1 Digestive Physiology and Nutrition of Swine

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Introduction

The domestic pig (*Sus scrofa*) belongs to the order of Artiodactyla suborder Suiformes (Simpson 1945). Many of the physio-anatomical features of the species *S. scrofa* can be related to dietary adaptations typical of a plant-dominated omnivore, characterized by a high fermentative capacity in the proximal hindgut.

In brief, the digestion of nutrients starts in the mouth and continues in the stomach and small intestine with the help of both mechanic and enzymatic mechanisms. Most dietary nutrients are digested into single moieties and absorbed before the gut content reaches the end of the ileum and enters the large intestine where fermentation occurs. Undigested compounds such as complex carbohydrates, reaching the large intestine, are fermented and utilized by the microbiota releasing mainly short-chain fatty acids (SCFA). This chapter reviews the main anatomical and physiological features relevant to the digestion and absorption of nutrients in the pig. A comprehensive understanding of the role of gut microbiota in the digestive physiology of pigs has not been included in this chapter.

Anatomy of the Porcine Digestive System

The Oral Cavity

The mouth is the necessary point of entrance for all solid and liquid nutrients essential to maintain metabolic homeostasis. The anatomical and physiological features of the oral cavity respond to three main functions relevant to eating: (i) food selection and apprehension, (ii) physical breakdown and grinding of ingredients including predigestion, and (iii) lubrication and swallowing. These functions have been related to three main organs: the tongue, the dental, and the salivary system.

The Tongue

The pig tongue consists of a muscle appendix protruding from the base of the oral cavity (lower mandibula) characterized for a high mobility essential to move oral contents and a dorsal epithelial layer containing mechanical and sensory papillae. The tongue plays a fundamental role in food acquisition (particularly the front mobile tip), food selection (through taste), and oral manipulation as part of the mastication and the act of swallowing (Lærke and Hedemann 2012). The mechanical

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papillae (known as filiform) facilitate a central role in moving the food bolus around the oral cavity for optimal processing (e.g., grinding, crushing, and lubrication) prior to and including swallowing.

In addition, the tongue plays a fundamental role in sensing dietary nutrients through the taste system. The basic organelle is the taste bud, with bundles of 100–150 taste sensory cells embedded in defined epithelial structures named as taste papillae. There are three types of taste bud-containing taste papillae: fungiform, foliate, and circumvallate. Pigs have many fungiform papillae covering the upper lingual surface. The foliate are located distal at each side of the tongue and is in contact with the oropharynx. The circumvallate papillae are two mushroom-shaped macroscopic structures, located and also in contact with the oropharynx but as part of the dorsal epithelia in pigs (Roura et al. 2016). The circumvallate papillae contain the highest amount of taste buds. A detailed explanation of the sense of taste and nutrient sensing mechanisms in the pig can be found in the section on "Nutrient Digestion."

The Dental System

The apprehension and oral processing of solid food occurs mainly due to the combined function of the lips, the tongue, and the dental system. The pig is a dental heterodont consisting of four types of specialized teeth: incisors (I), canines (C), premolars (Pm), and molars (M). The array of teeth is arranged in four identical and symmetric quarters two in each half of the upper and lower jaws. The number of tooth types differs in the various orders of mammals and is closely related to their feeding habits. Incisors and canines are primarily involved in food acquisition (stripping and rooting), while premolars and molars are involved in oral processing of foods (crushing, grinding, and shearing). Specific to the pig, the dentition consists of 44 permanent teeth with a basic dental formula in each quarter of 3-1-4-3 indicating the number of I, C, Pm, and M, respectively. The lower tusks are kept sharp by friction against the upper ones making them formidable weapons as well. Numerous tubercles make the occlusal surface of the molars very irregular and ideal for grinding and crushing food (Figure 1.1) (Sova et al. 2018).

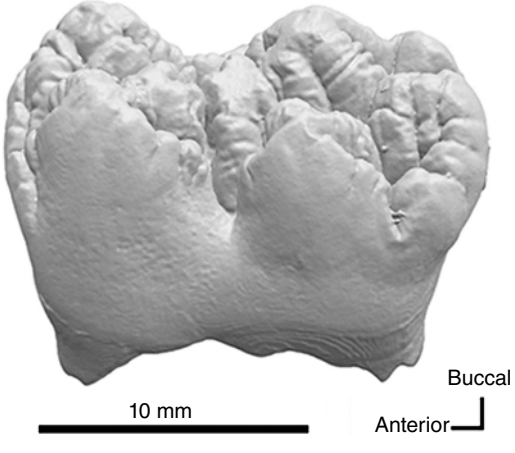


Figure 1.1 Pig molars have a complex fragmentary pattern with high crushing and grinding power. The enamel surface shows rounded, convex cusps with narrow intervening fissures. Porcine molars are difficult to distinguish from human molars. Source: Sova et al. (2018), Figure 03 [p. 04]/Frontiers Media S.A/CC BY 4.0.

The Salivary System

Adult pigs produce about 15 L of saliva daily. Saliva is a viscid, slightly acidic, and watery fluid secreted by the salivary glands present in the oral cavity that facilitates the mastication, digestion, lubrication, and deglutition of foods. The enzymatic digestion occurring before and after swallowing thanks to enzymatic activities present in saliva is further presented in the section "Nutrient Digestion."

The salivary glands are exocrine secretory acini with an intralobular system of intercalated and striated ducts. Pigs have three paired major salivary glands (parotid, submandibular, and sublingual) as well as hundreds of minor salivary glands embedded as part of the oral epithelia (Figure 1.2). Salivary glands produce three types of secretions referred to as serous, mucous, or seromucous (mixed). The main proteins present in serous secretions are alpha-amylase and the pig-specific enzyme ptyalin, both involved in the breaking down of starch into maltose and glucose. In mucous secretions, the main protein secreted is mucin acting mainly as a lubricant.

Pharynx, Esophagus, Stomach, and Omentum

When leaving the oral cavity, foods travel through the pharynx and esophagus before reaching the stomach. The esophageal submucosa is rich in bicarbonate and mucin-producing glands that lubricate the walls and the food protecting the epithelium, while also buffering contents with extreme pH.

The stomach is a food conditioning chamber preceding the main site of digestion and absorption of nutrients, the small intestine (duodenum). The size of the stomach represents 0.6% of the body weight (BW) in an adult pig reaching a volume of up to 6–8 L. The relative size decreases with the

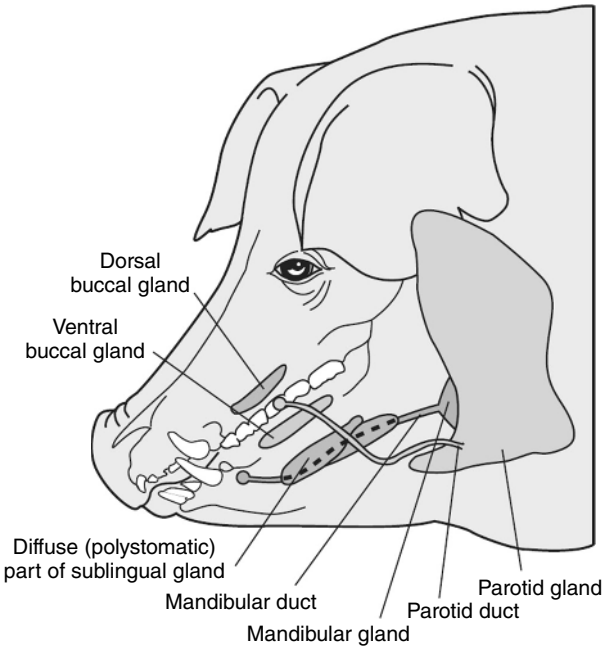


Figure 1.2 Schema of the distribution of the salivary glands in pigs. Source: Ducharme et al. (2017) / with permission of Elsevier.

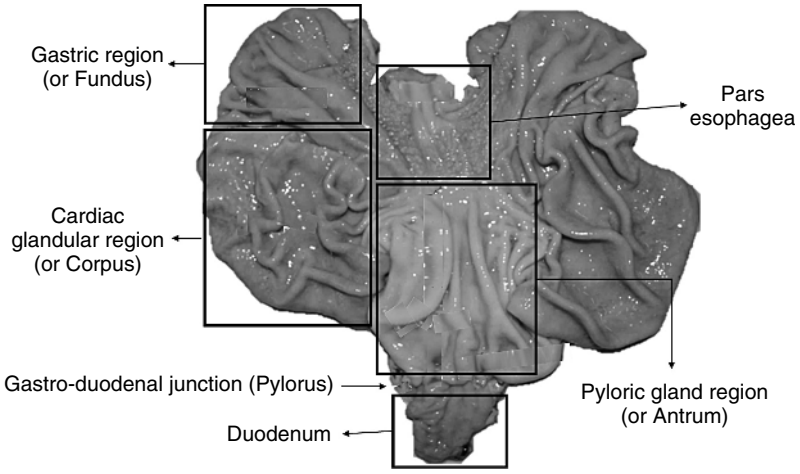


Figure 1.3 The stomach of a pig highlighting the four epithelial/glandular regions (*pars esophagea*, cardiac, gastric, and pyloric regions) and the gastro-duodenal junction (pylorus sphincter) gate to the duodenum.

age of the animal to the extent that in young pigs the relative size is around twice as much as in the adult (see the section on "Developing GIT in Piglets"). Based on the structure–function of the gastric mucosa, the porcine stomach can be divided into four main regions (Figure 1.3): the stratified squamous region named as *pars esophagea*, the cardiac glandular region (or *corpus*), the proper gastric region (or *fundus*), and the pyloric gland region (or *antrum*).

The most cranial region (*pars esophagea*) is a nonglandular extension of the esophagus located at the entrance of the stomach from the esophagus. In pigs, this region has a high risk in developing ulcers due to fine feed particle size or because of dealing with stressing events. The cardiac region contains mainly mucus-producing cells that protect the gastric mucosa from the entering bolus and the low pH gastric environment. Compared to other mammalian and avian species, the pig stomach has a very large cardiac region that is associated with having one of the lowest pH of around 1.5–2.5 (Smith 1965; Stevens 1977) (Figure 1.4). The fundus is also referred to as the proper gastric region because of the high density of HCl and mucus-producing glands (fundus glands). Fundus gland secretions are high in protease activity and contain pepsinogen (see "Nutrient Digestion" in this chapter below for additional descriptions). The stomach fundus is also rich in sensory cells identified as part of the endocrine/paracrine system described later in the section on "Nutrient Sensing and Gut-brain Axis." The pyloric region includes mucus; chief (zymogenic) cells, which oversee the production of pepsinogen and gastric lipase; and enteroendocrine cells (EEC).

The main function of the stomach is to precondition foods for further digestion in the small intestine, using mechanical and chemical processing. Mechanical digestion occurs thanks to the peristaltic movements that mix and soften the digesta. The apical entrance of the stomach is regulated by the cardiac valve that prevents the accidental regurgitation of highly acidic stomach contents. These movements increase in force as they reach the pylorus. The pylorus acts as a filter allowing the passage of only small particles into the duodenum. The digested food then slowly pushes into the duodenum through a process known as gastric emptying, regulated by neural and hormonal mechanisms involving ghrelin, cholecystokinin (CCK), glucagon-like peptide 1 (GLP-1), or peptide tyrosine-tyrosine (PYY) (see the section on "Nutrient Sensing and the Gut-brain Axis"). The chemical

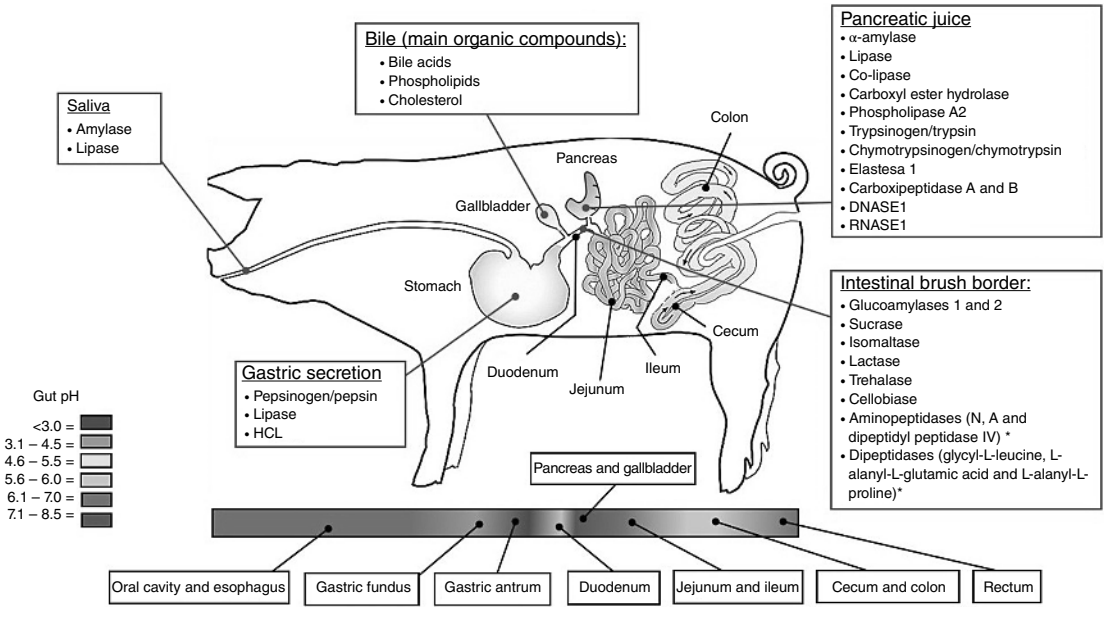


Figure 1.4 The porcine gastrointestinal tract: main enzymatic activities secreted by tissue and pH variations along the tract using color coding.

processing primarily consists of the secretion of hydrochloric acid that lowers the pH below 5. The acidic pH allows for the activation of pepsinogen to pepsin. In addition, gastric lipase is also secreted in the stomach. A more detailed accounting of the chemical digestion of foods in the stomach is presented in the next section.

