.* 1985). The gastric pH response varies with the type of meal ingested. After ingestion of a complete liquid test meal a pH drop below 4·0 was noticed within 10–20 min (Youngberg *et al.* 1985). With a meat based diet a drop in pH to below 6·0 was found after 60 min (Banta *et al.* 1979; Carrière *et al.* 1993).

Gastric emptying

Gastric emptying plays an important role in the time enzymes are in contact with food in the stomach. Rates of emptying are influenced by many factors such as volume, energy content, viscosity, density and particle size of gastric contents (Ehrlein & Pröve, 1982; Dressman, 1986; Cargill *et al.* 1988; Benini *et al.* 1994; Horowitz *et al.* 1994), temperature (Teeter & Bass, 1982; Benini *et al.* 1994), body weight (Allan *et al.* 1996) and amount of acid in the duodenum (Cooke, 1974; Cooke & Clarke, 1976). Also, a complex interaction exists between different meal components (Horowitz *et al.* 1994).

The rate of gastric emptying of a liquid meal is determined by the pressure gradient between the stomach and the duodenum (Carrière *et al.* 1993). In general, liquids empty in a monoexponential manner, whereas solids empty in a linear manner (Dozois *et al.* 1971; Gué *et al.* 1988; Gupta & Robinson, 1988; Hornof *et al.* 1989) after a lag phase (Horowitz *et al.* 1994). This lag phase is probably dependent on the time taken for redistribution of food from the proximal into the distal part of the stomach and the time for grinding solid food into small particles (Horowitz *et al.* 1994). After ingestion of a meal of solids and liquids, the stomach

retains solid food predominantly in the proximal part, until most (*c.* 80 %) of the liquid has disappeared (Horowitz *et al.* 1994).

Carrière *et al.* (1993) determined gastric emptying by the concentration of a liquid marker (phenol red) in duodenal and gastric contents at 15 min intervals. They found an average gastric half-time of emptying of a liquid test meal of 75 ± 8 min. This was in agreement with the results obtained with the empirical equation described by Hunt & Stubbs (1975):

$$t_{1/2} = V_0(0{\cdot}18 - 0{\cdot}17\, e^{-K})$$

where V_0 is the meal volume (ml) and K is its nutrient density (kcal/ml).

Both meal volume and density play a role in gastric emptying. Meyer *et al.* (1985) studied the effects of density of nondigestible solids in duodenal fistulated dogs. There was a trend for higher density particles to empty slower. The regulation of emptying by density depends upon the intraduodenal concentrations of products of digestion, either monosaccharides, acting through their osmotic pressure, or esters of fatty acids acting on duodenal receptors. Isocaloric concentrations of carbohydrates and triglycerides induce similar gastric emptying (Hunt & Stubbs, 1975). Although emptying of high density meals is slower, more energy is transferred to the duodenum in a given time than with low density meals (Hunt & Stubbs, 1975). A larger volume of fluid flows through the duodenum with meals of higher energy density than with meals of lower energy density. The same effect occurs with foods differing in osmolarity (Hinder & Kelly, 1977). Apparently, a greater stimulation of endogenous secretion occurs with the meals of high energy density, and a greater diffusion of water occurs into the duodenal lumen because of the high osmolarity (Meyer *et al.* 1989).

Gupta & Robinson (1988) studied the gastric emptying of liquids in the dog by collecting the effluent from a permanent Thomas cannula located in the duodenum about 15 cm from the gastroduodenal junction. The gastric emptying of volumes above 100 ml of water seems to follow an exponential curve with a half-time of discharge of *c.* 10 min. In fasted dogs, gastric emptying of liquids starts immediately after administration of test meals and most of the volume (80–100 %) is emptied within 40 min (Gupta & Robinson, 1988). Dozois *et al.* (1971) found a half-emptying time for liquid meals of 25 min. The discharge pattern of volumes of 100 ml or less was different from that of larger volumes. During the first 20–30 min after administration of water there was little or no emptying. Half of the administered volume was emptied between 35 and 45 min and the complete volume was emptied in 55–65 min (Gupta & Robinson, 1988). Lui *et al.* (1986) observed a longer gastric emptying time of $99{\cdot}8 \pm 27{\cdot}2$ (35·0–317) min after ingestion of 20–50 ml of water compared to the studies of Gupta & Robinson (1988) and Dozois *et al.* (1971). The mean resting volume in the stomach in the fasted state was about 25 ml and administration of small volumes ($\leq$100 ml) did not change the motility pattern. From these results it can be concluded that the volume transition to convert motility from a fasted to a fed state lies somewhere between 100 and 150 ml (Gupta & Robinson, 1988).

For liquid meal volumes smaller than 66 ml/kg of body weight, the volume emptied from the stomach in 30 min increased linearly with meal volume. For higher meal volumes, the gastric emptying seemed to approach a maximum at $0{\cdot}99 \pm 0{\cdot}052$ ml/min/kg (Leib *et al.* 1986). These results are in contrast with the results of Hunt & Stubb (1975) who conclude that nutrient density alone determines the volume of a meal emptied in 30 min, independent of the starting volume of a meal.

Meat leaves the stomach as particles smaller than 2 mm in diam. (Hinder & Kelly, 1977; Meyer *et al.* 1979, 1985; Burrows *et al.* 1985; Cullen & Kelly, 1996). It is therefore assumed

that a stomach containing food has a threshold or cutoff size, above which it retains material and below which it allows the food or particles to be moved to the duodenum (Meyer *et al.* 1985). Breaking down digestible solids to a smaller size speeds up gastric emptying. In contrast, coarse, indigestible solids are retained in the stomach until digestion of other food components is completed. Such indigestible solids are not swept out of the stomach until powerful, propulsive, gastric contractions in the fasting state take place (Hinder & Kelly, 1977).

Banta *et al.* (1979) studied the gastric emptying of both solids and liquids in dogs using two fluid markers; polyethylene glycol (PEG) and ^{51}Cr-labelled EDTA and radiopaque polyethylene tubing cut in particles of 2, 10 and 20 mm as a solid marker (Table 3). They concluded that the stomach appears to be the major site involved in regulation of particulate marker passage through the GIT; this is most obviously the case with the larger particles. Emptying of liquids (154 mM NaCl) and solids (solid plastic spheres, 1 cm in diam.) was also studied by Dozois *et al.* (1971) who concluded that the terminal antrum and pylorus are of minor importance in the regulation of gastric emptying of liquids but are of great importance in gastric emptying of solids. Allan *et al.* (1996), who used two different sizes solid particles, found no significant difference in the mean lag period between the large (5 mm) and small (1·5 mm) radio-opaque markers.

Miyabayashi *et al.* (1986) found a gastric emtpying time of 76 ± 16 min (range 30–120 min) in a barium sulfate contrast study. By using external scintigraphy, Theodorakis (1980) found an average gastric half-emptying time of 77 ± 23 min for 255 g of canned dog food in six beagles. Scintigraphy was also used for dry kibble food to determine solid-phase gastric emptying in beagles and mongrel dogs (Hornof *et al.* 1989). An average half-emptying time of 240 min was found in the beagles (*c.* 12 kg; $n = 6$) and 216 min in the mongrel dogs (5·4–35 kg; $n = 5$).

