Digestion and Absorption

Niall G MacFarlane, School of Life Sciences, University of Glasgow, Glasgow G12 8QQ.

Abstract

Carbohydrates are digested by salivary and pancreatic amylases to di-, tri- and oligo-saccharides, and then to monosaccharides by enzymes on the wall of the small intestine to allow them to be absorbed. Proteins are absorbed as amino acids and small peptides that are broken down to amino acids within the cells. Monosaccharides and amino acids pass into the liver via the portal vein. Fats are digested and absorbed as free fatty acids and glycerides which are then mostly reconstituted as triglycerides in the mucosal cells of the small intestine. They combine with phospholipids and a protein to form chylomicrons, which pass via the lymphatics and the thoracic duct into the systemic circulation. Fatty acids are re-esterified and stored as triglycerides in adipose tissue or oxidised for energy. Water is passively absorbed due to the osmotic gradient that results mainly due to the active absorption of sodium ions.

Keywords Amino acids; carbohydrates; fat; free fatty acids; monoglycerides and diglycerides; monosaccharides; protein; water and electrolytes

Royal College of Anaesthetists CPD matrix:

Learning objectives

After reading this article, you should be able to:

- understand the mechanisms whereby carbohydrate, fat and protein are digested
- explain where and how the products of carbohydrate, fat and protein digestion are absorbed
- understand water absorption and secretion, and the role of Na^+ and glucose in its absorption

Introduction

Digestion is the breakdown of food into smaller particles and then on to simpler molecules. It is accomplished with the help of secretions that are added to lubricate, liquefy and digest food as it moves through the gastrointestinal system. Normally digestion begins in the mouth with the action of salivary amylase to breakdown carbohydrate but food introduced directly into the stomach (*e.g.* via a nasogastric tube) can be digested by pancreatic amylase. Digestive enzymes cannot easily penetrate solid food and so any solids taken into the mouth should be chewed and broken down into small particles. When a bolus of food particles arrive in the stomach, protein digestion begins from the actions of hydrochloric acid and pepsin.

While peristalsis is chiefly responsible for moving material through the gastrointestinal system by alternating waves of muscle relaxation and contraction, not all the contractions propel the food particles along the tract. Mixing waves churn the ingested food particles and secretions within the stomach to form chyme that is passed on into the small intestine. Enzymes released from the pancreas and the intestinal lining completes the digestion of the food particles into large molecules and their component parts before absorption (though water, vitamins and minerals are absorbed without digestion). Absorption is the movement of small molecules out of the gastrointestinal system and into the circulation or lymphatic system via a range of transport mechanisms.

Carbohydrate

There are three main types of carbohydrate; starch (a polysaccharide), sugar (disaccharide and monosaccharide) and fibre. The two digestible carbohydrates are starch and sugar, and both are broken down into their elementary form along the gastrointestinal system and absorbed as a monosaccharide in the small intestine. Starch is digested within the luminal fluid and broken down into monosaccharide and disaccharide units (beginning in the oral cavity with salivary amylase and continuing through the small intestine with pancreatic amylase). The brush border of the small intestine epithelium possesses membrane-bound enzymes which further digest disaccharides into

an absorbable monosaccharide. The major enzymes include lactase, sucrase, and maltase (maltose being a disaccharide released from starch and composed of two molecules of glucose).

The end result of carbohydrate digestion is the production of a small selection of monosaccharides (glucose, galactose and fructose) which can be transported across the epithelium of the small intestine. The monosaccharides are quickly absorbed along the small intestine. Small, finger-like projections, called villi, are the sites where the membrane transporters for monosaccharides are found. Glucose and galactose transport is by a secondary active transport mechanism via Na^+-glucose or Na^+-galactose co-transporters (or symporters). The energy for this reabsorption is provided by a Na^+-K^+ ATPase on the basolateral membrane of small intestine enterocytes which reduces the cytosolic concentration of Na^+ and drives luminal resorption of sodium along with the monosaccharide. Fructose is transported by passive diffusion down an electrochemical gradient and, as a consequence, it is much less efficiently transported than either glucose or galactose.

Protein

The small intestine can only transport single amino acids or short polymers of two to three amino acids (*i.e*. dipeptides and tripeptides) and so large macromolecular proteins are enzymatically digested prior to absorption by a variety of peptidases in the stomach and small intestine. Digestion begins in the stomach with pepsin which is secreted by gastric chief cells of oxyntic glands in the form of pepsinogen. Pepsinogen is activated by the low pH environment in the stomach (where HCl is secreted by parietal cells).

