CHAPTER 16

The Role of Apolipoprotein A-IV as a Satiety Factor

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1. Sources of Lipid in the Lumen of the Gastrointestinal Tract

As much as 40% of the daily caloric intake in the Western diet is in the form of lipids ranging between 60 to 100 grams (Davenport, 1971). Triacylglycerol (TG) is the major dietary fat in humans. Major long-chain fatty acids present in the diet are palmitic (16:0), stearic (18:0), oleic (18:1), linoleic (18:2), and linolenic (18:3). In most infant diets, fat becomes an even more important source of calories. In human milk and in human formulas, as much as 50% of the total calories are present as fat (Hamosh, 1979). In human milk, there is also an abundance of medium-chain fatty acids. The human small intestine is presented daily with other lipids such as phospholipids (PL), cholesterol, and plant sterols. Both PL and cholesterol are major constituents of bile. In humans, the biliary PL is a major contributor of luminal PL and as much as 11 to 20 grams of biliary PL enters the small intestinal lumen daily, whereas the dietary contribution is only between 1 to 2 grams (Northfield and Hofmann, 1975; Borgström, 1976). The small intestinal epithelium undergoes rapid turnover that also contributes to the luminal PL and cholesterol. Although cholesterol is the predominant sterol of total dietary sterol in the Western diet, plant sterols account for 20% to 25% (Taylor and Gould, 1967; Gould et al., 1969).

2. Digestion of Lipids

Lipid digestion begins in the stomach. Lipase activity has been reported to be present in the human gastric juice (Schonheyder and Volquatz, 1946). In humans, the gastric lipase activity is contributed mainly by the stomach and the highest activity is detected in the fundus of the stomach. Human gastric lipase has a pH optimum of about 5.5 and, therefore, has

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Lipid is emulsified in the stomach (broken into small oil droplets). Lipid emulsion enters the small intestinal lumen as very fine lipid emulsion droplets less than 0.5 μm in diameter (Senior, 1964; Carey et al., 1983). The combined action of the bile and the pancreatic juice brings about a marked change in the physical and chemical form of the luminal lipid emulsion. Pancreatic lipase is secreted into the duodenum where it hydrolyzes TG to form 2-monoacylglycerol (2-MG) and FAs. The most potent gastrointestinal hormone that stimulates the release of enzymes by the pancreas is cholecystokinin (CCK; Solomon, 1994), and CCK-A receptor has been demonstrated to be present in the pancreas (Rosenzweig et al., 1983). The pancreatic lipase works at the oil and water interphase. As a result, the rate of lipolysis is influenced by factors modifying the physicochemical properties of the interface as well as the surface area (Brockerhoff, 1968; Mattson and Beck, 1956; Simmons, 1972).

In vitro studies using purified pancreatic lipase have demonstrated a potent inhibitory effect of bile salts on lipolysis of TG at concentration above the critical micellar concentration (Morgan et al., 1969; Benzonana and Desnuelle, 1968). The inhibitory effect of bile salt is physiological because the concentration of bile salts in the duodenum is normally higher than the concentration of bile salt that is needed to observe the inhibitory effect. If this is the case, why, then, is pancreatic lipase so efficient in digesting TG? The explanation lies in the fact that the pancreas secretes another protein that counteracts this inhibition. The factor is called colipase. This factor was first isolated by Morgan et al. (1969) from rat pancreatic juice. The structure and mechanism of action of colipase have been elucidated by the elegant works from the laboratories of Dr. Desnuelle (Maylie et al., 1971; Benzonana and Desnuelle, 1968) and Dr. Borgström (Borgström & Erlanson, 1973; Borgström et al., 1979). Colipase acts by attaching to the ester bond region of the TG molecule. In turn, the lipase binds strongly to the colipase by electrostatic interactions, thereby allowing the hydrolysis of the TG by the lipase molecule (Erlanson-Albertsson, 1992). Colipase is secreted as a procolipase and is converted to the active form through the removal of a five-amino-acid fragment by trypsin. The five-amino-acid fragment released is called the enterostatin. Enterostatin has been demonstrated to inhibit fat intake—an action independent of the route of administration. For instance, it has been reported that both the intraduodenal (Mei and Erlanson-Albertsson, 1996), intraperitoneal (Okada et al., 1996; Lin et al., 1994), intravenous (Mei and Erlanson-Albertsson, 1992), and intracerebroventricular administration of enterostatin reduces fat intake, but both the dose and the time required for the administered enterostatin to exert its action are quite different. The physiological role of enterostatin in the inhibition of fat intake has often been questioned because intestinal digestion of peptides are extremely efficient and therefore only amino acids, di- and tripeptides, are taken up by the small intestinal mucosa. If so, one wonders how enterostatin is taken up by the small intestine and then transported into the circulation. This criticism