Arnbjerg (1992) studied the time of passage of various commercial food items through the stomach of dogs (25–30 kg) by radiography. The types of food used were (1) dried food with 10 % moisture, (2) canned food with 70 % moisture and (3) fresh food (fish) with 75 % moisture. After food ingestion the animals had no access to water or to any other type of liquid. In group 1, the food remained unchanged in the stomach for 480 to 600 min (mean 534 min) after completion of the meal. After 900 ± 60 min the stomach appeared to be completely empty. In group 2, the food started to enter the duodenum after 270 ± 30 min. The stomach appeared to be empty 420–480 min after eating. In group 3, the food was observed in the duodenum 30 min after ingestion and emptying was complete 240–360 min after ingestion. However, this method is not very accurate due to problems with determining the very beginning of gastric emptying; besides, radiographs were taken at intervals of 60 min (Arnbjerg, 1992). The results of fresh meat emptying are in agreement with the results for labelled chicken liver reported by Cullen & Kelly (1996) who found a gastric emptying time of 214 ± 14 min, including a lag phase of 71 ± 9 min. However, Meyer *et al.* (1985) found a faster gastric emptying (180 min) for radiolabeled steak

Table 3. Gastric emptying time (min) for liquids and solids (different particle sizes) in dogs after feeding cereal or meat based diets (Banta *et al.* 1979)

Diet	Liquid emptying time (min)*	Solid emptying time (min)*		
		2 × 2†	2 × 10†	2 × 20†
Cereal based	102	186	564	600
Meat based	108	606	42	666

*Time required for 50 % of the solid particles appearing in the faeces
† particle size (mm × mm)

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and liver in large breed dogs (20–25 kg body weight). Compared to Meyer *et al.* (1985) Burrows *et al.* (1985) observed comparable results in half-emptying time in large breeds (26–32 kg body weight) using different isocaloric commercial diets. Canned meat based food (77 % moist), dry cereal based chow plus water (77 % moist) and dry cereal based food were emptied in 228 ± 36, 150 ± 36 and 144 ± 36 min respectively (differences not significant).

The large difference in half-emptying time of dry food between the studies is probably due to the fact that sometimes, like in the study of Arnjberg (1992), the dogs had no access to water.

Cullen & Kelly (1996) used the equation of Elashoff *et al.* (1982) to calculate the emptying curves of liquids and solids in the dog (Table 4):

$$f = 2^{-(t/t_{1/2})^{\beta}}$$

in which $t_{1/2}$ is the time (min) from the start of the meal until 50 % of the meal has been emptied and β determines the shape of the curve. This equation can be used to summarize and compare data on gastric emptying between meals or between groups. An overview of the different studies on gastric emptying in dogs is shown in Table 5.

Besides the effects of the food, motility (Pröve & Ehrlein, 1982; Azpiroz & Malagelada, 1984; Mandrek, 1991; Eagon & Kelly, 1993) and hormones (Landor & Wild, 1970; van Kruiningen *et al.* 1987; Patronella *et al.* 1988; Lawson *et al.* 1994; Jin *et al.* 1994*a, b*) play an important role in the regulation of gastric emptying. Although these parameters are very important, their effects are not discussed in this review because such parameters cannot be used in *in vitro* models.

Pancreas

A very important aspect in the digestion of food is the secretion of pancreatic juice into the proximal small intestine mainly due to the action of electrolytes and digestive enzymes.

Composition of pancreatic juice

The electrolyte composition of the pancreatic juice released into the intestine varies among animal species and, in most animal species, with flow rate. Intermittent feeders (eating at intervals), such as the dog, mainly secrete the juice during the digestive phase after the ingestion of a meal (Stevens & Hume, 1995*b*). The effects of different types and amounts of food are shown in Table 6.

Because the amount and type of food play a role in the composition and secretion rate of the pancreatic juice secreted, the range of the values is very wide (Table 7).

Dog pancreatic lipase and its catalytic properties are very similar to those of humans and pigs. The lipase activity is stable above pH 4·0 and the amount delivered into the duodenum is shown in Fig. 3 (Carrière *et al.* 1993). The concentration slowly decreases in the duodenum and jejunum between meal ingestion and at the end of digestion (Fig. 4) (Carrière *et al.* 1993).

Table 4. Gastric emptying parameters of liquids and solids in dogs (Cullen & Kelly, 1996)

	Solids	Liquids
$t_{1/2}$ (min)	246 ± 14	148 ± 14
β	$3{\cdot}0 \pm 0{\cdot}4$	$1{\cdot}4 \pm 0{\cdot}2$
Lag (min)	71 ± 9	14 ± 8

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Table 5. Overview of different studies of gastric emptying in dogs fed liquid meals, canned or fresh food or dry food

Method	Diet	Gastric emptying parameters	Reference
Fluid marker: phenol red	liquid test meal 14 g protein 52 g carbohydrate 12·5 g lipid	$t_{1/2} = 75 \pm 8$ min	Carrière *et al.* 1993
Thomas cannula	water > 100 ml	$t_{1/2} = 10$ min 80–100 % has left the stomach after 40 min	Gupta & Robinson, 1988
Fluid markers:		mean gastric emptying*	Banta *et al.* 1979
PEG	cereal based diet	102 min	
^{51}Cr-EDTA	meat based diet	108 min	
Aspiration from the stomach	154 mM NaCl	$t_{1/2} = 25$ min	Dozois *et al.* 1971
Heidelberg capsule	20–50 ml of water	gastric emptying time 99·8 ± 27·2 min (range 35–317 min)	Lui *et al.* 1986
Barium contrast	barium sulphate suspension	gastric emtying time 6 ± 16·7 min (range 30–120 min)	Miyabayashi *et al.* 1986
External scintigraphy	canned dog food	$t_{1/2} = 77 \pm 23{\cdot}3$ min	Theodorakis *et al.* 1980
Radiography	canned food (70 % moist)	first appearance duodenum: 270 ± 30 min emptying complete: 420–480 min	Arnbjerg, 1992
Radiography	fresh food (75 % moist)	first appearance duodenum: 30 min emptying complete: 240–360 min	Arnbjerg, 1992
γ-activity measurement	radiolabelled steak	$t_{1/2} = 180$ min	Meyer *et al.* 1985
	radiolabelled liver	$t_{1/2} = 180$ min	
Scintigraphy	radiolabelled chicken	$t_{1/2} = 214 \pm 14$ min	Cullen & Kelly, 1996
	^{111}In-labelled beef broth	ag phase: 71 ± 14 min	
Radio-opaque polyethylene tubing		particle size (mm) 2 × 2 2 × 10 2 × 20	Banta *et al.* 1979
	cereal based diet	186 564 600 min	
	meat based diet	606 642 666 min	
Scintigraphy	dry kibble food	beagles $t_{1/2} = 240$ min mongrel $t_{1/2} = 216$ min	Hornof *et al.* 1989
Radiography	dried food (10 % moist), no access to water	radiographic appearance remained unchanged for 480–600 min (mean 534 min) emptying complete: 900 ± 60 min	Arnbjerg, 1992

* time required for 50 % of the marker to leave the foregut or to be recovered in the faecal material

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Besides lipase, chymotrypsin is also an important pancreatic enzyme with significant activity (Table 8). A very high induction of chymotrypsin activity is caused by feeding protein-rich meals (especially animal protein) whereas lactose meals produce a very low chymotrypsin activity ($1{\cdot}45 \pm 0{\cdot}66$ U/kg wet weight) (Kienzle, 1988).

