

**Gastrointestinal motor function and
glycaemic control in diabetes**

A thesis submitted by

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THESIS ABSTRACT

This thesis focuses on the role of gastric emptying and gastrointestinal hormones in the regulation of glycaemia and appetite in health and patients with type 2 diabetes. The key issues relate to: 1) dietary strategies to improve postprandial glycaemia and appetite by modulation of gastric emptying and gut hormone release, 2) comparative patterns of incretin hormone secretion in response to known rates of small intestinal glucose delivery in healthy subjects and type 2 patients, and 3) whether non-nutrient substances impact on gastric emptying and hormone secretion.

The rate of gastric emptying and secretion of the incretin hormones, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulintropic polypeptide (GIP), are major determinants of glucose homeostasis. Dietary strategies that aim to increase endogenous GLP-1 secretion and slow gastric emptying are therapeutically appealing in type 2 diabetes. The study reported in Chapter 5 evaluated the acute effects of whey protein, when given as a „preload“, on gastric emptying, incretin hormones and postprandial glycaemia in patients with type 2 diabetes. Different doses of whey preload were evaluated for their effects on glycaemia, fullness and energy intake in Chapter 6. The study reported in Chapter 7 addressed the question of whether the acute effects of whey are sustained with „chronic“ administration.

The study reported in Chapter 8 evaluated plasma GLP-1 and glycaemic responses to a small load of enterically coated lauric acid, designed to be released over a long length of terminal ileum, after both breakfast (with which the formulation was given), and a subsequent lunch, in patients with type 2 diabetes.

Patients with type 2 diabetes have been reported to have impaired postprandial secretion of GLP-1, but gastric emptying was not quantified in these studies. It has been established that the rate of gastric emptying is an important determinant of incretin hormone secretion, and gastric emptying is frequently abnormally slow in patients with diabetes. In Chapter 9, glycaemia, insulinaemia, and incretin hormone release were evaluated in response to duodenal glucose loads in patients with type 2 diabetes, and were compared to healthy controls.

Sucralose, a noncaloric sweetener, has been reported to stimulate GLP-1 release from L-cells in vitro. The study described in Chapter 10 evaluated whether sucralose stimulated GLP-1 release or affected gastric emptying in healthy subjects. In rodents, sucralose stimulates glucose absorption by enhancing apical availability of the GLUT2 transporter. In the study reported in Chapter 11, the effects of exposure of the proximal small intestine to sucralose on glucose absorption and the glycaemic response were evaluated. Cephalosporin antibiotics mimic peptones and stimulate release of cholecystokinin (CCK) in rodents. In

Chapter 12, the acute effects of orally administered cefaclor on CCK release, gastric emptying, and postprandial blood glucose and insulin responses in healthy subjects were assessed.

DECLARATION

Name: Jing Ma

Program: Doctor of Philosophy

This work contains no material which has been accepted for the awards of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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PUBLICATIONS ARISING FROM THIS THESIS

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