The capacity of the stomach to absorb nutrients has often been underestimated. Absorption of simple molecules occurs including water and water-soluble vitamins, short- and medium-chain fatty acids, hormones (α-ketoglutarate, estrogens), and some AAs among others (Zebrowska et al. 1982; Ruoff and Dziuk 1994; Buddington et al. 2004).

The omentum is a membrane structure that covers the stomach and part of the liver in pigs. It helps anchoring the gastrointestinal tract to the body wall (along the spine) keeping the stomach in place. In addition, the omentum is one of the main fat body stores creating a network of adipocytes sitting around the blood vessels.

Small intestine

The small intestine is a tubular organ approximately 20 m long in the adult pig, extending from the stomach to the large intestine and located in the right abdomen. It is divided into three segments: the duodenum, jejunum, and ileum representing around 5, 90, and 5% of the total length, respectively (Adeola and King 2006). The small intestine consists of four membrane layers: in a distal to medial direction (from outside to inside the intestinal lumen), first is the serosa, then the muscularis, followed by the submucosa and the mucosa (Figure 1.5). The serosa or outermost layer has a squamous epithelium forming the mesentery that contains large blood vessels, connective tissue, and nerves. The muscular layer includes two sublayers, the outer consisting of longitudinal muscle

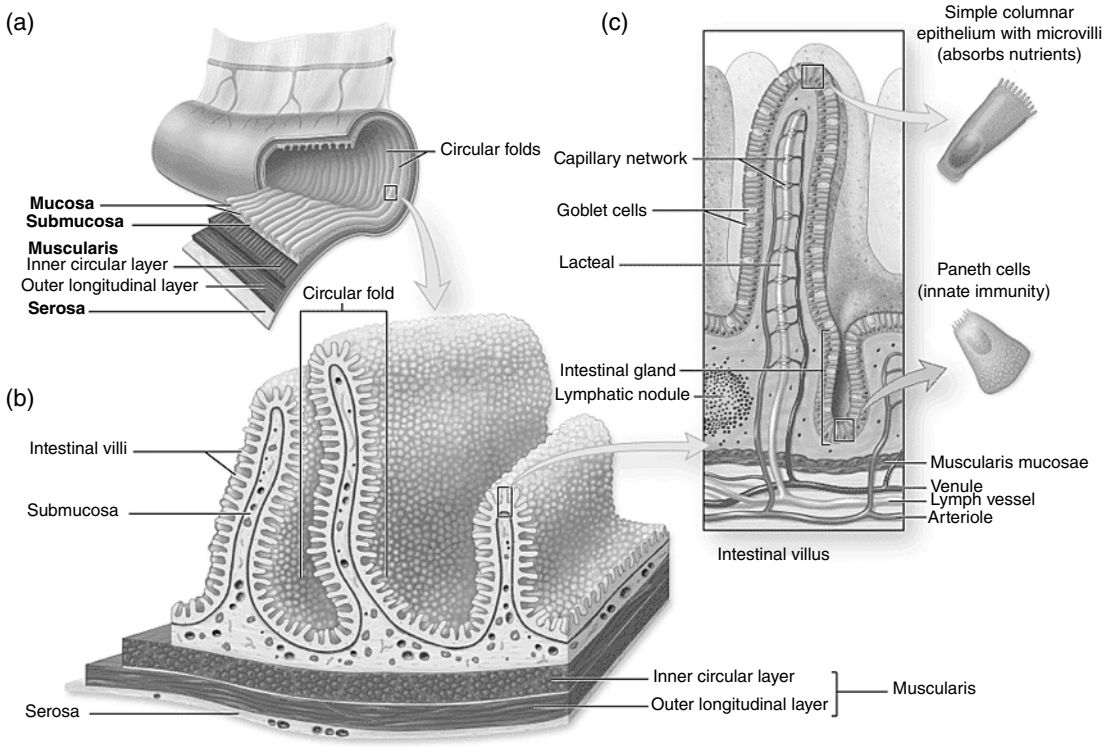


Figure 1.5 Anatomy of the small intestinal mucosa. The gut has five concentric layers (a). The most inner layer is the mucosa that consists of circular folds (b) and a covering of villi (c). Each villus contains connective tissue with microvasculature and lymphatics called lacteals and is covered with a simple columnar epithelium composed of enterocytes and goblet cells. The microvilli present in the apical cell membrane of enterocytes dramatically increase the absorptive area. Crypts are short tubular glands between villi with stem cells and Paneth cells. Source: Mescher (2009) / with permission of McGraw Hill LLC.

fibers and the inner consisting of circular muscles. Collectively, the synchronic contraction and relaxation of the muscles in the two sublayers define the rhythmic waves of intestinal motility also referred to as peristalsis that determines food passage rates (see the section on "Gut motility, transit time and the ileal brake"). The submucosa is made up of connective tissue and contains blood and lymphatic vessels and nerves. The mucosa, which is the most inner layer, is divided into three smaller layers: muscularis mucosa, lamina propria, and epithelium. Like the muscular and submucosa layers, the muscularis mucosa possess both inner longitudinal and outer encircling muscles, whereas the lamina propria contains blood vessels, gut-associated lymphatic tissue (GALT), and neurons. The epithelium consists of folds and villi that increase the contact between the chyme and the epithelial cells and crypts with high secretory capacity (Figure 1.5). The average height of the villi is constant throughout the duodenum and jejunum while slightly declining in the ileum (Table 1.1). In addition, the apical membrane of enterocytes consists of microvilli enabling higher digestive capacity (through brush border enzymes) and subsequent absorption of nutrients from the lumen. In addition to the enterocytes, the intestine has four specialized epithelial cell types: goblet, tuft, Paneth, and EEC.

Table 1.1 Anatomy and physiology of different cell and tissue types in porcine small intestine, colon, and rectum.

Item	Duodenum	Jejunum	Ileum	Colon	Rectum
Goblet cells[a]	Low density	Medium density	Medium-high density	High density increasing caudally	Very high density
Tuft cells[b]	0.5% of total cells	0.5% of total cells	0.5% of total cells	0.5% of total cells	—
Paneth cells[c]	—	Lieberkühn crypts	—	—	—
Enteroendocrine cells[d]	High in I cells; low in EC and L cells	Medium-high in EC and L cells in distal section	High in EC and L cells	High in EC and L cells	Very high in EC and L cells
GALT[e]	Low density	Medium density	Very high density	Lymphoid follicles only	Lymphoid follicles only
Villus height (μm)[f,h]	420 ± 15.0	480 ± 53.8	372 ± 43.0	—	—
Crypt depth (μm)[g,h]	367 ± 49.7	429 ± 59.9	316 ± 32.9	—	—
Surface area (m^2)[i]	0.090	60.000	60.000	0.250	0.015

GALT = gut-associated lymphoid tissue consisting of lymphoid follicles and PPs.
References: [a] Gonzalez et al. 2013; Vertzoni et al. 2019; Zhang and Wu 2020
[b] Banerjee et al. 2018
[c] Myer 1982; Kong et al. 2018
[d] Gunawardene et al. 2011; Ripken and Hendriks 2015
[e] Jung et al. 2010; Ruth and Field 2013; Urmila et al. 2019
[f] Lin et al. 2020
[g] Metzler-Zebeli et al. 2017
[h] Tian et al. 2020
[i] Kararli 1995.

Duodenum

The adult porcine duodenum extends from the pylorus of the stomach until the duodenal-jejunal junction located 70–95 cm down the tract divided in four segments: superior, descending, inferior, and ascending. After the chemical digestion occurring in the oral cavity and by stomach, the duodenum is the third organ involved in enzymatic/chemical digestion of foods. While accounting only for 5% of the length of the small intestine, the duodenum has a crucial role in receiving the main digestive juices essential for food digestion: the bile (i.e., bile acids) and pancreatic juices (i.e., pancreatic enzymes). Pancreatic enzymes and bile acids enter the duodenum through the common hepatopancreatic duct forming the major duodenal papilla located 2–5 cm from the stomach pylorus. Pigs have a secondary pancreatic duct (accessory) that opens at a minor duodenal papilla located 8–10 cm distally from the major duodenal papilla. The hepatopancreatic sphincter (Sphincter of Oddi) controls the flow of digestive juices into the duodenum. The optimization of the enzymatic digestion requires of a pH of around 6.4 (Figure 1.4). At the start of the duodenum, the pH is 6.1 and steadily rises to 6.4 thanks to the alkaline secretions released from Brunner's glands present in the duodenal submucosa facilitate the neutralization of the acidic digested contents received from the stomach via the gastric pylorus. Unique to the duodenal epithelium is the presence of CCK-secreting I cells (Table 1.1). The duodenum also plays a minor role in absorbing a small part of free nutrients.

Jejunum

The main site of digestion and absorption of nutrient is the jejunum. The length of a mature pig jejunum is between 14 and 19 m (this is 90% of the small intestine) that begins at the duodenojejunal junction transitioning into the ileum without any specific anatomical feature. This is the longest segment in the middle of the small intestine that is red in color (indicating very high vascularization) and consists of a relatively thick intestinal wall. At the beginning of the jejunum, the pH is 6.4 that rises to 6.6 before transitioning into the ileum back at 6.4 (Figure 1.4). Deep crypts, known as Lieberkühn, and highly developed villous are characteristics of the jejunal mucosa. The crypts contain a high density of Paneth cells with antimicrobial functions (Table 1.1). In addition, the many parallel circular folds in the mucosa (valves of Kerckring) further increase the surface area for nutrient absorption. Brunner's glands are also widely distributed up to the proximal part of the jejunum to ensure that the acidity has been neutralized by the alkaline secretions before comprehensive absorption occurs. The porcine jejunal submucosa is densely populated with Peyer's patches (PPs), lymphoid follicles rich B and T cells forming part of the so-called gut-associated lymphoid tissue (GALT).

Ileum

The ileum is the most distal tubular part of the small intestine. In an adult pig, the length of the ileum is between 0.70 and 1 m and has a pink color indicative of less vascularization than the jejunum. The ileocecal valve is a sphincter that regulates the movement of digested contents from the small to the large intestine that begins at the cecum. The primary role of this sphincter is to prevent the reflux of microbe-rich enteric fluid from the large intestine to the small intestine. At the entry point of the ileum, the pH was 6.4 increasing to 6.7 in the middle segments to fall back to 6.4 at the terminal end near the ileocecal junction (Figure 1.4). Compared to the duodenum and jejunum, digestion is minimal in the ileum, while nutrient absorption is maximized thanks to a relatively thin intestinal wall that reduces diffusion distance. Partially digested foods that have not been fully broken down to simple nutrients, particularly lipids at the proximal part of the small intestine have the capacity to induce the ileal brake. In pigs, the ileal submucosa also contains PPs with a unique composition consisting of 90% of the immune cells being B lymphocytes.

Epithelial Cells

Intestinal epithelia consist mainly of enterocytes and four highly specialized types of cells: goblet, tuft, Paneth, and EEC (Table 1.1). Enterocytes are nutrient-absorptive cells that line the surface of the finger-like projections referred as intestinal villi. These structures collectively amplify the intestinal surface area by 30-fold. Enterocytes differentiate from stem cells at the bottom of the crypts and mature as they migrate toward the tip of the villi. As the enterocytes move above the basal third of the villi, the digestive functions are activated such as border brush enzymes. When the enterocytes reach the upper to mid-level of the villi, the absorptive role begins to develop. When the mature cells reach the top of the villi, their active life terminates and are sloughed off into the lumen. Goblet cells are mucus-secreting cells that are distributed in the epithelial layer surrounded by enterocytes. There is a higher frequency of goblet cells found in the distal (ileum) compared with the proximal (duodenum/jejunum) small intestine. Tuft cells are chemosensory cells in the epithelial lining of small and large intestines. Their main function is to detect physiological disturbances associated with parasitic infections in the intestinal lumen and signal the immune system. In the intestine, tuft cells are the sole source of secreted interleukin 25. During helminth infection, IL-25 production initiates a feed-forward mechanism involving the activation of group 2 innate lymphoid cells (ILC2) that promote type 2 inflammation with the generation of IL-5, IL-9, and IL-13. During a helminth infection, tuft cell populations can become elevated to ten times their original frequency. Paneth cells are epithelial

cells located at the bottom of the crypts of Lieberkühn. They produce peptides such as defensins and lysozymes and proteins with antimicrobial activity that mediate the host–microbe interactions, including innate immune protection from enteric pathogens. EEC have the primary role of secreting gut peptides that facilitate the dialogue with the gut-brain axis of the central nervous system in response to specific nutrients present in the lumen. A description of the types and roles of EEC can be found in the section on "Enteroendocrine System."