Although the dog has no amylase activity in saliva, there is amylase activity in pancreas secretions. The amylase activity in pancreatic tissue of an adult dog has been reported to be 2316 ± 2017 (383 to 6625 U/g wet weight) ($n = 16$). As for chymotrypsin, maximum levels of amylase activity were found in the jejunum as well as in the ileum. In contrast to chymotrypsin activity, the activity of amylase is relatively high in carnivores (Kienzle, 1988). The amylase output is increased by wheat bran supplementation in the diet, as well as bicarbonate output and pancreatic juice flow (Stock-Damgé *et al.* 1983). Pancreatic enzyme levels can adapt to the type of food available; this is a physiological advantage that allows animals to digest food components and energy for metabolism as efficiently as possible (Ballesta *et al.* 1990).

Besides food, hormones, such as pentagastrin, can also stimulate the exocrine secretion of the pancreas: directly, resulting in a protein-rich secretion, and indirectly by virtue of their effect on gastric acid secretion and consequently the release of secretin and cholecystokinin when acid gains access to the duodenum (Gupta *et al.* 1973).

Bile

Composition of dog bile

Bile is continuously produced in the liver and is partly stored in the gall bladder between meals or between periods of ingestion. In fasting dogs 29 to 53 % (median 42 %) of newly produced bile is stored in the gall bladder. The remainder is directly released into the duodenum (Rothuizen *et al.* 1990). Bile is stored in a concentrated form and is actively evacuated into the duodenum in response to the ingestion of a meal (Camello *et al.* 1991). Therefore bile from the gall bladder differs in concentration from bile directly secreted from the liver (Table 9).

In a study with adult dogs (20–25 kg), Madrid *et al.* (1983) found results comparable to those of Altmann & Dittmer (1968) for basal secretion of bile (29 ml/kg/24 h), concentration of bilirubin (195 ± 14 mg/100 ml) and concentration of chloride ($70 \pm 4{\cdot}5$ mmol/l). Nakayama (1969), Wildgrube *et al.* (1986) and Washizu *et al.* (1990) studied the bile acid composition of gall bladder bile of dogs (Table 10). In the dog, more than 99 % of the bile acids are conjugated with taurocholic acid, taurodeoxycholic acid and taurochenodeoxycholic acid.

Gall bladder emptying

In response to food ingestion the gall bladder contracts (Fig. 5) and the pressure and the rate of emptying of the gall bladder increase. Emptying peaks are found at 30 min after a meal and the emptying decreases 2 h after food ingestion (Madrid *et al.* 1983; Traynor *et al.* 1984). Food is

Table 6. Amount, secretion time and composition of the pancreatic juice with different types and amounts of food given to dogs (Stevens & Hume, 1995)

Amount and type of food	Amount of juice (ml)	Time of secretion (min)	Dry matter (%)	Na_2CO_3 (%)
600 cm^3 milk	457	270	527	35
250 g bread	1624	465	322	56
100 g meat	1316	252	247	59

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Table 7. Composition of dog pancreatic juice as reviewed by Altman & Dittmer (1968)

Property or constituent	Value
pH	7·1–8·2
secretion rate	0·2–1·1 ml/min
ash	8400–9700 mg/l
solids total	14000–63900 mg/l
organic	4800–22000 mg/l
water	98·04 %
calcium	0·9–1·0 mmol/l
chloride	71–106 mmol/l
magnesium	0·1–1·7 mmol/l
potassium	2·5–7·0 mmol/l
sodium	142–162 mmol/l
bicarbonate	93–143 mmol/l
phosphate	0·4–1·8 mmol/l
glucose	250 mg/l
protein	5000–48000 mg/l
urea	240–585 mg/l
nitrogen total	1000–9360 mg/l
protein	748–843 mg/l
nonprotein	180–840 mg/l
lactate	0·1–0·7 mmol/l
amylase*	23900–47500 mg/l†
lipase*	9·75–33·25 ml 0·05 N NaOH/ml‡
trypsin*	407·5–2440·0 mg tyrosin/ml§

* secretin-stimulated
† starch substrate
‡ olive oil emulsion substrate
§ casein substrate

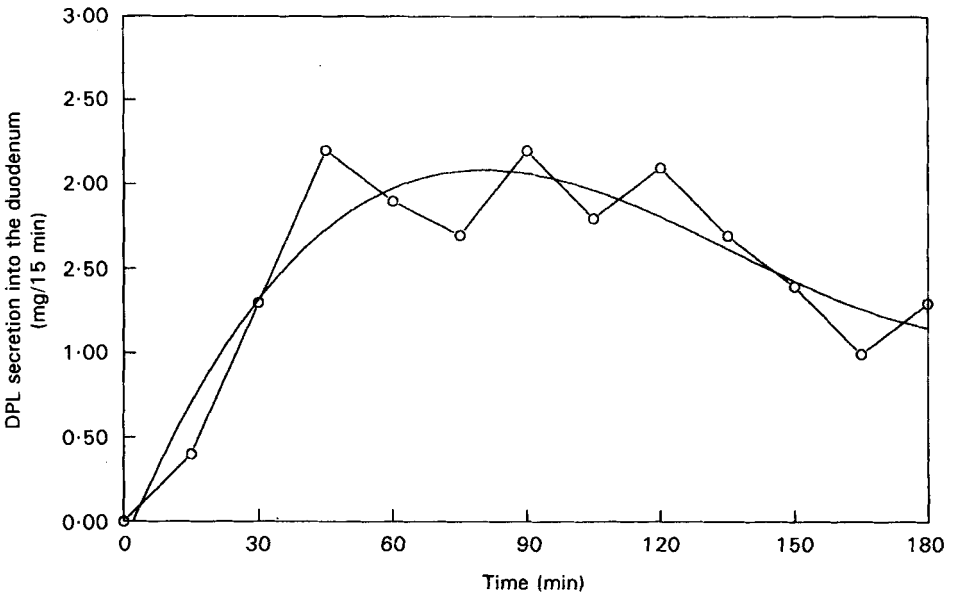

Figure 3. Rates of secretion of dog pancreatic lipase (DPL) secretion levels into the duodenum during digestion of a liquid test meal (14 g protein, 52 g carbohydrate and 12.5 g lipid) (Carrière *et al.* 1993).

