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Incretin and Lipid Metabolism

Young Min Cho
Seoul National University, Korea

In addition to glucose, fat ingestion is a physiologic stimulus of GLP-1 secretion in humans and rodents, and GLP-1 is thought to regulate fat absorption to decrease postprandial lipemia. In rats, intravenously administered GLP-1 inhibited Apo-B48 production, which was accompanied by decreased absorption of triglycerides but not cholesterol. In healthy humans, intravenous GLP-1 infusion suppressed postprandial increases in triglycerides and free fatty acids, possibly via delayed gastric emptying and suppression of lipolysis. Sitagliptin, a DPP-4 inhibitor, also decreased postprandial plasma triglyceride and Apo-B48 levels, as well as fasting plasma triglyceride levels (particularly the very low density lipoprotein fraction) in mice and hamsters. Exendin(9-39) abolished the lipid-lowering effect of sitagliptin, which suggests that endogenous GLP-1R signaling is critical for synthesis and production of intestinal Apo-B48(+) triglyceride-rich lipoproteins. In this regard, it is noteworthy that exendin-4 directly inhibits the synthesis of Apo-B48 from hamster enterocytes. Since DPP-4 inhibitors also decrease postprandial plasma triglyceride levels, delayed gastric emptying may not be a prerequisite of decreased fat absorption by GLP-1. In this lecture, I will overview the role of incretin hormones in lipid metabolism.