Large intestine

The large intestine consists of a highly lobulated tube that facilitates the development of microbiota and the fermentation of undigested material leaving the small intestine. It consists of the cecum, the colon, and the rectum. Following dietary adaptations where fibrous components are likely to increase with age, the development of the large intestine, particularly the colon, continues long after the small intestine has already been fully developed, reaching a total length of around 7.5 m long in mature individuals. Thus, the colon becomes the longest proportion of the large intestine. Consequently, pigs like humans have been defined as mainly colonic fermenters. The undigested chyme from the small intestine is released into the ileo-cecal junction passing into the ceca or directly into the colon. A series of pouches derived from longitudinal muscular bands from the cecum and proximal part of the spiral colon are referred to as haustra. These pouches compartmentalize the passage of luminal contents while facilitating the proliferation of the microbiota. Villi are absent in the mucosa of the large intestine a differential feature compared to the small intestinal mucosa. In contrast, the large intestine mucosa consists of columnar epithelial cells with microvilli that form straight tubular crypts. The epithelium of the large intestine consists of enterocytes as the main cell type, and goblet, tuft and EEC (Table 1.1). Goblet cells play an important role in the large intestine by secreting a sulfated carbohydrate-protein complex, which lubricate columnar epithelial cells that absorb water from the chyme.

Cecum

The cecum is a highly lobulated cylindrical blind sac with three teniae running along its length, located at the proximal end of the colon, and lying transversely on the left side of the abdomen. The apex of the cecum points caudoventrally. The cecum's pH is kept at 6.1, which is a noticeable decline from the 6.4 at the terminal end of the ileum (Figure 1.4). There are no villi throughout the cecum epithelium. Segmental contractions induce absorptive and microbial activity, which is followed by mass movements that transfer the chyme to the colon. In pigs, soluble fiber is fermented in the cecum, while insoluble fiber is mainly fermented in the colon. A thick mucous membrane makes up the internal wall of the cecum through which water and salts are absorbed. While the mucosa has mucous glands, these are absent in the submucosa. The lamina muscularis particularly in the distal section of the cecum has large lymphatic nodules (PPs).

Colon

The porcine colon begins at the ascending colon, which is an elongated, coiled, and cone-shaped structure. It is attached to the dorsal abdominal wall, where the apex is oriented ventrally, that ascends cranially (anterior direction) until encountering the liver where it turns at a right angle to move horizontally. This bend is referred to as the hepatic flexure marking the start of the transverse colon. Over a short distance along the colon, there are three teniae coli of smooth muscle (mesocoloic, free, and omental coli) that run longitudinally along the surface of the large intestine, which contract to form rows of sacs known as the haustra. The pH rises from 6.1 to 6.4 across the

proximal segment of the colon (Figure 1.4). The transverse colon then extends horizontally until it turns at a right angle at the spleen to descend caudally (posterior direction). The splenic flexure is the term for this bend between the transverse colon and the descending colon. The pH across the middle section of the colon remains at 6.5 from start to end. The descending colon moves caudally toward the pelvis until it begins to turn medially and transition into the sigmoid colon. The sigmoid colon is an "S" shaped part of the colon in the lower left quadrant of the left abdomen that is attached to the dorsal pelvic wall of a mesentery called the sigmoid mesocolon that provides mobility to the sigmoid colon. The pH across the distal section of the colon slightly rises and remains at 6.6 (Figure 1.4). Eventually, in the spiral colon region, there are two teniae and two haustra that are no longer identifiable in the centrifugal section. No villi are found in the colon, but there are microvilli that line the simple columnar epithelium of the mucosa that assist in the absorption of water that leads to the thickening of the stool. Anaerobic fermentation of indigestible components such as the insoluble fiber cellulose by the intestinal microflora, which inhabit the crypts of Lieberkühn, is another major role played by the colon. Large lymphatic nodules are also found in the submucosa of the colon. The temporary storage and transport of feces across the large intestine is enhanced by a layer of mucus secreted by an abundance of goblet cells distributed throughout the colon that provides lubrication. The teniae coli of the smooth muscle in the sigmoid colon broaden to form a complete layer within the rectum at the rectosigmoid junction in the large intestine that marks the end of the sigmoid colon and the start of the rectum.

Rectum, Anal Canal, and Anus

The rectum follows the posterior end of the large intestine and is the last straight part of the digestive system connecting with the anus in the anal canal. It is surrounded by bands of muscles required to move the waste product of digestion (feces) out of the body. Goblet cells are abundant throughout the rectal mucosa to lubricate the feces as they pass into the anus. The median pH of the porcine rectum is 6.3. The ampulla is the last segment of the rectum that relaxes to accumulate and transiently store feces. The recto-anal junction functions thanks to the longitudinal layer of the tunica muscularis and the lamina muscularis in the rectum. As feces accumulate in the ampulla, pressure sensitive receptor cells detect increasing distension that initiates the defecation reflex. The combination of both voluntary and involuntary process involves the rectum to forcefully contract and subsequently relax the internal anal sphincter regulating defecation. The anal sinuses are furrows in the anal canal that contain glands in charge of secreting mucus to lubricate the feces as it passes through to the external environment. The median pH of the porcine anal canal, like the rectum, is 6.3. The anus is referred to the exterior opening surrounded by the anal sphincter.

The Pancreas

The pancreas is both an endocrine and an exocrine organ, associated with the digestive system located in the inner side of the duodenum loop (part of the proximal small intestine). In the pig, the pancreas is composed of two glandular lobes and a pancreatic duct that drains into the duodenum 20–25 cm from the pylorus and closely distal to the bile duct from the gallbladder. Acinar cells, present in the exocrine pancreas, oversee the production and release of enzymes and zymogens into the duodenum when stimulated. The pancreatic enzymes are essential to digest proteins, carbohydrates, lipids, and nucleic acids. The endocrine pancreas produces hormones that regulate the utilization of the absorbed digested products and it is structured in islets named after Professor Paul Langerhans (islets of Langerhans). The islets consist of α-cells producing the peptide glucagon,

β-cells producing insulin and amylin, δ-cells producing somatostatin, and F-cells producing pancreatic polypeptide. More detail on the endocrine and exocrine roles of pancreatic secretions can be found in sections "Nutrient Digestion and Nutrient Sensing and the Gut-brain Axis."

The Liver

The liver is a complex organ with several essential functions in the maintenance of metabolic homeostasis including detoxification of hazardous metabolites, synthesis of a wide range of proteins, and other compounds necessary for digestion and growth. The liver is an accessory but crucial organ to the digestive system that produces bile, an alkaline fluid containing cholesterol and cholesterol-derived bile acids required for the breakdown of fat. The liver in pigs is divided into six lobes by deep interlobular fissures: the left lateral and medial, the right lateral and medial, the quadrate, and the caudate lobes. The gallbladder (3–5 cm, 25 mL), a small pouch that sits just under the liver, stores the bile produced before it is released into the small intestine to complete digestion. Hepatocytes are the main functional liver cells that produce the bile juice (0.6–1.1 mL kg^{-1} BW/h) (Swindle 2015). The bile juice is moved through the intrahepatic bile ducts to the extrahepatic biliary system consisting of a cystic duct, connected to the gallbladder, and a bile duct, that drains in the duodenum, approximately 2–5 cm distal to the pylorus. Different from the pancreas, bile juices are produced constantly and stored in the gallbladder until nutrient stimulation. The presence of nutrients in the proximal small intestine, particularly lipids, triggers the sphincter of Oddi to relax, and the gallbladder contracts allowing the release of bile juices into the duodenum.

The Gut-Associated Lymphoid Tissue (GALT)

The GALT is the specialized intestinal immune system that protects the gut mucosa avoiding microbial invasion. The distribution of GALT through small and large intestine has been outlined in Table 1.1. The GALT includes PPs, the mesenteric lymph nodes (MLNs), and isolated lymphoid follicles. PPs are transmucosal clusters with dendritic cells in the dome and interfollicular areas as antigen-presenting cells. PPs are present in the small intestine (Jejunum -JPP- and Ileum -IPP-) and the large intestine, with isolated lymphoid follicles (ILF; Liebler-Tenorio and Pabst 2006). In pigs, pancreatic polypeptides in the jejunum are richer in T cells than B cells (65% vs. 35%, respectively), while in the ileal submucosa, pancreatic polypeptides consist of 90% of B cells. This suggests that the jejunum has a stronger role in cell-mediated immunity compared to the ileum that is dependent on humoral (antibody mediated) immunity. Microfold cells are specialized epithelial cells, which facilitate the transport of antigens from pathogenic microorganisms to the B lymphocytes, that elicit the immune response. In addition, individual lymphoid nodules have been observed in the submucosa and lamina propria of the gastric cardia region in pigs.

Gut Motility, Transit Time, and the Ileal Brake

The transit time of the food bolus and chyme through the gastrointestinal tract determines the efficiency of the digestion and absorption of nutrients ultimately affecting appetite and feeding behavior. Gut motility is an essential feature to understand the passage rate of gastrointestinal contents

and is mainly a result of (i) tissue-specific sequences of contraction–relaxation patterns of the smooth muscle layers, (ii) the presence of two valves (epiglottis and cardia) and four sphincters (pyloric, ileo-cecal, and internal and external anal) with a "stop-go" flow function in critical points of the gastrointestinal tract determine bolus and chyme passage rates (Figure 1.5).

Smooth Muscle Layers

Smooth muscle layers are present in two locations throughout the gastrointestinal tract, in the mucosa outside the lamina propria (muscularis mucosae) and surrounding the submucosa (external muscular layers). The muscularis mucosae is a continuous thin layer separating mucosa from submucosa, consisting of crossed fibers of smooth muscle that facilitate the expel and mixing of glandular crypt secretions into the lumen and a gentle agitation of the epithelial surface and gut contents. The external muscular layers trigger the sequential waves that will further mix and move the bolus or chyme down the gastrointestinal tube, also referred to as gut peristalsis. There are two main types of external smooth muscle layers, the middle circular just outside but in contact with the submucosa and the outermost longitudinal. Circular muscles result in slow waves that promote the mixing of particles and digestive secretions while preventing the reflux of the chyme. Longitudinal muscles stimulate the aboral movement of the chyme through combining contraction–relaxation sequences that result in shortening–lengthening of the tube. The result of the two external muscle layers working together is the mixing and propelling of gut contents.

Enteric Myogenesis and Enteric Nervous System (ENS)

The regulation of gut motility is a combination of myogenic and neural impulses generated by the enteric nervous system (ENS), the second largest accumulation of nerve cells in the body. Enteric myogenesis refers to the capacity of the myocyte itself to initiate a contraction and is responsible for initiating intestinal motor patterns. Smooth muscle fibers are electrically connected by gap junctions. In addition, the gastrointestinal tract contains interstitial pacemaker cells (cells of Cajal) between muscle layers that generate electrical rhythmicity in the smooth muscle cells allowing for coordinated generation of slow waves. The ENS, in turn, is based on an autonomic neural system (thus capable of operating independently from the central nervous system) with thousands of small, interconnected ganglia that form the myenteric and submucosal plexus coordinating muscle activity and mucosal secretion and absorption of nutrients, respectively. In addition, the vagal innervation of the gut has the capacity to modulate the autonomic nervous system to help regulate digestive functions and to synchronize the digestive system with other vital systems (e.g., blood flow). In the pig, the vagal innervation is dominant in the motility of esophagus and stomach, while the autonomic system is dominant in small and large intestines. Furthermore, gut peptides also play a relevant role capable of modifying the electrical and contractile pattern within the gut. For example, motilin and ghrelin promote the gastrointestinal motility, while CCK and GLP-1 inhibit gastric emptying and proximal small intestine motility as part of the ileal brake (see additional details below).

Tissue-specific functions related to gut motility are briefly explained next.

Deglutition and Esophagus

Deglutition (or swallowing) is the passing of foods from the oral cavity (oral phase) to the esophagus through the pharynx (pharyngeal and esophageal phases). The oral phase is based on skeletal muscle (mainly tongue), while the pharyngeal and esophageal phases are regulated by the autonomic nervous system following activation with mechanoreceptors. The act of deglutition requires synchronization with the closure of the trachea thanks to the epiglottis preventing the accidental passage of foods to the upper respiratory system. In addition, swallowing is associated with the primary peristaltic contractions

resulting from the circular muscles of the esophagus that lead the bolus to a rapid transit into the stomach. Secondary peristaltic contractions are triggered by the distension caused by material left in the esophagus. The primary contractions are mediated by central mechanisms through the vagal nerve, while the secondary contractions are locally mediated by mechanoreceptors in the esophageal lining.