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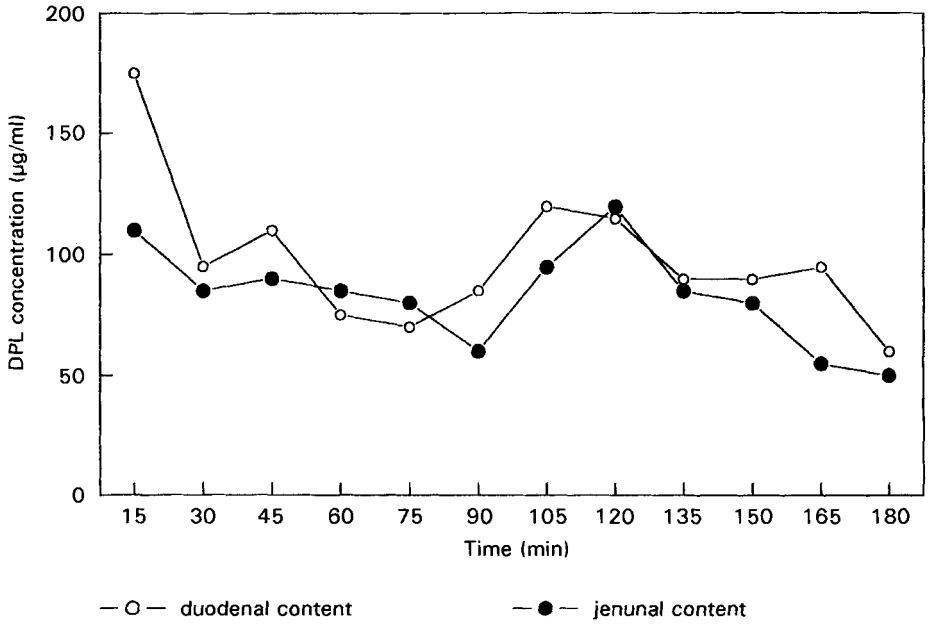

Figure 4. Dog pancreatic lipase (DPL) concentration in duodenal and jejunal contents, obtained from enzymic activity measurement (Carrière *et al.* 1993)

an inducer of circadian rhythms in the gall bladder. These contraction – relaxation cycles are synchronized with periodic dilution – concentration processes (Camello *et al.* 1991).

The gall bladder empties only partially (5–65 %; median 31 %) after a meal (Rothuizen *et al.* 1990). The time course of (partial) postprandial gall bladder emptying is reflected by the parameters of the power-exponential function. Values for the gall bladder half-emptying time $t_{1/2}$ of 47·3 ± 4·7 min and for the curve shape parameter S of 0·866 ± 0·036 were reported by Jonderko *et al.* (1994). During feeding the gall bladder bile concentration shows circadian rhythms peaking immediately before meal time in all biliary compounds (Camello *et al.* 1991). This finding suggests that periodic food ingestion plays a role in the circadian rhythms of gall bladder bile composition (Camello *et al.* 1991). The duodenal activity has also an influence on

Table 8. Activity (U/g wet weight) of chymotrypsin in the chyme of adult dogs in relation to the amount of protein in the diet (Kienzle, 1988)

Part of the intestine	Protein content in food dry matter		
	< 25 %* n = 10	35–45 %† n = 4	> 50 %‡ n = 4
duodenum	3·9 ± 6·2	31·0 ± 26·8	13·8 ± 8·1
jejunum	13·9 ± 15·3	53·1 ± 8·0	84·9 ± 100·1
ileum	20·4 ± 22·1	25·0 ± 8·4§	148·1 ± 99·8

*diets: meat meal with sucrose, meat meal with lactose, dry type of dog food, soyabean meal with tapioca starch
† diets: soyabean meal, soya bean meal with fat
‡ diets: raw meat, raw lungs
§ n = 11

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Table 9. Composition of bile secreted from the gall bladder and from the liver of dogs (Altman & Dittmer, 1968; Nakayama, 1969); mean ± SD or range

	Gall bladder (Nakayama, 1969)	Gall bladder (Altman & Dittmer, 1968)	Liver (Altman & Dittmer, 1968)
secretion rate mg/kg body wt/24 h		–	12·0 (5·2–52·5)
pH		5·18–6·97	7·1–8·5
dry matter g/l		114–246	23–45
solids, total	196·6 ± 122·9		
salts g/l		79–150	5–24
calcium mmol/l		131	1·9–3·6
chloride mmol/l			70 (59–105)
iodine g/l		130×10^{-6}–1130×10^{-6}*	
iron g/ ml		$0{\cdot}9 \times 10^{-3}$–$1{\cdot}8 \times 10^{-3}$	18×10^{-3}–160×10^{-3}
magnesium mmol/l			1·8 (1·1–2·5)
total phosphorus g/l		0·87–2·8	0·1–0·15
potassium mmol/l			5·1–6·0
sodium mmol/l			168 (150–203)
bicarbonate mmol/l		–	7–34
choline, total g/l		3·4–11·1	0·39–0·58
cholesterol g/l	1·37 ± 0·75	0·8–1·0	0·004–0·15
fatty acids, total g/l	0·25 ± 0·23	16·0–50·0	1·75–2·70
monoacylglycerol	2 ± 3		
diacylglycerol	2 ± 4		
triacylglycerol	0		
total protein g/l		1·9–5·2	1·3–2·1
total lipid g/l	193·5 ± 49·8		
bilirubin g/l	0·021 ± 0·014	0·92–1·70	0·42–0·55
total bile acids†	37·9 ± 20·6		
phospholipids	20·3 ± 15·4		

*Source of bile not specified
† Sum of cholic, chenodeoxycholic, deoxycholic, lithocholic, hyocholic, and hyodeoxycholic acids

the output of bile components (Table 11). Drugs (Jonderko *et al.* 1994) and hormones (Rothuizen *et al.* 1990; Keane *et al.* 1980; Stevens & Hume, 1995*a*) also can influence the motility.

