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Abstract

An Animal Model to Investigate Postprandial Metabolism †

Larissa Rodrigues [1,*], Tushar More [2], Carlos Mario Donado-Pestana [1], Amanda Domingos Vasconcelos [1], Vinicius Bonfieti Mantovam [1], Karsten Hiller [2] and Jarlei Fiamoncini [1]

[1] Department of Food Science and Experimental Nutrition, School of Pharmaceutical Sciences, University of São Paulo, São Paulo 05508-000, Brazil; donadopestana@usp.br (C.M.D.-P.); amandavasconcelos@usp.br (A.D.V.); viniciusbmantovam@usp.br (V.B.M.); jarlei@usp.br (J.F.)

[2] Department of Bioinformatics and Biochemistry, Braunschweig Integrated Center of Systems Biology, Technische Universität Braunschweig, 38106 Braunschweig, Germany; t.more@tu-braunschweig.de (T.M.); karsten.hiller@tu-braunschweig.de (K.H.)

* Correspondence: larissarodrigues@usp.br

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Abstract: Background and Objectives: Bile acids (BA) are recognized as metabolic integrators that participate in the regulation of energy metabolism and inflammation. Their concentration in the plasma increases several-fold after a meal. The postprandial period is characterized by physiological changes to accommodate the alterations in nutrient availability and a systemic inflammatory response. An animal model would be an important tool to investigate postprandial metabolism, but there is no fully characterized model, and it is uncertain whether human responses to a meal can be reproduced in animals. This study aimed to characterize an animal model for investigating postprandial metabolism and inflammation, with a focus on the role of BA in the modulation of postprandial inflammation. Methods: Changes in plasma BA levels and hepatic cytokine concentrations were investigated in male Sprague-Dawley rats (n = 50) at different time points after the ingestion of a high-fat meal (fasting, 60, 120, 180, and 300 min). Results: Plasma BA levels were quantified using liquid chromatography-mass spectrometry (LC-MS/MS), and hepatic inflammatory marker content was assessed using Western blotting. As a result, we observed that unlike humans, rats showed a predominance of unconjugated BA (~70%) both during fasting and throughout the postprandial period in the plasma, with cholic acid being the most abundant species (~36%). On the other hand, rats exhibited a postprandial inflammatory response with a temporal resolution like that observed in humans. In the liver, two hours after meal ingestion, the content of Toll-like receptor 4 (TLR-4) was 30% higher than in the fasting state (p = 0.0071). Discussion: TLR-4 is a receptor that interacts with intracellular adaptors to activate tumor necrosis factor κB (NF-κB), which also increased in the liver three hours after meal ingestion (p = 0.0208). Increased hepatic mRNA expression of interleukin 6 (IL-6) and interleukin 1β (IL-1β) was also observed at 60 min. Preliminary analysis demonstrated that rats exhibit postprandial inflammation in the liver and may constitute a valid experimental model to investigate postprandial alterations also observed in clinical trials.

Keywords: bile acids; post-prandial; energy metabolism; meta-inflammation; metabolomics

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