Stomach

The bolus enters the stomach through the cardiac valve that functions as a barrier to prevent reflux of the potentially damaging highly acidic gastric content. The primary motility is also governed through the ENS. Characteristic of the stomach is the inner oblique muscle layer that coordinates the mechanical digestion promoting the grinding and mixing of large feed particles with gastric juices to release a more liquified state, also known as chyme. A second main function of the contraction of smooth muscle in the stomach is the forced passage of small quantities of chyme through the pyloric sphincter into the duodenum, a process also known as gastric emptying. Distal gastric contractions and gastric emptying through the pyloric valve are triggered by the volume of feed as well as by the distension of the stomach through the stimulation of mechanoreceptors. Large grain particles modulate gastric emptying by delaying the passage rate into the duodenum. The middle circular muscular layer forms part of the pyloric sphincter, while the longitudinal layer participates in coordinating a radially symmetrical contraction and relaxation of muscles that stimulates the aboral movement of food into the pyloric region and duodenum. In addition, CCK and gastrin contribute to the modulation of gastric motility by stimulating the ENS (vagal nerve).

Small intestine and the Ileal Brake

The arrival of the chyme to the duodenum triggers chemical and mechanical stimulus that mediate the onset of peristaltic and secretory reflexes. The chemical signals are sensed through EEC in the intestinal mucosa that release the neurotransmitter serotonin that in turn stimulates the vagal nerve (see the section on "Nutrient sensing and the gut-brain axis" for more information on nutrient sensing). The mechanical sensing activates the ENS. The motility consists of slow waves that allow for the mixing of the chyme with intestinal, pancreatic, and biliary secretions as well as longitudinal or peristaltic waves responsible for the aboral passage. Peristaltic waves do not propagate along the entire intestine, but instead help propel the chyme only a few centimeters into the duodenum. In pigs, the number of duodenal waves is positively correlated with the flow rate of the chyme (Ruckebusch and Bueno 1976). The physical distension and the presence of undigested nutrients into the duodenum, jejunum, and ileum trigger the so-called brakes consisting of negative feedback mechanism increasing the retention time in proximal parts of the gut (Roura and Navarro 2018). The ileal brake has the strongest impact slowing down the passage rate of the chyme by inhibiting intestinal motility, delaying gastric emptying, digestive secretions, and hunger, altogether resulting in feed intake suppression.

Ileo-cecal Junction, Large intestine, Rectum, and Anal Canal

The ileum generates strong contractions to propel batches of digesta into the cecum at 7–12 minutes intervals. At the ileo-cecal junction, there is a sphincter consisting of a circular smooth muscle layer with the main function of preventing reflux of cecal contents into the ileum. The motility pattern in the colon is characterized by segmentation contractions within the haustra that mix luminal contents and peristaltic contractions that facilitate the movement of digesta through haustra and into the rectum. As the fecal matter reaches the distal colon, contractions speed up, but their force declines leading to a slower passage to facilitate water absorption. In addition, the motility of the large intestine includes reversed peristalsis contractions that propel the digesta back toward the ileum resulting

in the accumulation of fecal matter in the proximal colon. This allows for additional capacity to absorb water and electrolytes and extends the time for microbial fermentation. The ejection of fecal matter through the anal sphincters (defecation) involves giant contractions (or mass movements) involving most of the large intestine and providing the major force required. In pigs, the mass movements occur at intervals of around seven minutes in coordination with the ileal strong contractions (Hipper and Ehrlein 2001). Passed the rectum, fecal content accumulates in the anal canal where the internal anal sphincter is formed by an involuntary circular layer of the tunica muscularis in the upper two-thirds of the anal canal, whereas the external anal sphincter is a voluntary muscle composed of skeletal muscles that surrounds the lower two-thirds of the anal canal. Mechanoreceptors in the anal canal will result in the relaxation of the internal sphincter leaving the defecation as a voluntary act to relax the external sphincter.

Transit Time

The time required for food to travel through the gastrointestinal tract varies with the age and size of the animal and the physicochemical characteristics of the diet. In adult-size pigs, the mean retention time (MRT) has been estimated in 1, 4, and 38 hours for stomach, small intestine, and large intestine, respectively (Figure 1.6). Thus, the passing time in cecum and colon represents 70–85% of the total. However, depending on the composition of the bolus/chyme, the contents may stay up to 24 hours in stomach, 15–20 hours in small intestine, and up to 50–55 hours in the large intestine. Importantly, the amount of chyme present in the small intestine at any given time is relatively small indicating the relevance of a high enzyme-to-substrate ratio for an effective digestion. Dietary factors that increase transit time in the stomach include large food particles (>2 cm) or food with high water holding capacity. Diets rich in soluble fiber can also dramatically increase the passage rate of the chyme through the small and large intestines, attributed to their water holding capacity (Jørgensen et al. 1997). The size of the large intestine increases with age (and weight), which, in turn, results in longer MRT in the whole gastrointestinal tract. MRT increased from 32 to 44 hours and above 80 hours for a 28, 85 kg pig and mature sows, respectively (Holzgraefe et al. 1985; Potkins et al. 1991). In contrast, increasing insoluble fiber content in feeds does not affect gastric transit time while potentially decreasing retention time in small and large intestines in pigs. As previously mentioned, the activation of the ileal brake following the presence of undigested nutrients into the small intestine increases the retention time in proximal parts of the gut through negative feedback mechanisms. As to the effect of animal age and size, older pigs have a longer retention time compared to young pigs associated with a longer intestinal tract and a better digestion and absorption of nutrients (Ratanpaul et al. 2019). In addition, sows have a much longer MRT than growing and finishing pigs potentially lasting more than 80 hours.

Nutrient Digestion

Nutrient digestion is defined as the process by which food is dissected into simple chemical compounds (nutrients) that can be absorbed along the gastrointestinal tract. In pigs, enzymatic digestion takes place mainly in the small intestine and fermentation in the large intestine. The composition of the diet determines the type of digestion, absorption capacity, and secretion of gut peptides involved in the regulation of energy homeostasis. The main digestive enzymes, their sources, and roles are summarized in Table 1.2 and illustrated in Figure 1.4 together with variations of pH along the gastrointestinal tract.

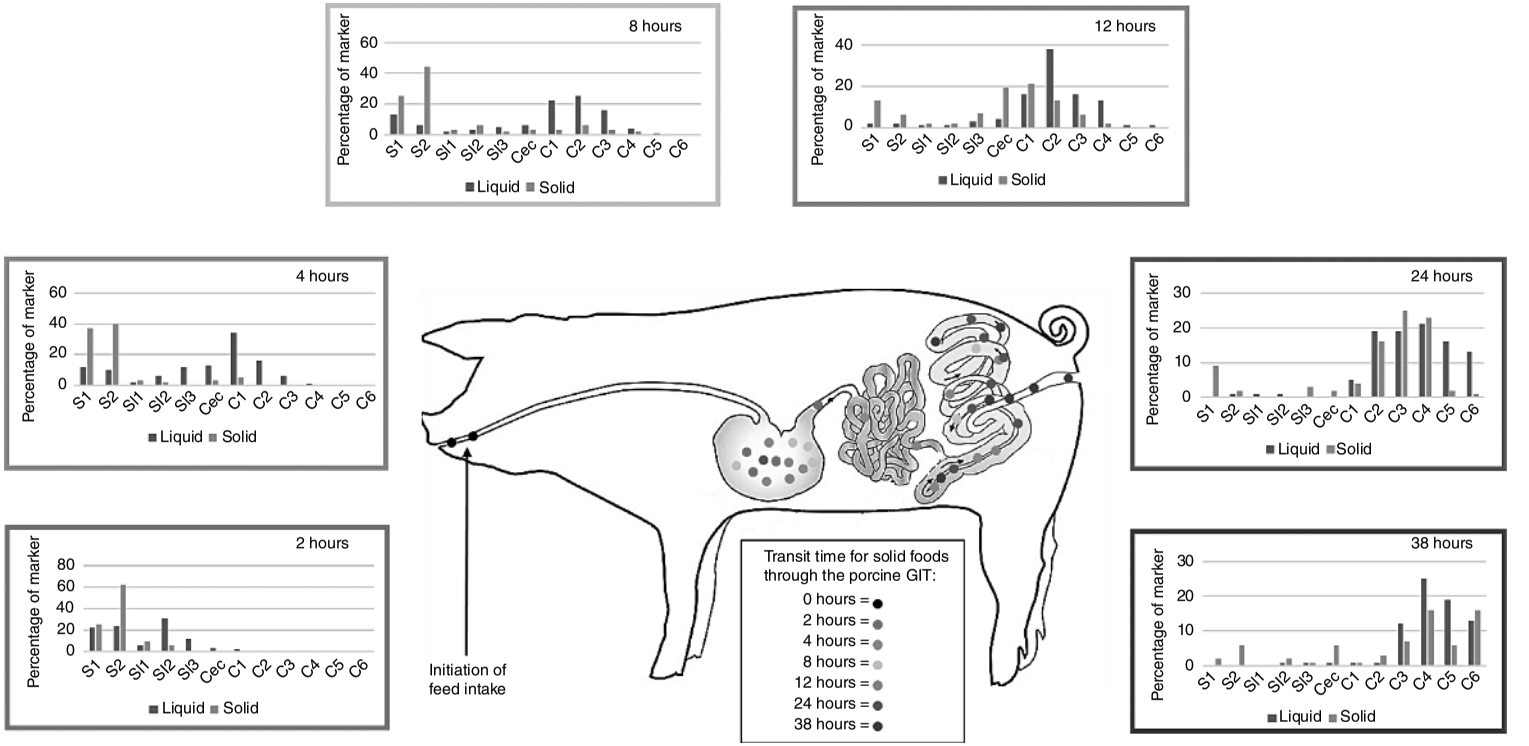


Figure 1.6 Transit time of liquid and solid particles through the gastrointestinal tract in young pigs. Dietary components may stay up to 24 hours in the stomach depending on particle size among other aspects. The amount of chyme in the small intestine is relatively small at any given time. The transit time in cecum and colon represents 70–85% of the total. Source: Adapted from Stevens and Hume (1995). Abbreviations: S1 = stomach cranial, S2 = stomach caudal, SI1 = duodenum, SI2 = jejunum, SI3 = ilium, Cec = cecum, C1 = colon cranial, C2 = colon medium 1, C3 = colon medium 2, C4 = colon medium 3, C5 = colon distal, C6 = rectum.

Table 1.2 Main digestive enzymes with main location in the gastrointestinal tract of the pig, substrate and end products, and hydrolysis site.

Enzyme	Location/secretory glands or organs	Nutrient target and product	Hydrolysis site
Carbohydrases			
α-amylase	Parotid gland and pancreas	Polysaccharides → oligosaccharides (mainly di- and tri-saccharides)	α-1,4 internal links
Glucoamylases (1 and 2)	Brush border of enterocytes	Oligosaccharides → glucose	α-1,4 internal links
Sucrase	Brush border of enterocytes	Sucrose → glucose and fructose	α-1,2 internal links
Isomaltase	Brush border of enterocytes	Dextrins and maltose → glucose	α-1,4 and α-1,6 internal links
Lactase	Brush border of enterocytes	Lactose → glucose and galactose	α-1,4 internal links
Trehalase	Brush border of enterocytes	Trehalose → glucose	α-1,4 internal links
Cellobiose	Brush border of enterocytes	Cellobiose → glucose	β-1,4 internal links
Lipases			
Lipase	Von Ebner's glands, stomach, and pancreas	Triglycerides → FFA and glycerol	Ester bonds (sn-1 and sn-3)
Co-lipase	Pancreas	Triglycerides → FFA and glycerol	Cofactor for pancreatic lipase
Carboxylic/cholesterol-ester hydrolase	Pancreas	Triglycerides, phospholipids, and cholesteryl esters → Non-esterified cholesterol, FFA, and glycerol	Ester bonds (sn-2)
Phospholipase A2	Pancreas	Phospholipids → Lysophospholipids and FFA	Ester bonds (sn-2)
Proteases			
Pepsinogen/Pepsin	Stomach	Proteins → polypeptides	Peptide bonds-aromatic AA
Trypsinogen/Trypsin	Pancreas	Proteins and polypeptides → Free AA and oligopeptides	Peptide bonds-basic AA
Chymotrypsin/-ogen	Pancreas	Proteins and polypeptides → Free AA and oligopeptides	Peptide bonds-aromatic AA
Elastase 1	Pancreas	Proteins and polypeptides → Free AA and oligopeptides	Peptide bonds-hydrophobic AA
Carboxypeptidases A/B	Pancreas	Polypeptides → Free AA and small oligopeptides (tri- and di-peptides)	Peptide bonds, C-terminalaromatic, basic or BC AA
Aminopeptidases*	Cytoplasm and brush border of enterocytes	Polypeptides → Free AA and small oligopeptides (tri- and di-peptides)	Peptide bonds, N-terminal
Dipeptidases**	Cytoplasm and brush border of enterocytes	Dipeptides → Free AA	Di-peptide bonds
Nucleases			
DNASE1	Pancreas	DNA → nucleic acids	5′-phosphooligonucleotide
RNASE1	Pancreas	RNA → nucleic acids	3′-Cy and Ur nucleosides

Abbreviations: AA = amino acids; BCAA = branched chain amino acids; FFA = free fatty acids; C-terminal = carboxyl terminal; N-terminal = amino terminal; RNA = ribonucleic acid; DNA = deoxyribonucleic acid; sn-1, -2,-3 = stereospecific numbering system; Cy = cytidine nucleoside; and Ur = uridine nucleosides.