Small intestine

Electrolytes and enzymes

The pH value, concentrations of constituents and activity of some enzymes in different parts of the small intestine are listed in Table 12. The results of the reviews of Alexander (1965) and Altman & Dittmer (1968) both show that there is a large variation between results of different studies.

pH

Digesta are rapidly neutralized as they pass from the stomach into the duodenum. The average pH in the proximal duodenum is 6·2 (6·0–7·2) with diets based on cereal or meat (Banta *et al.*

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Table 10. Bile acid composition of gall bladder bile of the dog (% of total bile acid concentration (Wildgrube *et al.* 1969; Washizu *et al.* 1990)

Bile acid*	Washizu *et al.* 1990	Wildgrube *et al.* 1986	Nakayama, 1969
TUDC	1	–	nd
TC	732	743	nd
TCDC	60	53	nd
TDC	201	149	nd
TLC	1	nd†	nd
C	–	nd	774
CD	nd	nd	49
DC	nd	nd	177
LC	nd	nd	–
GUDC	–	–	nd
GC	4	–	nd
GCDC	–	–	nd
GDC	nd	–	nd
GLC	1	nd	nd

*TUDC, tauroursodeoxycholic acid; TC, taurocholic acid; TCDC, taurochenodeoxycholic acid; TDC, taurodeoxycholic acid; TLC, taurolithocholic acid; C, cholic acid; CD, chenodeoxycholic acid; DC, deoxycholic acid; LC, lithocholic acid; GUDC, glycoursodeoxycholic acid; GCDC, glycochenodeoxycholic acid; GDC, glycodeoxycholic acid; GLC, glycolithocholic acid.
† nd = not determined

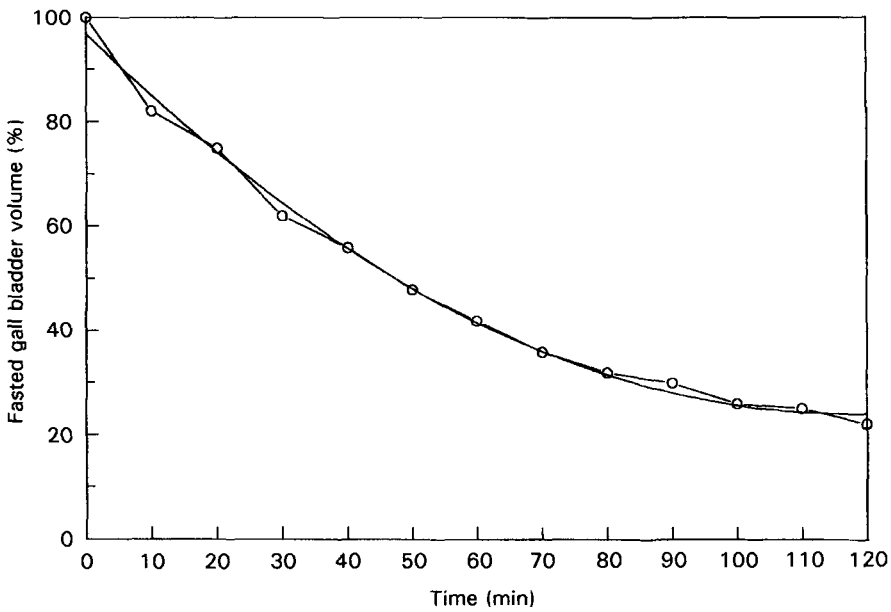

Figure 5. Time course of the meal-induced gall bladder emptying in dogs (Jonderko *et al.* 1994)

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Table 11. Bile acid and bicarbonate outputs related to different phases of duodenal activity (Keane *et al.* 1980)

Mean output (μmol/min)	Phase I*	Phase II*	Phase III*	Phase IV*
Bile acids	0·17 ± 14	23·6 ± 4·6	7·1 ± 1·6	2·7 ± 1·5
Bicarbonate	0	10·6 ± 2·5	21·3 ± 5·2	6·03 ± 5·3

* Phase I, period of complete motor quiescence (no spikes); Phase II, gradual increase in spiking activity; Phase III, series of strong contractions with spikes on every slow wave; Phase IV, rapid return to quiescence and hence to phase I of a new cycle (Eeckhout *et al.* 1984)

Table 12. Composition of gastrointestinal content presented as mean and/or range (in parenthesis) in the duodenum, jejunum and ileum

	Duodenum*	Jejunum†	Ileum‡	Reference§
pH	84	6.8 (6.3–7·2)	7·6–8·7)	1
Inorganic matter mg/g	926	–	–	1
Organic matter mg/g	615	–	–	1
Solids, total g/l	15.41 mg/g	17 (12–23)	(13–18)	1
Calcium mmol/l	–	1·4 (0·8–2.7)	(2.5–2.8)	1
Magnesium mmol/l	–	0·6 (0·1–1·0)	–	1
Chloride mmol/l	136 (130–140)	147 (141–153)	78 (68–88)	1
			101 (98–104)	1
		61 ± 3.4	54 ± 5.0	2
Sodium mmol/l	145 (136–150)	141 (126–152)	151 (146–156)	1
		75 ± 2	109 ± 8	2
Potassium mmol/l	6.3 (4.5–8·0)	6.3 (4.2–10·2)	4.7–6.8	1
		59 ± 3.5	44 ± 4.3	2
Bicarbonate mmol/l	17 (14–22)	22 (5–30)	92 (70–114)	1
		20 ± 3.8	28 ± 4	2
Phosphate mmol/l	–	1·6 (0·6–4.0)	–	1
		44.5 ± 5.5	41·5 ± 6.0	2
Pepsin units/ml	15	–	–	1
Lipase (as fatty acid) g/l	–	61 (49–74)	22 (18–29)	1
Amylase (as reducing sugar) g/l	–	600 (500–680)	240 (200–300)	1

* Brunner's glands and and duodenal mucosa fistula
† isolated loop or fistula, during fasting
‡ loop or transplant; during fasting
§ 1, Altman and Dittmer (1968); 2, Alexander (1965)

1979). This is much lower than the pH of 8·4 reported by Florey & Harding (1934). The difference probably can be explained by the method used to measure the pH.

Gupta & Robinson (1988) studied the effect of administration of different volumes of water to a fasted dog on pH of the duodenal effluent collected from a permanent Thomas cannula (15 cm distal from the gastroduodenal junction). The mean pH of the duodenal discharge during one activity period without the administration of a test meal was 7·7. The pH was maintained between 7 and 8 after the administration of volumes up to 100 ml. This compares well with the results of Lui *et al.* (1986) who found a maximum pH of 7·7 20 min after gastric

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empyting. The pH gradually declined thereafter (pH 7·2 180 min after empyting). The overall mean intestinal pH was 7·3 ± 0·09. However, a reduction in pH of the effluent was seen as the volumes were increased to 100 ml or more. The range of pH for volumes up to 100 ml was 4·3–8·3 whereas it was 1·5–8·3 for 150 ml and more. From these results it can be concluded that the pH of the duodenal effluent in dogs indirectly depends on the volume of water ingested. Large volumes apparently induce acid secretion in the stomach (by stimulation of gastrin release) and thus lower the pH to values as low as 1·5 in the lumen of the proximal duodenum. The movement of acid chyme from the stomach into the small intestine stimulates the secretion of pancreatic juice into the duodenum. The large amount of bicarbonate in pancreatic juice and bile accounts for the increase in pH of digesta passing from the stomach to the duodenum (Banta *et al.* 1979).

Fig. 6 shows the pH of the intestinal contents of beagles fitted with chronic duodenal and jejunal fistulas, inserted opposite to the biliary canal and 30 cm below the angle of Treitz, respectively (Carrière *et al.* 1993).