Pancreatic digestive enzymes perform the majority of protein digestion in the lumen of the small intestine. Proteolytic enzymes from the pancreas include trypsin, chymotrypsin, elastase and carboxypeptidase and break proteins down to short chains of a few amino acids, termed 'oligopeptides'. The final stage of occurs on the brush border of the small intestine epithelium where membrane-bound peptidases complete digestion of oligopeptides to single amino acids, dipeptides or tripeptides.

The single amino acids, dipeptides and tripeptides are transported, via secondary active transport over the enterocyte luminal membrane via a range of symporters. Once inside the enterocyte the dipeptides and tripeptides are cleaved to form individual amino acids by cytosolic peptidases. Individual amino acids are then passively transported over the basolateral membrane and into the portal bloodstream.

Lipid

The major dietary lipids include triglycerides, phospholipids, cholesterol and cholesterol esters (but about 90% of the dietary lipids are triglycerides). Lipid digestion only occurs in an aqueous environment; however, being water insoluble, lipids form large globules that provide little exposure to an aqueous environment and need to be emulsified. Emulsification is where large lipid globules are broken down into small droplets (with a high surface area-to-volume ratio). Emulsification aids lipid digestion by providing a greater surface area for digestive enzymes to act on the droplet. The main emulsifiers are bile acids and the phospholipid lecithin (both made in the liver and secreted in bile) but dietary proteins act as weak emulsifiers too. Emulsification is aided by the continual churning of chyme in the gastrointestinal system.

Lipid digestion is primarily in the small intestine (however, the stomach and salivary glands secrete small amounts of lipases that begin the process although this is not vital). The pancreas makes the main enzymes that digest lipids:

- pancreatic lipase breaks down triglycerides into component fatty acid and 2-monoglycerides (with the aid of colipase)
- pancreatic cholesterol esterase breaks down cholesterol esters into component cholesterol and fatty acid
- pancreatic phospholipase A_2 breaks down phospholipid into component head groups and fatty acid

Importantly, derived amphipathic fatty acids produced by these enzymatic processes also contribute to emulsification.

The products of lipid digestion are hydrophobic and will cross plasma membranes easily by diffusion but the process is made easier with the close proximity of the lipids to the enterocyte luminal membrane. This is accomplished by the action of bile acids surrounding small aggregations of lipids to form micelles (approximately 5 nm in diameter). Since bile acids are amphipathic they can orientate lipids within the micelle (with the hydrophobic region towards the core and the hydrophilic region at the surface). As a result, the micelles can get close enough to the small intestine brush border and the lipid digestion products diffuse across the enterocyte plasma membrane. Bile acids do not cross, because they are amphipathic, and are left in the lumen to collect more lipid digestion products and carry them to the small intestine brush border.

Free fatty acids and cholesterol are toxic if released into the bloodstream at high concentration. So, they are converted to triglycerides and cholesterol esters within the enterocyte cytosol and packed within macro-molecular structures called chylomicrons that are released from the basolateral membrane into a lacteal (a specialized lymphatic vessel) and then onto the bloodstream.

Water and Minerals

Approximately 8 L of fluid is secreted into the gastrointestinal system (along with 2 L of ingested fluid); but normally only a 0.1-0.2 L of fluid is excreted. Thus, over 9 L of fluid, composed of water and minerals, must be absorbed each day. Water and electrolyte absorption primarily occurs in the small and large intestines (and any upset can lead to diarrhoea or constipation).

Water is always absorbed in the gastrointestinal system by passive osmosis (mostly via a paracellular route between enterocyte tight junctions). Consequently, water reabsorption is primarily actuated by active absorption of osmotic minerals, especially sodium (Na^+). In cases where solutes remain

unabsorbed in the lumen of the gastrointestinal system, their high concentration means water cannot be reabsorbed and results in osmotic diarrhoea.