* The main aminopeptidases studied in pig are N, A, and dipeptidyl peptidase IV.

** The main dipeptidases studied in pigs are glycyl-L-leucine, L-alanyl-L-glutamic acid, and L-alanyl-L-proline.

Protein and Amino Acid Digestion

Protein digestion in pigs starts in the stomach, through the action of pepsin and hydrochloric acid (HCl). HCl is required to lower the stomach pH below 5, to transform pepsinogen into its active form, pepsin. Pepsin, in turn, increases the susceptibility of the ingested protein to the activity of pancreatic proteases by altering their quaternary and tertiary structure and exposing their AA residues.

Once the digesta reaches the proximal small intestine, pancreatic and intestine enzymes break down proteins and polypeptides further (Table 1.2). Among pancreatic enzymes, trypsin, chymotrypsin, and elastase are responsible for the initial breakdown of protein and polypeptides into small peptides and free AA within the small intestine. Nevertheless, these enzymes are secreted in their inactive forms. Pancreatic trypsinogen is activated within the duodenum through the action of brush border enzymes (enteropeptidase) into trypsin, which activates other zymogens including other trypsinogen proenzymes (trypsinogen, chymo-trypsinogen, procarboxypeptidase, and pepsinogen). Smaller peptides are then digested by carboxypeptidases secreted by the pancreas as well as by aminopeptidases present in the brush border of the small intestinal enterocytes. Thus, the final product of lumen digestion is free AA, di- and tripeptides that can be easily absorbed and further processed by cytosolic enzymes within the enterocytes (Krehbiel and Matthews 2003).

The rate-limiting step in the digestion of protein seems to be the rate at which the protein source is dissolved and hydrolyzed. For example, skim milk powder has a higher and more rapid digestion than soybean meal which in turn has a higher and more rapid digestibility than corn gluten meal (Asche et al. 1989). Digestion of protein from diets based on barley and soybean meal fed to growing pigs occurs rapidly based on the net portal appearance (NPA) of amino acids (AAs), and this can be affected by the inclusion of materials such as betaine and conjugated linoleic acid (CLA) in the diet. The NPA of essential, nonessential, and total AAs for pigs following a single feed is shown in Figure 1.7.

Nonfiber Carbohydrates Digestion

Although carbohydrate breakdown starts in the mouth, the digestion that occurs in the oral cavity by salivary α-amylase produced by the sublingual glands is negligible compared to the digestion processes that occur in the intestinal lumen, partly due to the rapid inactivation of α-amylase by the low pH in the stomach.

Within the stomach, carbohydrate digestion is limited for both sugars and starches. The gastric digestion of carbohydrates is mainly due to fermentation and leads to the production of SCFA and lactic acid, which can only be absorbed in limited amounts by the gastric mucosa.

In the small intestine, most of the starch consumed is degraded by pancreatic α-amylase into maltose, isomaltose, maltotriose, alpha limit-dextrins, and some free glucose. These new di-, tri-, and oligosaccharides are then further processed by brush border enzymes (oligosaccharidases) as enterocytes membrane transporters cannot absorb molecules bigger than monosaccharides (Table 1.2). Among oligosaccharidases, glycoamylases can remove 1,4 linked glucose residues, whereas α-dextrinases (isomaltases) and sucrases can cleave the nonreducing terminal α-1,6 and α-1,2 links, respectively. The products of carbohydrate enzymatic digestion are monosaccharides mainly glucose, fructose, and galactose. Glucose is then actively transported inside enterocytes by the sodium-potassium ATPase system, which pumps the intracellular Na^+ across the basolateral membrane (Drochner 1993). The Na^+/glucose cotransporter (SGLT1) is the major route for the

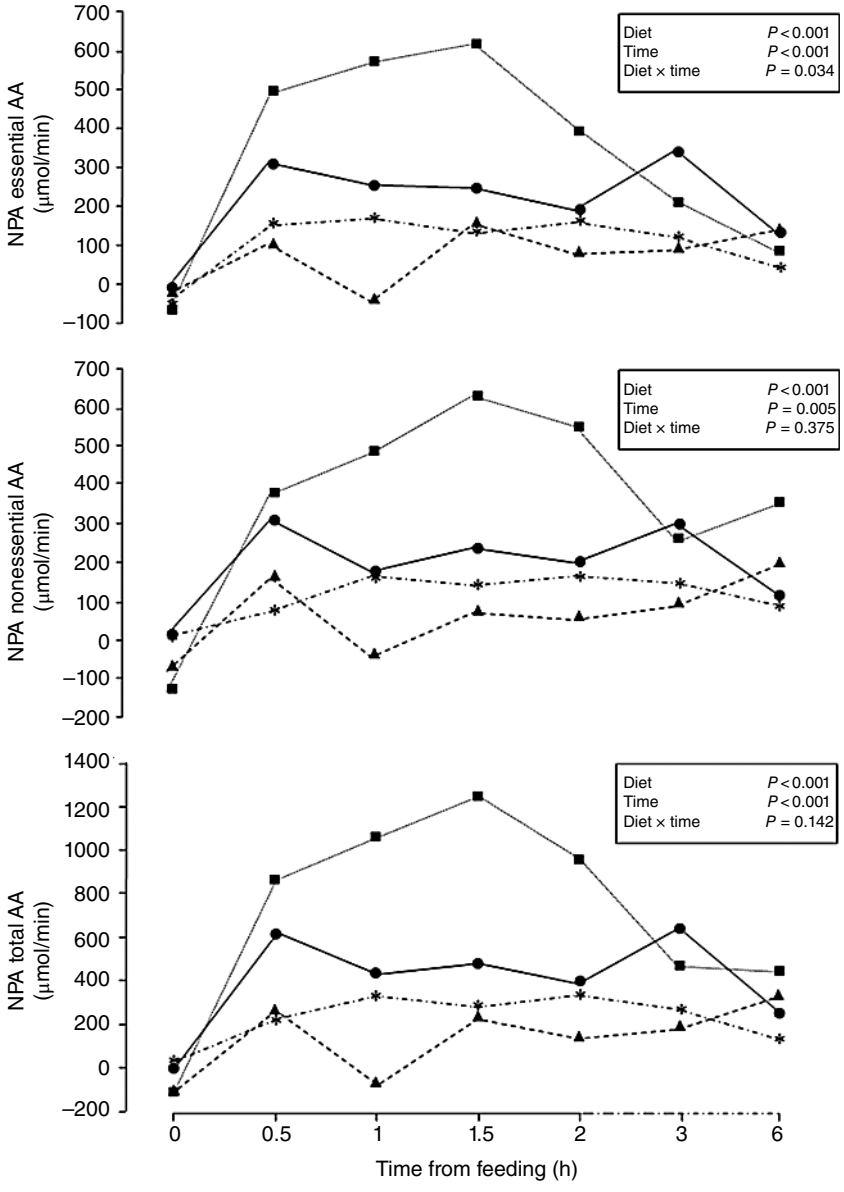


Figure 1.7 From top to bottom: Net portal appearance (NPA) of essential, nonessential, and total amino acids (AA) of Iberian growing pigs fed control (●), betaine (■), CLA (▲), or betaine + CLA diets (*). Values are means for four pigs. Source: Lachica et al. (2021) / with permission of Elsevier.

transport of dietary sugars from the lumen of the intestine into enterocytes. Regulation of this protein is essential for the provision of glucose to the body and avoidance of intestinal malabsorption. It has been demonstrated that dietary sugars and artificial sweeteners increase SGLT1 expression and the capacity of the gut to absorb monosaccharides. Fructose is transported by the Na^+-independent fructose transporter, GLUT5, transporting fructose from the lumen of the intestine

into enterocytes down its concentration gradient. These monosaccharides, when accumulated in the enterocytes, exit the cell across the basolateral membrane into the systemic circulation by another Na^+-independent monosaccharide transporter, GLUT2, a bidirectional transporter that can move glucose out of or into the cell depending on its concentration gradient (Shirazi-Beechey 1995).

Starch digestibility is affected by molecular features such as the degree of porosity of the granular surface, particle size, and degree of gelatinization such as after grain processing (i.e., pelleting or extrusion), all the above ultimately affecting the accessibility of digestive enzymes to the glucose polymers. A more detail explanation on the effects of grain processing and starch structure on digestibility have been explained in the section on "Effects of grain processing and starch structure on nutrient digestibility."

Fiber Digestion

Degradation of dietary fiber in the stomach and small intestine is limited compared to that of the cecum and large intestine. Dietary fiber will pass the ileo-cecal sphincter mainly intact, becoming substrate for the microbiome in the large intestine. Bacteria in the cecum and colon use the soluble fiber through fermentation producing SCFA including propionate, acetate, and butyrate, as well as other products such as lactic acid, methane, carbon dioxide, hydrogen, water, and heat. The final content of SCFA depends on the degradability of the substrate that reaches the large intestine. While oligosaccharides are easily fermented by the microflora in the colon, other elements such as cellulose show a much slower breakdown, resulting in only a moderate production of SCFA in comparison (Drochner 1993).

As illustrated by Pekas (1991), the size and weight of the digestive system increase with age and BW, with a longer hindgut in 270 kg BW pigs (7.5 m) than in 70 kg BW pigs (5.4 m) or in 30 kg BW pigs (4.3 m). Le Goff et al. (2002) reported neutral detergent fiber digestibility was 8–17% higher for pigs weighing 77 kg than those weighing 34 kg. Digestibility of NDF did not differ between pigs of different weight when a low fiber control diet was fed. In contrast, the difference in NDF digestibility for the same higher fiber diets when fed to sows was 18.5 and 9.4% higher than that measured in pigs weighing 77 kg when fed diets containing maize or wheat bran, respectively. There was no difference in NDF digestibility between the heavy pigs and sows when either were fed the lower NDF control diet or a diet containing sugar beet pulp as the fiber source.

In an earlier study, Noblet and Shi (1994) measured the digestibility of maize bran, wheat bran, and sugar beet pulp in grower pigs, finisher pigs, and in sows. The results for organic matter and neutral detergent fiber digestibility are shown in Figure 1.8. They demonstrate how the animal and the source of fiber affect energy and nutrient digestibility.

Fat Digestion

Like carbohydrate digestion, lipid breakdown (triglycerides) starts, to a small extent, in the oral cavity with the activity of lingual lipase. Digestion is then continued in the stomach by gastric lipase, where a part of the emulsification of dietary fats and fat-soluble vitamins occurs (the physical breakdown of fat globules into smaller size droplets).

Lipids then enter the duodenum mixing with bile salts and pancreatic juices that contain lipase, colipase, phospholipase A2, and carboxyl ester hydrolase (Table 1.2). While bile salts promote the solubilization of lipids, facilitating their digestion, pancreatic lipolytic enzymes (lipase, phospholipase

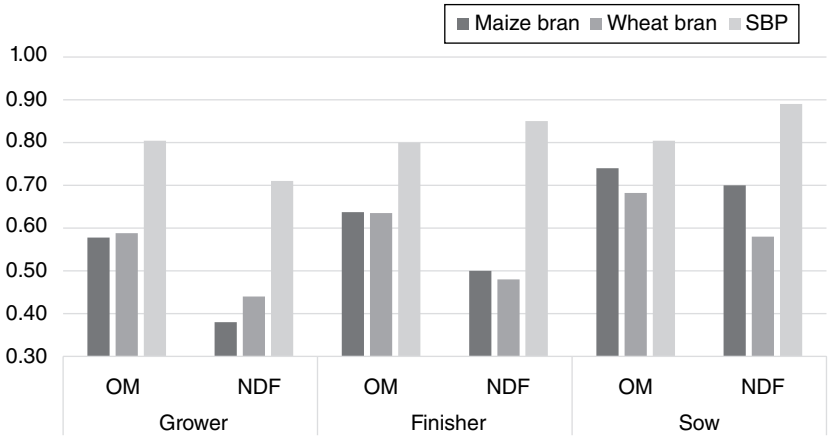


Figure 1.8 Effects of animal type (grower, finisher, and sow) and fiber source on the digestibility coefficient for pigs of organic matter (OM) and neutral detergent fiber (NDF). SBP: sugar beet pulp. Source: Based on Noblet and Shi (1994).

A2, and carboxyl ester hydrolase) help in the breakdown of triglycerides into more polar and smaller molecules such as free fatty acids (FFA), free cholesterol, and lysophospholipids. Colipase prevents the inhibition of lipase by bile salts within the duodenum. FFA (mono- and diacylglycerols) can then be easily absorbed by enterocytes and used for the biosynthesis of new triglycerides within the cell. Absorption of FFA is nearly complete at the distal ileum and has been attributed to both passive diffusion as well as to protein-dependent models (fatty acid transporters). Within enterocytes, triglycerides can then, together with cholesterol, be packaged into phospholipid vesicles (chylomicrons) enabling their transport/movement through the lymphatic and circulatory system. Any fatty acid that is not absorbed in the small intestine becomes substrate for microbial hydrogenation in the cecum and colon. Saturated fatty acids have lower ileal digestibility than unsaturated fatty acids.