Absorption

One of the main functions of the small intestine is the absorption of digested products. The absorption of water and electrolytes from the jejunal lumen has been studied in dogs using a 25 cm proximal jejunal Thiry-Vella loop and 400 g of a standard mixed canine meal (52 % protein, 36 % fat, 12 % carbohydrates). In the basal period the F_{H2O} (flux of water) averaged 171 ± 44 µl/min, the net F_{Na+} averaged 20 ± 6 µmol/min and the F_{Cl-} averaged 10 ± 5 µmol/min. (Yeo *et al.* 1990). After ingestion of a standard mixed meal there was a significant increase ($P < 0{\cdot}0001$) in the net absorption of water and electrolytes at all post-prandial observations, peaking at 75 min after a meal. The maximum ΔF_{H2O} at 75 min after a

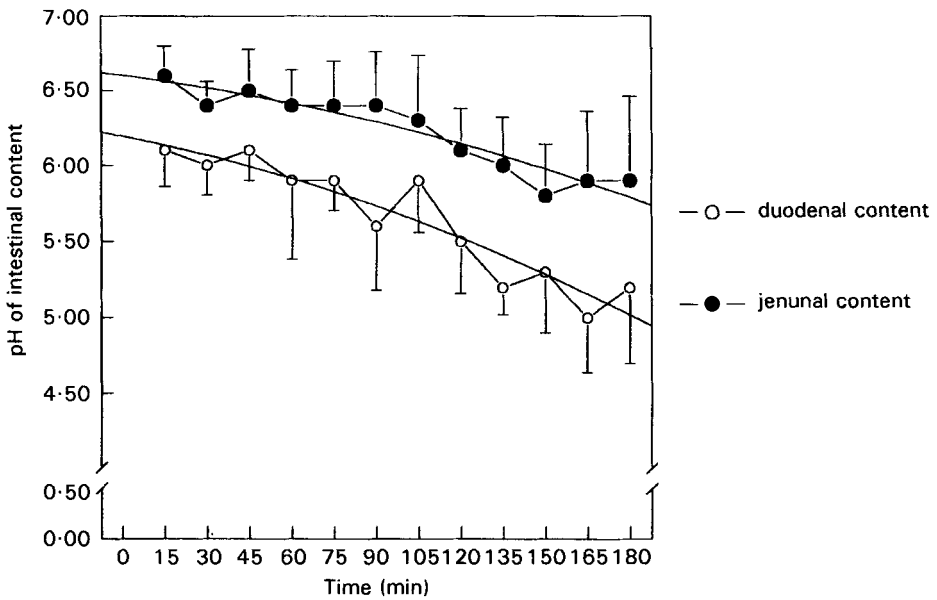

Figure 6. Curve fitted pH curves of the duodenal and jejunal contents measured in fistulated beagles (Carrière *et al.* 1993).

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Table 13. Recovery of test substances in effluent* of the proximal jejunal loop determined in 15 min samples after infusion of an electrolyte solution† (Hakim *et al.* 1992)

Parameter	Amount infused	Median	Range
Fasting state			
H_2O (ml)	42	291	24·5–29·6
Sodium (mmol)	5880	3590	3460–4200
Potassium (mmol)	210	162	144–179
Chloride (mmol)	5250	3710	3460–4150
Glucose (μg)	42	230	1·31–3·80
Folate (%)	–	66	35–77
$t_{1/2}$ (min)	–	56	4·0–8·0
Fed state			
H_2O (ml)	42	242	22·8–24·8
Sodium (mmol)	5880	3590	3460–4200
Potassium (mmol)	210	151	130–157
Chloride (mmol)	5250	3710	3455–4150
Glucose (μg)	42	121	0–2·47
Folate (%)	–	54	31–66
$t_{1/2}$ (min)	–	73	6·1–8·0

*six dogs, three experiments per dog at each time point
† isomolar solution containing NaCl (120 mmol/l), $NaHCO_3$ (20 mmol/l), KCl (5 mmol/l), glucose (5·6 mmol/l), ^{3}H-folic acid (10 μCi/l), unlabelled folate (1·5 mg/l), and 5 g/l PEG labelled with ^{14}C-PEG (5 μCi/l).

meal was 206 ± 33 μl/min, while the maximum ΔF_{Na+} and ΔF_{Cl-} were 25 ± 4 and 17 ± 3 μmol/min, respectively (Yeo *et al.* 1990).

This is in contrast with the results of Hakim *et al.* (1992) who studied the net absorption of water, glucose, electrolytes and folate in a 80 cm modified Thiry-Vella loop of the proximal jejunum. The enteric neural continuity with the duodenum and proximal jejunum was maintained. All effluent was collected from the jejunostomy at 15 min intervals to determine net absorption during a fasting state and a fed state (meal of 500 g porcine liver) (Table 13). When net absorption of water during fasting was compared to the absorption after feeding at different times, no statistically significant differences were detected ($P > 0{\cdot}05$). However a tendency towards absorption of more infusate after feeding was noticed as indicated by median values. Similar results were found with sodium, potassium, chloride, glucose and folate.

Meyer *et al.* (1989) studied the absorption of water, sodium and potassium in the small intestine in ileal fistulated dogs during 25 feeding trials. Water was always absorbed in the small intestine at a rate of 15–65 ml/kg body weight or 30–90 % of the water intake. Sodium absorption in the small intestine generally corresponded with sodium intake. The absorption of potassium is strongly correlated to potassium intake. Sodium and potassium had an absorption of *c.* 90 % of the intake or more. Only with some specific foods (e.g. tapioca starch) absorption was less. The sodium concentration in the ileum varied from 0·3 to 3·0 g/kg chyme. The potassium concentration varied from 0·3–0·5 g/kg chyme. The sum of both ions reached a value of 90–130 mmol in the ileal chyme.

Intestinal transit

The movement of digesta along the GIT is regulated *via* structural and physiological properties of the digestive tract. It is also influenced by physical as well as nutritional characteristics of the diet (Clemens & Stevens, 1980).

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Chyme is usually propelled through the small intestine mainly by the direction of propagation of the small intestinal pacesetter potentials (Soper *et al.* 1990). The motility of the intestine can be distinguished in different phases (Sarr & Kelly, 1980) and can be influenced by several factors, such as food components, hormones and the nervous system (Bueno *et al.* 1975, 1981; Berhns & Sarr, 1994; Dreznik *et al.* 1994; Eeckhout *et al.* 1984; Neri *et al.* 1991).

Miyabayashi *et al.* (1986) studied the small intestinal transit and emptying time in dogs given orally 60 % w/v barium sulphate solution. In this study small intestinal transit time was determined by identifying the head of contrast medium column within the caecum or ascending colon. The small intestinal emptying time was defined as the passage of the contrast medium into the caecum and colon. Sequential radiographs were made every 30 min. A transit time of 73·0 ± 16·4 (range 30–120) min was found and a small intestinal emptying time of 214·0 ± 25·1 (180–300) min (n = 5, three samples/dog). More frequent measurements would produce shorter times, since the experimental design allowed sampling errors of 29 min. The results suggest that both small intestinal emptying time and transit time correlate positively with gastric emptying time.