Luminal membrane Na^+ reabsorption occurs through a range of co-transporters and counter transporters in the small and large intestine (powered by Na^+-K^+ ATPase transport protein). This protein actively transports Na^+ across the basolateral enterocyte membrane, reducing the intracellular Na^+ concentration and creating an electrochemical gradient for Na^+ transport. Reabsorption also occurs in the duodenum and jejunum by a variety of Na^+-Nutrient co-transporters (but these mechanisms are constitutively active and not physiologically regulated). Na^+ reabsorption in the large intestine is similar to that occurring in the kidney (observed in the principal cells of the distal tubule and collecting duct). Briefly, diffusion through Na^+ luminal ion channels is powered by a basolateral Na^+-K^+ ATPase and, as observed in the late distal tubule and collecting duct, aldosterone significantly enhances sodium reabsorption in the large intestine through enhanced protein expression of basolateral Na^+-K^+ ATPase and luminal Na^+ ion channels. The majority of chloride (Cl^-) is reabsorbed in the small intestine, especially in the duodenum and jejunum. Reabsorption of Cl^- mainly occurs by passive diffusion via the paracellular route. Substantial active reabsorption of Na^+ can create a negative charge in the lumen, and provide a strong electrochemical gradient for passive reabsorption of Cl^-.

A large amount of bicarbonate is included with pancreatic secretions and so maintenance of good acid-base balance will require some reabsorption. When Na^+ is reabsorbed, moderate amounts of hydrogen ions (H^+) are secreted into the lumen of the intestine in exchange (using a Na^+-H^+ counter transporter) and the H^+ combines with bicarbonate ions (HCO_3^-) to form carbonic acid (H_2CO_3), which then dissociates to form water and carbon dioxide (CO_2). The water remains as part of the chyme and CO_2 is absorbed by the blood and expired. This is often termed ‘active reabsorption of bicarbonate ions’.

Vitamins

In addition to metabolic nutrients, water and important minerals the gastrointestinal system has to absorb several essential small molecule vitamins. The hydrophobic, fat soluble, vitamins (A, D, E and K) are absorbed together with other lipids using general mechanisms of lipid absorption. Most water-soluble vitamins are absorbed through secondary active transport by vitamin-specific Na^+-vitamin co-transporters in the small intestine. However, Vitamin B_{12} has a unique mechanism for absorption.

Dietary vitamin B_{12} is normally bound to proteins in food (substantially from animal origins) and so will require pepsin and the low stomach pH to release it. The free vitamin B_{12} binds to one of three binding proteins, haptocorrin, that is produced by the salivary glands and the parietal cells in the stomach. The higher duodenal pH is allows pancreatic proteases to degrade haptocorrin and the vitamin B_{12} is released before re-binding to a second binding protein, intrinsic factor, that is produced by parietal cells. In the distal ileum the vitamin B_{12}-intrinsic factor complex is recognised by special receptors (cubulin) in the mucosal cells. Vitamin B_{12} then enters the blood with the majority (70-80%) bound to haptocorrin and a smaller proportion (20-30%) bound to transcobalamin (forming a complex known as holotranscobalamin or active B_{12} and this is only form that vitamin B_{12} can be used by the cells of the body).

Protective Factors

The gastrointestinal system, particularly the stomach and small intestine, possess a remarkable ability to remain intact despite being constantly bathed in acid and proteolytic enzymes that digest virtually anything that we eat. Gastrointestinal system therefore possesses powerful mechanisms for mucosal defence and repair.

Goblet cells in the mucosa secrete large quantities of protective mucus that lines the mucosal surface and HCO_3^-, trapped inside the layer of mucus, buffer any HCl that penetrates and creates a pH gradient to maintain a near neutral pH at the epithelial cell surface. In humans, bicarbonate secretion is an active process (responding to vagal stimulation and fundic distension).

There are several mechanisms at the epithelial level that contribute to maintenance of an intact mucosal barrier. Surfactants in apical cell membranes prevent water-soluble agents from the gastric lumen reaching and damaging the epithelium and a rapid cell turn-over and restitution processes keep the epithelial lining intact. For sub-epithelial protection, mucosal blood flow is essential in supplying the epithelium with nutrients and oxygen and for disposal of H^+ and noxious agents permeating the mucosa. Prostaglandins maintain blood flow and prevent vascular endothelial injury caused by ethanol by direct cytoprotective actions and sucralfate, aluminium containing antacids, carbenoxolone and bismuth are mild irritants that liberate endogenous prostaglandins in the mucosa.

FURTHER READING

Leonard R. Johnson. Mosby Physiology Monograph Series: Gastrointestinal Physiology, 8th Edition. Elsevier 2013.