Nutrient During Digestion

Dietary fiber has the biggest effect on the digestibility of other nutrients. This interaction has been associated to fiber's physicochemical properties such as solubility (thus affecting chyme's viscosity) and consists of partially interfering with the digestion of mainly proteins and fats. It has been estimated that each 1% of NDF in the diet reduces by 0.5% the ileal apparent digestibility of dietary protein and the coefficient of energy digestibility by 1% in pigs. In contrast, the effects on insoluble fiber on ileal nutrient digestibility are less relevant (Dégen et al. 2007). A mechanism of action contributing to how soluble fiber effects fat digestibility in pigs has been described by Gunness et al. (2016a, b) showed that soluble fiber (e.g., as β-glucans and arabinoxylan) inhibit bile acid availability.

The impact of dietary fiber affects the digestibility of the overall diet. This is shown in Figure 1.9 for OM in pigs fed a low fiber and a high fiber diet over four periods when weight increased from 35.8 to 74.3 kg. Both diets were based on corn, barley, wheat, and soybean meal. The low fiber diet contained 10% NDF and 3.4% ADF. The high fiber diet contained 20% NDF and 9.5% ADF. The high fiber diet contained 15% wheat bran, 10% soybean hulls, and 5% sugar beet pulp. Both diets had the same crude protein level and digestible lysine to NE ratio. The results show that OM digestibility increased with period/weight and was lower for the high fiber diet. The digestibility of most other nutrients also increased with period/weight. The digestibility of energy and N was also

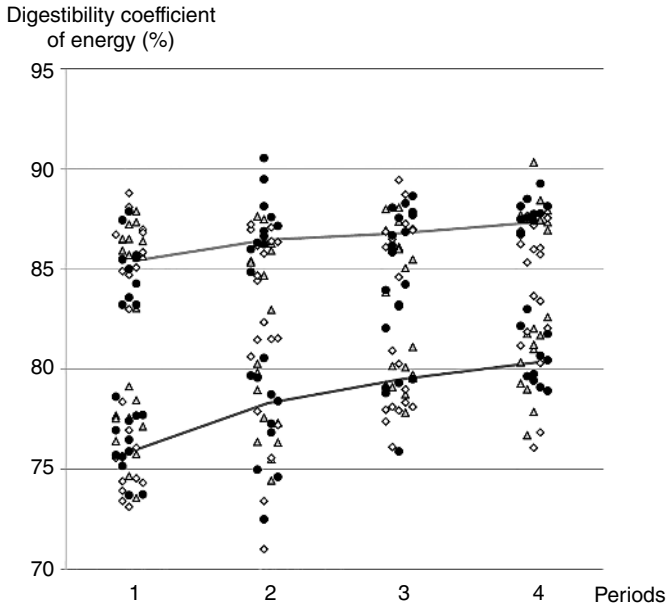


Figure 1.9 Evolution of digestibility coefficient of energy (in %) across four periods for a low-fiber (bold line on the top) or high-fiber (bold line on the bottom) diets in Duroc (▲), Large-White (◇), and Piertrain (●), pigs. Source: Le Sciellour et al. (2018) / PLOS ONE / CC BY 4.0.

reduced in pigs fed the high fiber diet. The digestibility of fiber components was higher for pigs fed the high fiber diet. The negative effect of NDF on OM and protein digestibility is quite dramatic and results in reduced growth performance (Le Sciellour et al. 2018).

Divalent minerals can also reduce the digestibility and bioavailability of liposoluble gut contents. Increasing dietary Ca reduces linearly the digestibility of fat by forming soaps that are excreted in feces. In particular, an increase from 0 to 6 g kg^{-1} of dietary Ca led to a fourfold increase ($P \leq 0.05$) in excreted palmitic and stearic acids in diets containing tallow or palm olein as major fat sources. More than 80% of these excreted fatty acids were present as soaps in feces. For the tallow-based diets, stearic acid digestibility decreased from 91 to 66% ($P \leq 0.01$), while palmitic acid digestibility dropped from 96 to 83% ($P \leq 0.01$). In contrast, dietary Ca excess did not influence fatty acid (or soap) excretion when the main oil sources where olive oil or soybean oil.

Effects of Grain Processing and Starch Structure on Nutrient Digestibility

The main limiting step in the digestion of grains is the access of digestive enzymes to their target substrates such as starch or proteins, which depends on the physical structure, including the intactness of cell walls. Thus, the digestibility of grains (the main energy source in pig diets) and other ingredients can be affected by particle size and how they are processed, and this is not always considered when allocating energy values to ingredients in diet formulation. Reducing particle size disrupts plant cell walls improving the digestion of starch due to the increased surface area of interaction with digestive enzymes (termed "outside-in" hydrolysis). The removal of the large particle size fraction in feeds significantly improves feed utilization in pigs (Al-Rabadi et al. 2017). In addition,

the structure and porosity of the starch granules also determines enzyme access and the degree of resistance to digestion. Starch granules with smooth continuous surfaces can be surprisingly resistant to enzyme hydrolysis, whereas other starches have granules with surface pores that allow for the entry of enzymes into the granules' interior (termed "inside-out" hydrolysis). Figure 1.10 illustrates the hydrolysis behavior of potato and maize starch granules. Maize starch has surface pores allowing the "inside-out" rapid digestion independent of granule size, whereas potato starch has no surface pores allowing only the slower "outside-in" hydrolysis, the latter being highly dependent on granule size.

The apparent total tract digestibility (ATTD) of gross energy (GE) improves in most grains when particle size is reduced to less than 400 microns with the improvement being more evident in grower pigs than weaner pigs and for corn compared to wheat. In contrast, the effect on protein digestibility is generally small and inconsistent. The effect of reducing diet particle size on performance is reflected mainly in feed efficiency, which is consistent with the process improving grain and diet

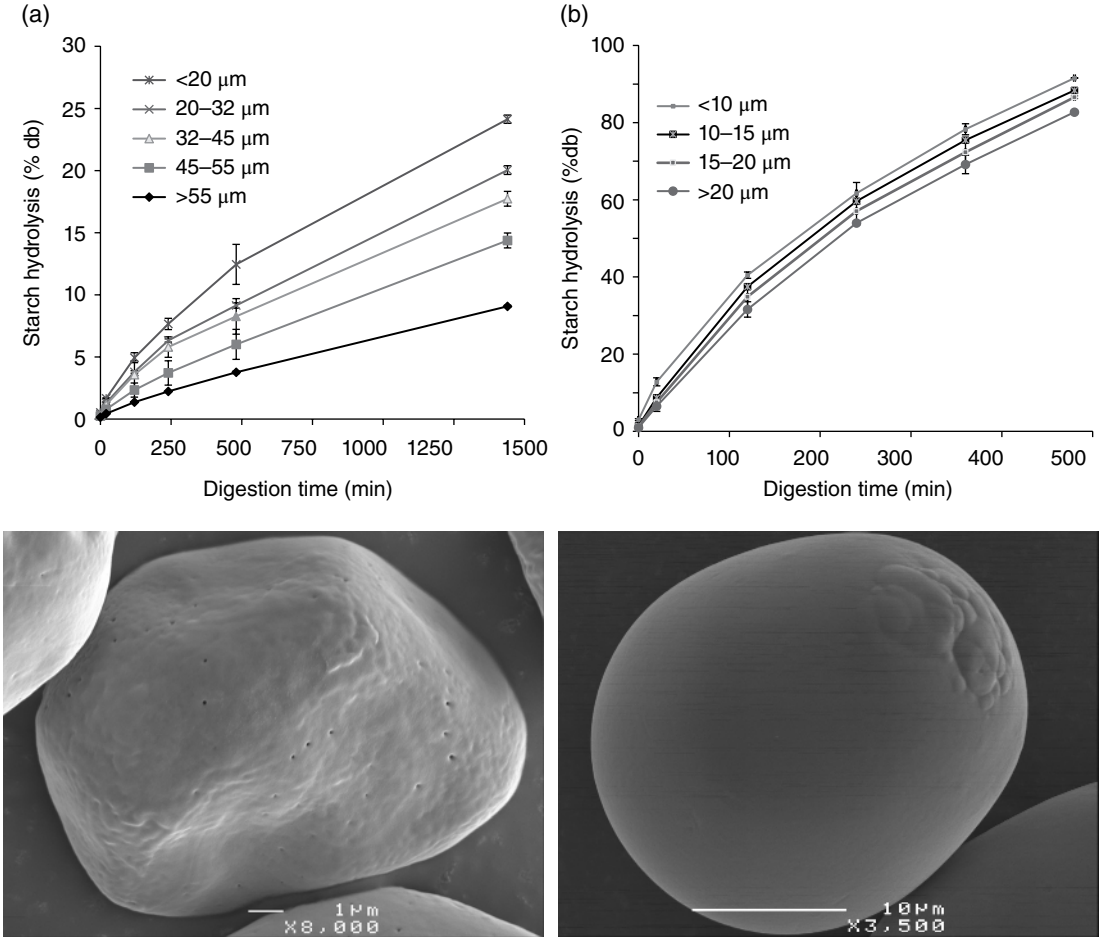


Figure 1.10 (a) Potato starch granule electron micrograph showing no surface pores and the rate of "outside-in" hydrolysis highly influenced by particle size; (b) maize starch granule electron micrograph showing surface pores allowing "inside-out" hydrolysis and rate of hydrolysis independent of particle size. Source: Dhital et al. (2010), Figure 02 & 03[p. 483 & 484]/with permission from Elsevier.

energy availability (Lancheros et al. 2020). The optimal particle size depends on the type of cereal that, in turn, reflects the molecular structure and the accessibility or diffusion rate of digestive enzymes in pigs as previously mentioned when comparing maize to potato starches. In ground oats, a reduction in the geometric mean of the particles to c. 600 micron improved ATTD of NDF, hemicellulose, and GE, while a further reduction to c. 570 micron reduced the ATTD of Ca and P but not NDF, hemicellulose, and GE. The effects of particle size on the DE, ME, and NE of the ground oats are shown in Figure 1.11. The values determined for the coarse ground oats were the closest to those derived from current prediction equations, but the DE, ME, and NE values for the medium ground oats were 4.6, 5.4, and 12.1% higher than those for the coarse ground oats. Finer grinding did not further improve the energy values of the ground oats.

Pelleting pig diets alters the structure of starch also making it more accessible to digestive enzymes and improving energy digestibility particularly in weaner and grower pigs where the ATTD of GE was improved 10.2 and 5.8%, respectively, compared with pigs offered the same diets in the mash form. The apparent discrepancy between energy digestibility and feed efficiency may be associated with the effects of pelleting on protein digestibility and on reducing feed wastage (Lancheros et al. 2020).

Extrusion consists of continuous cooking under pressure, moisture, and elevated temperature (Vatansever et al. 2020), which involves the use of shear force, and may be applied to feed ingredients to increase absorption and utilization of nutrients (Li et al. 2011). Extrusion improves the digestibility of energy and improves the digestibility of AAs in corn-soybean diets and in peas. In contrast to the effect observed in pelleting, the effects of extruding diets on growth performance were more evident in grower than weaner pigs, and the average improvement in feed efficiency for grower pigs was 11.1% (Lancheros et al. 2020).

Overall, reducing particle size of pig feed improves the digestibility of starch in the absence of surface pores such as in potato starch granules but not in highly porous starches such as maize that allow the "inside-out" hydrolysis to occur. Small particle sizes enable quite marked increases in NDF and energy availability. The responses differ with the ingredients involved, the age/weight of the pig, and what equipment is used to reduce particle size. Pelleting pig feeds have a more consistent effect on starch digestion and a larger effect than reducing particle size on pig feed efficiency. The latter is probably associated with the effect of pelleting diets on reducing feed wastage.

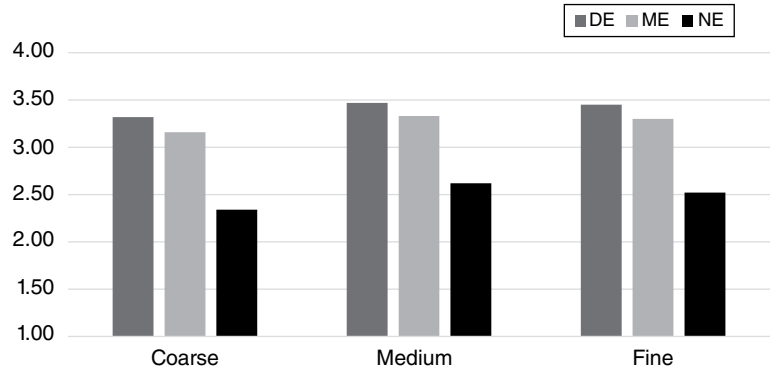


Figure 1.11 Effects of oats ground coarse, medium, or fine on the measured digestible energy (DE), metabolizable energy (ME), and net energy value (NE) expressed as Mcal/kg. The geometric mean particle size of the course, medium, and fine ground oats was 765, 619, and 569 microns, respectively.