Banta *et al.* (1979) used PEG and ^{51}Cr-labelled EDTA as a fluid and a solid marker, respectively, to determine the passage of liquids and particles in a meat diet through the gastrointestinal tract (Fig. 7). The fluid marker passed rapidly through the stomach and small intestine regardless of the diet. In dogs fed a cereal diet the distribution of the marker after 4 h was *c.* 25 % in the stomach, 45 % in the small intestine and 30 % in the colon. Species with a simple stomach and a short, nonsacculated, nonvoluminous colon, such as the dog, display no selective retention relating to the size of the particles. This means that no differences exist in

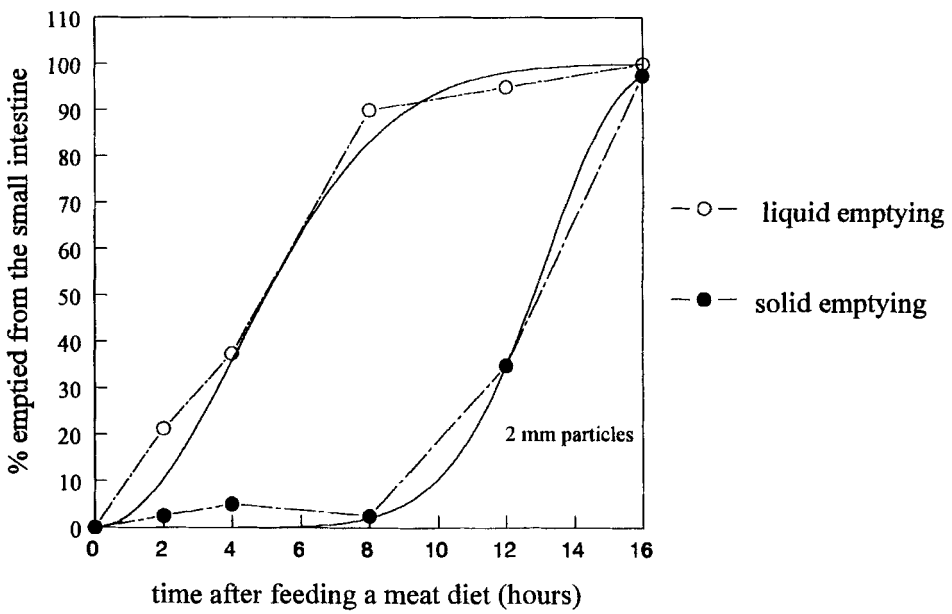

Figure 7. Percentage of liquids and solids (2 mm particles) emptied from the small intestine in a given time after feeding a meat diet (Banta *et al.* 1979).

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Table 14. Transmit time and flow rate of digesta through a 200 cm jejunal segment from 2 to 4 h after feeding 500 g of a standard diet, or mixed with 30 g of bran, cellulose or gum (mean ± SD, n = 6) (Bueno *et al.* 1981)

	Control	Bran	Cellulose	Gum
Transit time* (min)	9·5 ± 2·7	12·2 ± 4·3	82·3 ± 10·3†	14·3 ± 3·6†
Flow rate of digesta (ml/h)	172 ± 41	161 ± 34	55 ± 16†	285 ± 54†

* retention volume calculated from the flow rate (ml/min) of digesta and the mean transit time (min)
† significantly different ($P < 0·05$) from control values

Table 15. Half-emptying time of the small intestine (min) in the fasting state, early postprandial state and late postprandial state (Neri *et al.* 1991)

$t_{1/2}$	Fasting	EPP*	LPP*
Ileum–ileum‡	16·3 ± 4·6	8·7 ± 2·7	5·1 ± 0·7†
Ileum–colon‡	44·8 ± 6·7	25·2 ± 8·8	9·6 ± 3·4†

* EPP = early postprandial period, which extend from ingestion of the meal to its arrival in the terminal ileum; LPP = late postprandial period, which extend from the arrival of the meal in the terminal ileum to the end of the study (4 h after ingestion of the meal).
† $P < 0·05$ *v.* fasting
‡ ileum–ileum, from the infusion catheter 32 cm proximal to the ileocolonic sphincter (ICS) to the aspiration catheter 1 cm proximal to the ICS
ileum–colon = from the infusion catheter 32 cm proximal to the ICS to the cannula 5 cm distal to the ICS in the proximal colon

the rate of transit between the different particles sizes of the marker (Clemens & Stevens, 1980).

To determine the transit time of canned dog food the concentrations of labelled markers can be measured in ileal or jejunal samples using liquid scintillation spectroscopy (Tables 14 and 15) (Bueno *et al.* 1981; Neri *et al.* 1991).

Besides radiography, scintigraphy and radio-opaque plastic markers, the oro – caecal transit time can be assessed by ingestion of an unabsorbable but fermentable carbohydrate in a test meal and determining the time needed for a sustained increase in exhaled hydrogen (Papasouliotis *et al.* 1993). In this study the median oro – caecal transit times were 105 min (range 45–135 min) for a standard meal of canned food, 113 min (range 53–203 min) for a standard meal with the addition of wheat bran and 105 min (range 75–195 min) after addition of guar gum. A possible explanation for the difference between the study of Bueno *et al.* (1981) and that of Papasouliotis *et al.* (1993) maybe the amount of fibre added to the diets: Bueno *et al.* (1981) added 30 g fibre and Papasouliotis *et al.* (1993) added 7·7 g. The amount of fibre can influence the viscosity of the meal, which in turn influences the transit time.

The results of transit experiments can be misleading for two reasons. The single value ($t_{1/2}$) in no way indicates how the bulk of material moved through the GIT, neither does it consider the structure, volume or length of the GIT (Clemens & Stevens, 1980).

