A mathematical model for investigation of intestinal changes on the postprandial bile acid profile

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F.L.P. Sips[1], H.M. Eggink[2], P.A.J Hilbers[1], M.R. Soeters[2], A.K. Groen[3,4], N.A.W. van Riel[1,3]
1. Department of Biomedical Engineering, Eindhoven University of Technology, The Netherlands
2. Department of Endocrinology and Metabolism, Academic Medical Centre, University of Amsterdam, The Netherlands
3. Amsterdam Diabetes Center, Department of Vascular Medicine,
Academic Medical Centre, University of Amsterdam, The Netherlands
4. Departments of Pediatrics and Laboratory Medicine, University of Groningen,
University Medical Center Groningen, The Netherlands
E-mail: f.l.p.sips@tue.nl, h.m.eggink@amc.uva.nl, p.a.j.hilbers@tue.nl,
m.r.soeters@amc.uva.nl, a.k.groen@amc.uva.nl, n.a.w.v.riel@tue.nl

1. Introduction

Bile acids (BA) have surfaced as potential regulators of metabolic health. Although much is known about the elements that drive the enterohepatic circulation of BA, comprehensive understanding of BA dynamics in metabolic health and disease remains a challenge. Systemic understanding of BA metabolism is impeded by the complexity of BA metabolism and the difficulty in obtaining direct measurements of the main BA pools in the enterohepatic circulation. In order to investigate the dynamics of BA metabolism and the relationships between the sizes of the various pools of BA, we have developed a mathematical model of the enterohepatic circulation of BA.

2. Materials & Methods

The model is composed of a system of differential equations describing BA circulation as transportation between connected components. The model encompasses the complete enterohepatic and systemic circulation of BA. In particular, intestinal BA metabolism is included in detail (Fig 1). Intestinal transit is non-homogeneous, and is affected by a postprandial increase of transit which propels the intestinal contents forward.

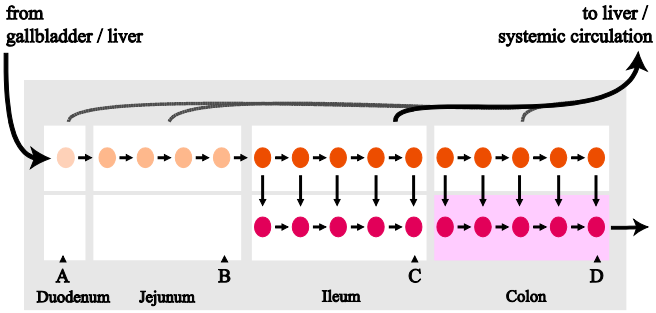

Figure 1. Intestinal detail of the model. In the intestine compartments, BA metabolism comprises transit and passive and active uptake, deconjugation of conjugated BA (orange) to unconjugated BA (red) and biotransformation (of unconjugated BA in the colon).

3. Results

Results show the model reproduces main characteristics of the healthy postprandial BA response. The simulated postprandial response consists of two phases (Fig 2). First, the gastro-colic reflex causes an immediate rise of ileal BA concentrations, and thus, systemic BA concentrations. Following this initial response, the pool of BA released by the gallbladder after the meal arrives in the ileum, causing a secondary peak.

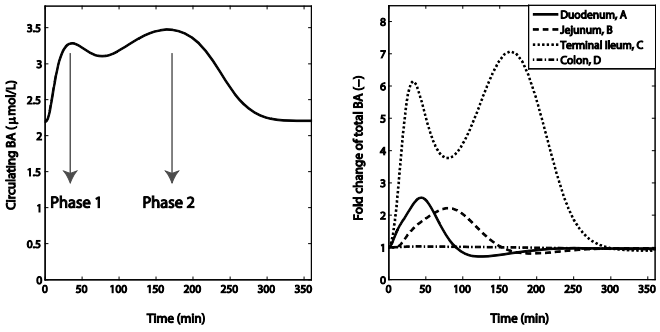

Figure 2. Postprandial response of the model. Left – Postprandial total BA in a healthy individual. Right – intestinal BA content during the meal at 4 locations in the intestine. Letters (A-D) denote the compartment (see Fig 1).

4. Discussion

The model has applications in elucidating effects of dietary or genetic perturbations on BA kinetics. As the model includes a more detailed description of intestinal transit than previously published models of BA circulation [1], it is particularly suited to investigate BA metabolism after changes of the gastrointestinal system, such as the increase of peripheral BA seen following Roux-en-Y Gastric Bypass.

5. References

1. Hofmann AF, Molino G, Milanese M, Belforte G. "Description and simulation of a physiological pharmacokinetic model for the metabolism and enterohepatic circulation of bile acids in man. Cholic acid in healthy man." *J Clin Invest.* 71: 1003–1022, 1983