Nutrient Sensing and the Gut-Brain Axis

Nutritional chemosensing is a scientific discipline that studies the perception of nutrients in biological systems linking molecular sensing mechanisms to genomic, metabolic, physiologic, and behavioral responses (Roura et al. 2016). Nutrient sensing in mammals starts in the nasal and oral cavities, as both taste and smell provide critical information to the central neuronal system (CNS) regarding the nutritional value of foods. The sense of smell is essential to the perception of food flavors. The retronasal smell relevant to foods is a response to volatile compounds released in the oral cavity reaching the olfactory epithelium (OE) through the nasopharynx. Pigs have an extremely sensitive olfactory system with one of the largest OE known in mammalian species. The OE, located in the upper wall of the nasal cavity, is composed of three main cell types: olfactory sensory neurons (OSN), supporting cells, and basal or progenitor cells. Food odorants stimulate olfactory receptors present on the plasma membrane of the cilia projected by the dendrite of OSN within the OE (Figure 1.12). OSN transduce the chemical stimulus into an electrical stimulus through membrane depolarization, reaching the olfactory bulb in the first instance and transferring the stimulus to mitral cells that will reach the primary olfactory cortex in the CNS (Roura and Tedo 2009).

The sense of taste is the result of perceiving nonvolatile compounds present in food in the oral cavity. Taste has been classified into five categories based on human sensing and believed to be conserved in pigs (Table 1.3): sweet (evoked by simple carbohydrates such as sugars), umami (associated mainly to AAs and peptides), salty (triggered by mineral salts), sour (sensing acids), and bitter (related to potentially toxic or antinutritional compounds). The taste system in the pig is based on c. 19 900 taste buds located in the oral cavity clustered in groups of 100–150 specialized epithelial cells projecting microvilli into the mucus layer of the tongue and grouped in macroscopic structures known as taste papillae (Figure 1.12). In pigs, there are three types of taste papillae: fungiform (scattered uniformly through the upper surface of the rear half of the pig tongue), circumvallate or vallate (two mushroom-shaped epithelial structures carved in the rear epithelia of the tongue in contact with the oropharynx and surrounded by deep crypts with the presence of von Ebner's

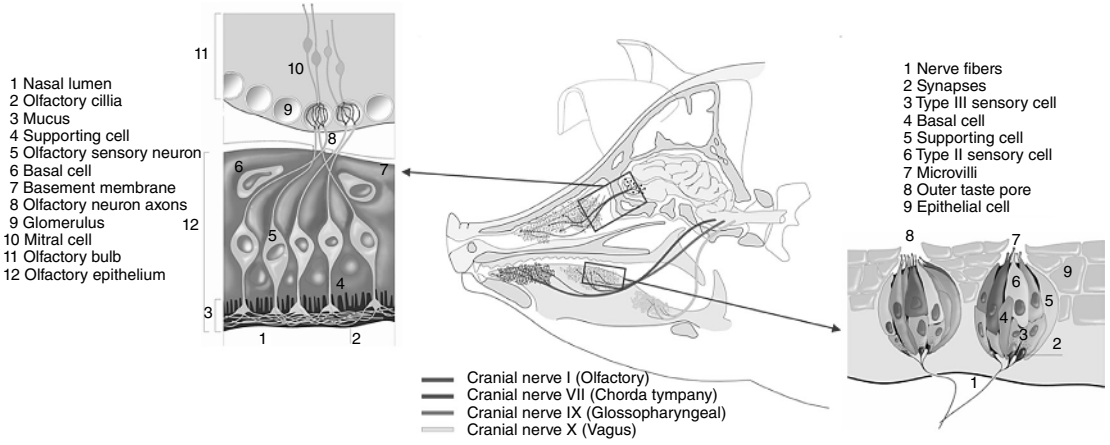


Figure 1.12 Drawing showing the four cranial nerves responsible for smell (I) or taste (VII, IX, and X) sensing. The olfactory epithelium and olfactory bulb showing how sensory neurons reach the lumen of the nasal cavity through the mucosa by setting a net of olfactory cilia. The axons of the neurons reach the glomerulus in the olfactory bulb where mitral cells will take the signal to the primary olfactory cortex. Lingual epithelium showing the main taste types and other functional structures in taste buds. Source: Adapted from Roura and Tedo (2009); Original artwork by Joaquim Roura.

Table 1.3 Main taste-types and taste-active compounds known in pigs.

Taste-type	Chemical groups	Main ligands known	Taste-receptors
Umami	Free AA	L-AA: Lys, Glu, Asp, Ala, Gln, and Asn	T1R1/T1R3
Unknown taste	Peptides and free AA	Peptone, L-Hyp, L-Ser, L-Thr, aromatic, and basic AA	CASR, GPRC6A, GPR92, mGluR1 and 4
Sweet	Sugars, alcohols, free AA, and other	Monosaccharides (e.g., glucose, fructose, galactose, and mannose); oligosaccharides (e.g., maltose, lactose, melibiose, sucrose, and trehalose); polyols (e.g., xylitol and sorbitol); D-AA (e.g., Ala, Asn, Gln, Phe, Ser, Thr, Trp) and Gly; high-intensity sweeteners (e.g., sucralose, rebaudioside A, acesulfame-K, saccharine, dulcin)	T1R2/T1R3, SLGT1/ SLGT3, GLUT4
Non-sweet	High-intensity sweeteners	Aspartame, cyclamate, NHDHC, perillartine, monellin, and thaumatin	None
Starchy “taste”	Glucose polymers	Malto-oligosaccharides	Unknown
Fatty “taste”	Triglycerides and FFA	Long-, medium-, and short-chain fatty acids (saturated and unsaturated)	FFAR1, 2, 3 and 4; GPR84
Bitter	Diverse	Caffeine, quinine, denatonium benzoate, L-Trp	16 T2Rs
Sour	Acids	Citric, ascorbic, tartaric, formic, lactic, and phosphoric acids	Otop1
Salty	Salts	NaCl, LiCl, KCl	ENACα, β, γ

Abbreviations: AA = amino acids; FFA = free fatty acids; NHDHC = neo-hesperedin dihydrochalcone.

salivary glands), and foliate (bilateral striated cuts in the back of the tongue). Some taste buds have also been found in the epiglottis and the soft palate epithelium. Taste buds are composed of four types of cells: taste cells I, II, III, and a basal/progenitor cell type. Taste cells I can sense sour compounds, whereas cell types II oversee umami, sweet, and bitter sensing. Type III cells perceive salty taste together with playing a fundamental role as presynaptic cells that connect taste sensory cells to sensory neurons of cranial nerves VII, IX, or X (Figure 1.12).

The lingual nerves connect directly with the primary gustatory cortex (i.e., insular cortex). Subsequently, multimodal sensory signals (e.g., smell, taste, and somatosensing) convey in secondary brain centers such as the orbitofrontal cortex involved in hedonic responses. In pigs, quinine (bitter) and sucrose (sweet) both promote the activation of the gustatory cortex while differentially activating other regions. Sucrose activates the putamen, which is involved in the reward circuits of perception. In contrast, quinine strongly activates the amygdala, a brain region involved in associative conditioning such as taste aversion. The sweet and bitter brain activation patterns found in pigs are concordant to results from human studies indicating the similarity between the two species in terms of taste perception (Coquery et al. 2018).

The activation of taste cells occurs when nutrients interact with the specific taste receptors (TR) located in the apical transmembrane (Figure 1.12 and Table 1.3). Taste perception of sweet and umami tastes in the tongue is mediated by two dimers of the T1R family of G-protein-coupled receptors (GPCR). The T1R1/T1R3 dimer perceives umami taste responding to L-Ala, L-Asn, L-Asp, L-Glu, L-Gln, Pro, and Thr (Roura and Fu 2017). The T1R2/T1R3 dimer elicits sweet taste responding to mono and oligosaccharides, polyols, some D-AA, and some sweet compounds known to be of high intensity (HIS) in humans such as sucralose or rebaudioside A, among others. In contrast, other HIS such as aspartame and cyclamate have failed to elicit sweet responses in pigs. In addition, other AAs associated with taste-type responses in pigs include L-Hyp, L-Ser, L-Thr, aro-

matic and basic AA, and peptones. Based on other mammalian data (mostly mice), the receptors responsible for the oral sensing of other AA may be G-protein-coupled receptors such as CaSR, GPRC6A, T1R1/T1R3, mGluR1, mGluR4, GPR92, as well as AA transporters/systems including the Pept1 receptor. Similarly, based on rodent data, some monosaccharides, such as glucose, galactose, and fructose, seemed to be sensed by a pathway independent to the T1R2/T1R3 involving the sodium glucose-linked transporter SGLT-1, SGLT-2, GLUT2, or GLUT5.

Other taste types and their ligands described in pigs include bitter, salty, sour, fatty, and starchy tastes (Table 1.3). The perception of bitter compounds is performed by a second family of TR known as T2R. The T2R family in pigs consists of 16 functional receptors (da Silva et al. 2014). Salty taste is evoked mainly by ionic sodium when in contact with the epithelium sodium channel receptors EnaC-α, -β, -γ, whereas sour taste has been linked to the abundance of hydrogen ions perceived through the ion channel Otop 1. FFA sensing has been linked with a variety of GPCR mainly FFAR1, 2, 3, 4 and GPR84 (Table 1.3).

The molecular mechanisms involved in nutrient/taste sensing in the mouth are also present throughout the intestinal tract. These so-called chemosensors are strategically positioned as part of the gut mucosa. They are continuously monitoring the presence and concentration of the nutrients, digestion products, and microbial metabolites in the gut playing a pivotal role in the regulation of gastrointestinal digestive secretions, passage rates and absorption, as well as the hunger/satiety cycle. Nutrient sensors are expressed by EEC and mediate the secretion of gut peptides that orchestrate feeding behavior.

Enteroendocrine System (EES)

The EES is a network of EEC present in the gastrointestinal mucosa that responds to foods by releasing gut peptides that coordinate digestion and absorption of nutrients involving biliary and pancreatic secretion and the modulation of gut motility. In addition, the EES senses toxic/harmful substances to initiate protective responses such as the delay of gastric emptying, the induction of vomiting and diarrhea, and the increase of intestinal secretions. The sensing of nutrients by EEC occurs through the same transmembrane receptors described as part of the taste system in the oral cavity (see Table 1.3). EEC represent approximately 1% of the intestinal epithelia accounting for the largest endocrine organ in the body. EEC are classified based on the expression and secretion of gut peptides. Gut peptides interact with neural circuits including the hypothalamus (the main organ controlling food intake) orchestrating the hunger-satiety cycle a pathway known as the gut-brain axis. The brain receives input via gut peptides secreted by EEC in response to ingested nutrients. Gut peptides are believed to stimulate brain structures (such as the hypothalamus) directly via blood or indirectly through efferent vagal nerve signals. A full classification can be found in the review by Fothergill and Furness (2018). Gut peptides are often coexpressed in the same cell, such as PYY with GLP-1 or gastric inhibitory peptide (GIP) in duodenal L-cells in pigs. The main gut peptides studied to date in pigs are ghrelin, CCK, the two incretins GLP-1 and GIP, and PYY (Table 1.4).

Ghrelin

Ghrelin is an appetite stimulatory (or orexigenic) peptide produced and secreted mainly by enteroendocrine A/X-like cells located in the fundus and corpus of the stomach and in decreasing amounts from duodenum to colon (Peeters 2005). Ghrelin has a positive impact on appetite increasing eating time and growth by activating the growth hormone secretagogue receptor (GHS-R) in pigs (Reynolds et al. 2010). In addition, ghrelin has been linked to GIT motility and pancreatic

Table 1.4 Main gut hormones, associated enteroendocrine cell (EEC) types, and physiological impact in pig.