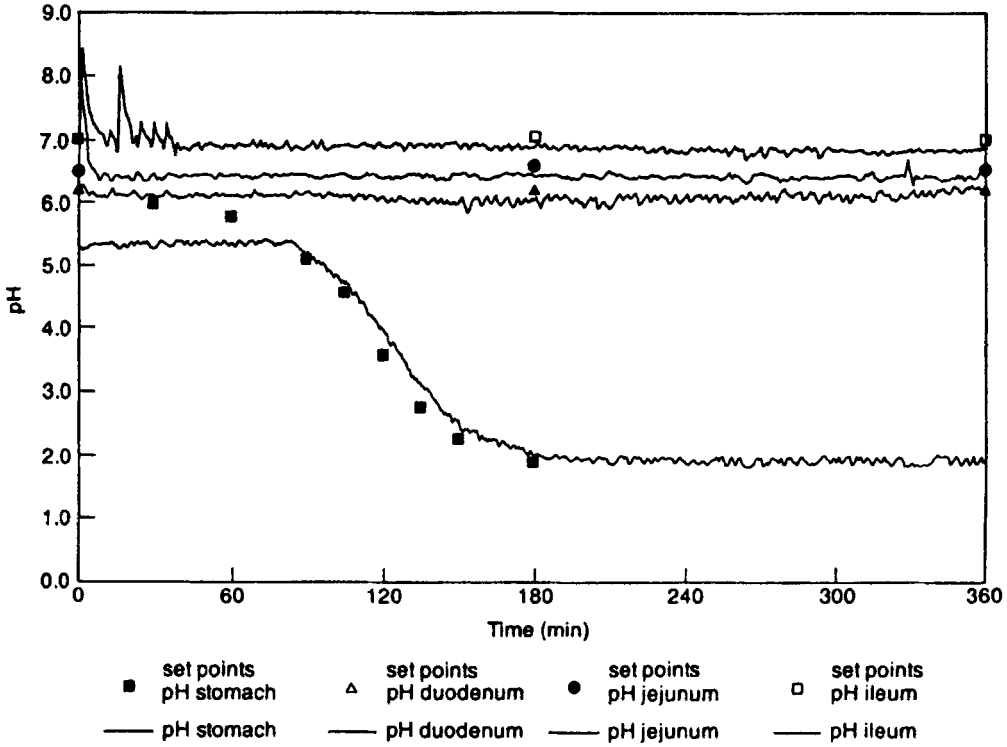

Figure 8. Comparison of the pH set points (markers) in the stomach and small intestinal compartments and the actual pH values in the canine model during an experiment with dry dog food ground to different particle sizes (< 1 mm and < mm).

Conclusions

In order to develop *in vitro* systems for simulation of digestion it is necessary that the digestive processes take place in an environment which simulates these processes as measured *in vivo*. Therefore we gathered literature on various aspects of the physiology of the stomach and small intestine of the dog. In this respect it is important to note that studies on physical conditions and rate of passage are not unanimous: between them variation was noted in relation to diets fed, to the type of dog and to the experimental methods.

Parameters needed for simulation of digestion are transit times, pH, composition of the secretions and the rate of secretion in the different parts of the GIT. Based on the data in literature it can be concluded that the concentration of electrolytes in saliva and gastric juice are in the same range and that dogs' saliva does not contain amylase. This means that in the model the secretion of saliva and gastric juice can be combined. Mimicking this by the computer program can therefore derive physiological conditions. Gastric juice should consist NaCl, KCl, $CaCl_2$, $NaHCO_3$ and the enzymes lipase and pepsin.

The mean secretion rate of gastric juice is $\sim 0{\cdot}25$ ml/min. To mimic the pH in the stomach the pH-curve found by Carrière *et al.* (1993) can be used. Transit of the chyme through the stomach can be derived using the equation described by Elashoff *et al.* (1982). Physiological values for $t_{1/2}$ and β should be 90 and 1, respectively.

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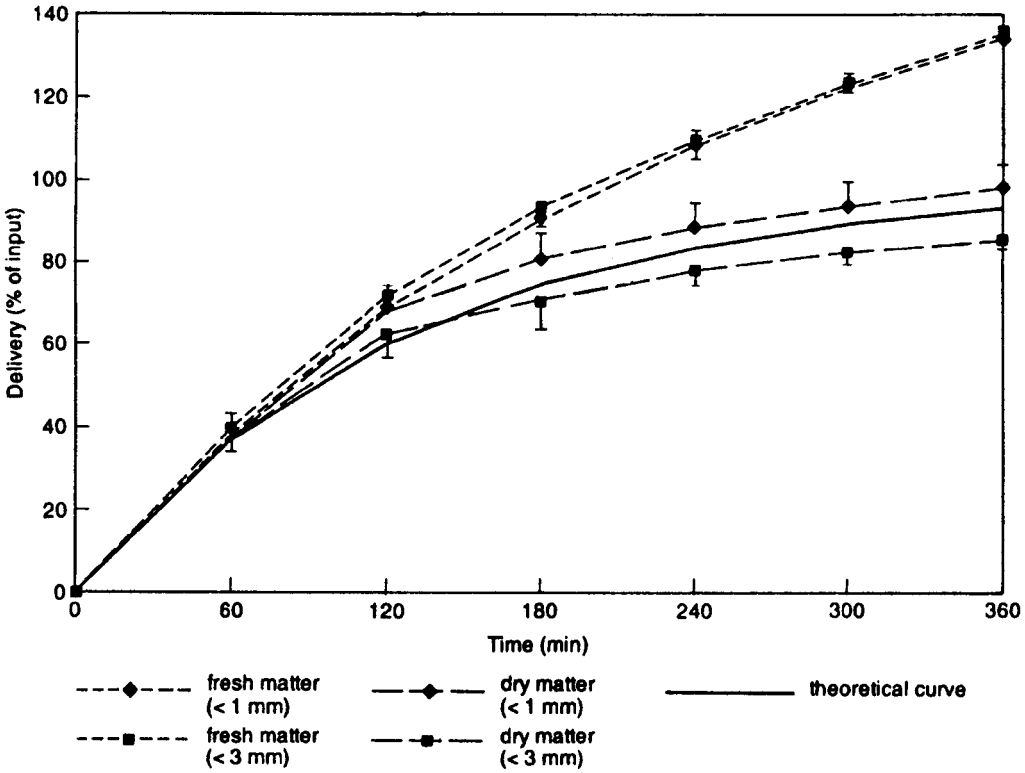

Figure 9. Comparison of the set points of gastric emptying and the emptying rate of fresh matter (food + secretions) and dry matter of the stomach during an experiment with dry dog food ground to different particle sizes (< 1 mm and < 3 mm).

For mimicking the secretion of pancreatic juice and bile porcine pancreas and bile extracts can be used. Besides pancreatic juice and bile, an electrolyte solution consisting of NaCl, KCl and $CaCl_2$ must be added in the duodenum. Based on the literature the rate of secretion of pancreatic juice and the electrolyte solution should be in the same range as the secretion rate of the stomach juice. However the secretion of bile must be higher than that of pancreatic juice (0·5 ml/min).

The pH in the small intestine can be set at 6·2 in the duodenum, 6·5 in the jejunum and 7·0 in the ileum. If these values can be incorporated in the model the condition may mimic the *in vivo* situation. Transit of chyme through the small intestine can be derived with a similar equation as used for transit through the stomach. Correct parameters to be used for the small intestine will be $t_{1/2}$ about 270 min and β about 2.

In conclusion the literature gives sufficient data for the development of a dynamic model of the canine GIT on the basis of the general concept of the GIT model developed at TNO Nutrition and Food Research. A fairly reliable composition of artificial saliva, gastric juice, bile and pancreatic juice can be made for secretion in the laboratory model of the canine GIT. Also the values derived for gastric and intestinal transit and for pH of the dog can be used to simulate the physiological situation when using the model as described. Although most parameters are influenced by factors such as meal components, hormones and the nervous system and although a large variation exists

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between individuals, a selection of these data can be made, within the physiological range, to mimic the parameters which are needed for the development of an *in vitro* dog model.

A protocol was consequently set up and the computer programme was adapted to simulate the physiology of the dog. Preliminary results showed that successive physiological parameters, such as gastric and intestinal pH (Fig. 8) and gastric emptying (Fig. 9), could be mimicked.

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