Digestive system hormones	EEC-type	Nutrients known to stimulate EEC hormone release (in pigs)	Gut tissue	Feeding and gastrointestinal effects
Ghrelin	X/A	Peptones, L-AA (L-Trp and L-Phe), SCFA, LCFA, LPA, bitter compounds	Stomach	↑ Feed intake, ↑ gastric acid secretion and emptying, ↑ pancreatic enzyme secretion
Serotonin	EC	Casein, LC FA	Stomach, small and large intestine	↓ Feed intake[b], ↑ intestinal motility[b]
Somatostatin	D	Unknown	Stomach, small intestine	↓ Gastric acid secretion and emptying
Gastrin	G	Peptones, L-AA (Trp and Phe), LPA	Stomach, duodenum	↑ Gastric emptying and acid secretion
Secretin	S	LCFA	Proximal small intestine	↑ Biliary and pancreatic bicarbonate secretion
Cholecystokinin	I	Mono/disaccharides, polyols, di/tripeptides, L-AA (Trp, Phe, Arg, Leu, Ile, and Lys), LCFA, LPA, bitter compounds	Proximal small intestine	↓ Feed intake, ↓ gastric emptying, ↑ gall bladder contraction, ↑ pancreatic enzyme secretion
GIP	K	Mono/disaccharides, polyols, peptones, L-AA (Trp and Phe), LCFA	Proximal small intestine	↓ Feed intake[b], ↑ insulin, ↓ gastric acid secretion and emptying[b], ↓ intestinal motility[b]
Motilin	M	Unknown	Proximal small intestine	↑ Gastric emptying and pepsin secretion[b], ↑ intestinal motility[b]
Insulin	β-cells[a]	Mono and disaccharides, polyols, L-AA, LCFA, bitter compounds	Pancreas	↓ Feed intake
Neurotensin	N	Unknown	Distal small intestine	↓ Feed intake[b], ↑ Pancreatic enzyme secretion
GLP-1	L	Mono/disaccharides, polyols, peptones, di/tripeptides, L-AA (Trp and Phe), SCFA, LCFA, LPA, BA, bitter compounds	Distal small intestine, colon	↓ Feed intake, ↓ gastric emptying and acid secretion, ↓ intestinal motility, ↓ pancreatic enzyme secretion, ↑ insulin
GLP-2	L	LCFA, BA	Distal small intestine, colon	↑ Pancreatic enzyme secretion, ↑ intestinal enzyme activity, ↑ epithelial proliferation, ↑ barrier function, ↑ blood flow[b]
PYY	L	Mono and disaccharides, polyols, peptones, L-AA (Trp and Phe), SCFA, BA	Distal small intestine, colon	↓ Feed intake, ↓ gastric emptying and acid secretion, ↓ intestinal motility, ↓ pancreatic enzyme secretion
Oxyntomodulin	L	Unknown	Distal small intestine, colon	↓ Feed intake[b], ↓ gastric emptying[b]

Abbreviations: AA = amino acids; BA = bile acids; SCFA = short-chain fatty acids; GIP = gastric inhibitory polypeptide; GLP-1,2 = glucagon-like peptide 1 or 2; LCFA = long-chain fatty acids; LPA = lysophosphatidic acid; PYY = peptide tyrosine-tyrosine.

[a] β-cells have been described in the pancreas and are not part of the enteroendocrine system.

[b] Indicates effects observed in laboratory rodents not confirmed in pigs.

enzyme secretion, cardiovascular functions, and cell proliferation and reproduction, among other activities in the pig (Dong et al. 2009). Zinc oxide and tryptophan are strong secretagogues of ghrelin in pigs (Zhang et al. 2007; Yin et al. 2009).

Cholecystokinin (CCK)

The CCK is a gut peptide strongly associated with meal termination/satiation produced by enteroendocrine I-cells located mainly in the proximal segments of the small intestine (duodenum and proximal jejunum) in pigs. Recent studies have shown that CCK function is related to at least two isoforms CCK-8 and CCK-58 associated with short- or long-term activities, respectively. CCK modulates appetite through the activation of the CCK-1R located mainly in vagal afferents nerves or by acting directly on the CNS in pigs (Ripken et al. 2015). CCK secretion is stimulated by the intraluminal presence of products from the hydrolysis of carbohydrates, proteins, and lipids. Free AA including Arg, aromatic AA (Phe and Trp), and branched-chain AA (Leu and Ile) have been described to significantly stimulate CCK secretion through interaction with GPCR, such as CaSR and T1R1/T1R3 in ECC. In addition, CCK has been associated with improved nutrient absorption via stimulating GI secretion and motility, gallbladder contraction, pancreatic enzyme secretion, and/or delayed gastric emptying (Müller et al. 2021).

Glucagon-like Peptide 1 (GLP-1) and Gastric Inhibitory Peptide (GIP)

The GLP-1 and GIP are often referred to as incretin hormones because of the role as stimulants of insulin secretion. As such, they are both considered anorexigenic hormones (thus stimulating meal termination or satiation) (Renner et al. 2018). GLP-1 arises from the processing of proglucagon and is secreted by L-cells in a biphasic manner following meal ingestion. First, GLP-1 is released and linked with duodenal neurohumoral mechanisms, whereas the second peak of secretion seems to be mediated by the activation of L-cells in the ileum and colon in response to the intraluminal presence of nutrients such as glucose and sucrose, lipids, and proteins in pigs (Steinert et al. 2013; Ripken et al. 2014). The GLP-1 receptors (GLP-1R) are expressed in many organs including pancreas, brainstem, hypothalamus, and vagal afferents in the gut. In addition, the incretin hormones have been related to the activation of the ileal brake, which may contribute to nutrient digestion and absorption as well as satiety by delaying gastric emptying and reducing proximal intestinal motility. GLP-1 and GIP are often coexpressed with PYY in enteroendocrine L-cells located in the porcine distal gut.

Peptide Tyrosine-Tyrosine (PYY)

The PYY is an anorexigenic gut peptide that activates the Y2 receptors located in vagal afferents and the CNS. Glucose, lipids, and proteins/AA have been shown to trigger PYY release in the proximal small intestine (duodenum/jejunum) where 40–50% of the EEC have been identified as PYY-producing cells in pigs (Cho et al. 2015; Wewer Albrechtsen et al. 2016). In addition, PYY also inhibits gastric acid and pepsin secretion, pancreatic exocrine secretion, gastric emptying, and intestinal motility. Thus, like GLP-1, PYY participates in the ileal brake system, reducing the speed at which nutrient transport occurs in the GIT (Sheikh et al. 1989).

Developing GIT in Piglets

Pigs are born with a markedly immature digestive system. This affects feeding behavior and feed preferences early in life particularly under commercial conditions where piglets are weaned very young and abruptly compared to the natural process in the wild. In brief, the immature

digestive system implies impaired digestive and absorptive capacities compared to a grown pig, which have profound implications in terms of nutrient supply and feeding and feed formulation practices.

The innate dentition of piglets consists of 8 deciduous teeth that increase to 32 early in life, reaching the full set of 44 permanent teeth by 18 months of age. Other differences relevant to anatomical metrics, small intestine development (villi height and crypt depths), and digestive enzyme activities between weaner and finisher pigs are highlighted in Table 1.5. The size of the stomach seems to increase linearly with BW. Similarly, as the pig's BW increases, an increment in small intestine weight, length, and mucosal weight occurs proportionally. The relative length of the small intestine segments changes with age. At birth they are 7–10%, 78–84%, and 9–12% for duodenum, jejunum, and ileum, respectively, while in older pigs, the corresponding proportions are 4–5%, 88–91%, and 4–5% (Adeola and King 2006). Relevant to the nutrient digestion and absorption capacity, immature pigs have shorter villi and decreased crypt depths than older pigs. In addition, the most dramatic change relates to digestive enzyme secretion. Compared to adult pigs, the relatively low enzymatic activities seen in piglets are compatible with an immature digestive system that explain the constraint in digesting feeds in early life. The shortage in enzymatic activity is particularly dramatic for the protease trypsin (Table 1.5).

Table 1.5 Main anatomical and physiological differences relevant to the gastrointestinal tract between weaner (approximately 5 kg) and finisher (approximately 100 kg) pigs.

	Length (m)				Weight (g)	
Organ size:	Weaner[a]		Finisher[a]		Weaner[b]	Finisher[c]
Stomach	—		—		20–35	600–680
Small intestine	7.65–9.10		16.5–19.73		180.5–230	1530–2000
Large intestine	1.2–1.5		4.13–5.0		53.12	1280[c]
Villus height and crypt depths (μm):	Duodenum		Jejunum		Ileum	
	Weaner[d]	Finisher	Weaner[d]	Finisher[g]	Weaner[d]	Finisher[g]
Villus height	328 ± 16.2	420 ± 15.0[e]	332 ± 13.4	480 ± 53.8	299 ± 22.7	372 ± 43.0
Crypt depth	207 ± 18.6	367 ± 49.7[f]	208 ± 17.0	429 ± 59.9	202 ± 18.4	316 ± 32.9
Enzyme activities (U g-1 digesta):	Weaner[h]		Finisher[i]			
Lipase	10		175.5			
Trypsin	0.25		957.7			
Amylase	25		2,807			

Abbreviations: GI = gastrointestinal.
References: [a] McCance 1974
[b] Marion et al. 2002
[c] Lærke and Hedemann 2012
[d] Yu et al. 2010
[e] Lin et al. 2020
[f] Metzler-Zebeli et al. 2017
[g] Tian et al. 2020
[h] Hedemann and Jensen 2004
[i] Pluschke et al. 2018.
The measures of enzyme activities were obtained from the proximal small intestine (caudal to the hepatopancreatic duct).

Digestive Secretions in the Young Pig

Some of the most relevant differences affecting pig nutrition practices relate to the low production of digestive juices, particularly enzymes in young pigs. The weaning process is particularly disrupting causing a decline in gastric protease and pancreatic trypsin, chymotrypsin, amylase, and lipase, all fell the week after weaning with amylase declining by 72% and chymotrypsin by 59% (Jensen et al. 1997).

Gastric protease chymosin, a milk clotting enzyme with low proteolytic activity, is one of the few enzymes highly expressed in the stomach during the first weeks following birth. Chymosin may initially help gastric development by stimulating gastric distention through milk clotting. With the increase in pepsinogen and HCl secretion during the weeks following weaning, pepsin replaces chymosin, becoming the dominant protease in the stomach of growing pigs (Rezaei et al. 2013). However, parietal cells in young pigs are not able to secret high amounts of HCl. The result is an inefficient conversion of pepsinogen into the active form pepsin (which requires a pH below 4.0). The low production of gastric pepsin together with the low secretion of pancreatic enzymes such as trypsin, chymotrypsin, and carboxypeptidases A and B is the cause of the low protein digestibility observed in piglets and is often associated with early weaning stress and diarrhea (Hedemann and Jensen 2004).

During lactation, the lactic acid produced from the lactose-rich maternal milk helps maintain a low stomach pH in piglets (Suiryanrayna and Ramana 2015). Thus, under commercial early-weaning practices, keeping a source of lactose seems to alleviate digestive problems in the early postweaning phase. Lactase levels are rather high during the suckling period but rapidly decrease around weaning partly related to an ontogenic decline of the enzyme activity in the intestinal brush border (Heo et al. 2013). Digestion of main complex carbohydrates (i.e., starch) is also impaired by the limited secretion of pancreatic α-amylase in young pigs (Pierzynowski et al. 1993).

In addition to the limited protein and carbohydrate digestive capabilities, lipase, colipase, and carboxyl ester hydrolase activity is also low in young pigs. During the suckling period, carboxyl ester hydrolase is the most prevalent fat hydrolase secreted by the pig. However, in the post weaned pig, colipase and lipase are the main enzymes. The low activity of pancreatic fat hydrolases described at weaning has been attributed to the abrupt changes in the dietary fat content (sow milk vs. weaner feed) and relative low feed intake (Lindemann et al. 1986). In addition, age and BW seem to also be major contributors in the changes of pancreatic lipase, colipase, and carboxyl ester hydrolase activity in young pigs as concentrations of these enzymes increase in the weeks following weaning. Gastric lipase activity increases at weaning and then remains relatively constant significantly contributing to the hydrolysis of triacylglycerols (Jensen et al. 1997).

A high level (173 g d^{-1}) compared to a low level (45 g d^{-1}) of DM intake in the five days immediately after weaning at 14 days of age resulted in greater villus length and higher maltase and glucoamylase activities, while lactase or sucrase activities were not affected. However, despite having a more developed GIT and higher enzyme activities, the digestion of DM, CP, OM, and CHO was significantly higher for pigs fed at the lower level. The digestibility values ranged from 87.1% for CP to 94.7% for CHO illustrating the digestive capacity of piglets even in the period immediately after weaning can be high and that enzyme activities were able to cope with the substrates consumed even by pigs on the high DM intake treatment (Kelly et al. 1991).

Postweaning Feeding Practices

The exposure to a complete feed (changing from the sow's milk to a solid diet) contributes to an increase in HCl and digestive enzyme secretions, indicating the adaptive capacity of the gastrointestinal tract in young pigs (Marion et al. 2003). The decline in most digestive enzyme activities in the

period immediately after weaning is well established as is the fact that piglet feed intake during this period is often very low. These factors have resulted in the use of specialized diets during the first 10–12 days after weaning. The main aspects of a postweaning diet for optimal nutrition can be summarized as (partially adapted from Pluske et al. 2018):

- Use of highly palatable feed ingredients to promote early feed intake.
- If allowed, these diets may benefit from high levels of ZnO that increase feed intake and reduce the incidence and severity of diarrhea.
- Low crude protein content diets using highly digestible protein sources (e.g., skim milk powder, fish meal and whey powder, and plasma protein) balanced with synthetic AAs.
- Increase sulfur amino acid to lysine ratio to 65%, the Trp to Lys ratio to 22%, and the Thr to Lys ratio to 70%.
- Low inclusion of soluble nonstarch polysaccharide (NSP) and add a source of insoluble NSP.
- Use processed starch sources to improve the digestibility.
- Use enzyme supplementation including carbohydrases (xylanase, β-glucanase), where appropriate, and consider phytase super-dosing.
- Low levels of PUFA (particularly keeping a low n-6 to n-3 ratio) and inclusion of medium-chain triglycerides/fatty acids.
- Reduce Ca levels by 10–20% and supplement with organic acids (to reduce buffering capacity in the stomach).
- Consider other additives that will have impacts on mitigating inflammation and immune function such as antioxidants and plant-derived extracts/essential oils.

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