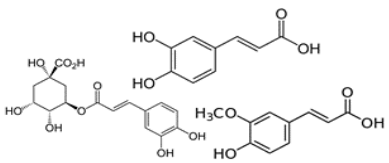

# Bioaccessibility, Bioavailability and Bioactivity of Polyphenols and Their Microbial Metabolites Following Simulated Dynamic Gastrointestinal Digestion

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## Abstract

Polyphenols have been indicated to exert protective effects against a number of chronic diseases including cancer. The bioactivity of polyphenols depends on their bioaccessibility and bioavailability from the gastrointestinal (GI) tract after undergoing digestion and microbial biotransformation processes followed by first pass intestinal and hepatic metabolism. Despite the functional significance of the polyphenols' metabolites, there is a paucity of knowledge with regards to microbial biotransformation of polyphenols and the bioactivity of the generated metabolites. The present work performed a series of studies involving the combination of a simulated gut digestion with cell culture systems for the investigation of the biotransformation, bioavailability and bioactivity of commonly consumed polyphenols including chlorogenic, caffeic, ferulic acids and rutin and their metabolites. The results from the in vitro digestion study highlighted the significant role of colonic gut bacteria in the process of digestion and metabolism of the tested polyphenols with minimal biotransformation of the native polyphenols seen in the upper GI vessels and extensive bacterial breakdown occurring in the colonic compartments. The biotransformation process led to differing antioxidant activities and short chain fatty acid profiles in the colonic compartments. The study of anti-colon cancer effects of chlorogenic acid and its major microbial metabolites (caffeic, 3-phenylpropionic and benzoic acids) indicated that the combination of chlorogenic acid and its metabolites enhanced the anti-cancer efficacy as anti-proliferative, apoptotic and cell cycle arrest effects were seen at several-fold lower concentrations of those compounds within the equimolar mixture than when they were provided singly. To further elucidate the transport and metabolism of polyphenols and their metabolites, we developed a testing approach that coupled the microbial digests generated from the simulated dynamic GI digestion system with a co-culture of human intestinal Caco-2 and hepatic HepG2 cells. Digestion of polyphenol-rich potato extract in the GI model led to generation of the microbial-derived metabolites of the polyphenols that were poorly transported across the Caco-2 cells. A two- to three-fold increase in the concentrations of ferulic acid and microbial metabolites such as dihydrocaffeic, 3-hydroxyphenylpropionic and coumaric acids after 3 h incubation with HepG2 cells demonstrated a major contribution of hepatic metabolism in the generation of those compounds despite their poor Caco-2 cellular transport. Overall, the combined approach using simulated gut digestion and cell culture systems developed in the current work provides a unique platform for the detailed study of mechanisms involved in biotransformation, bioavailability and bioactivity of polyphenols and their metabolites, which is otherwise difficult to perform in vivo.

## About the Candidate

Shima Sadeghi holds a M.Sc. degree in Human Nutrition from Shiraz University of Medical Science, Iran. She joined Dr. Kubow's research group to pursue her Ph.D. in Human Nutrition. Her Ph.D. project focuses on the in vitro investigation of biotransformation, bioavailability and anti-colon cancer effects of common dietary polyphenols including chlorogenic, caffeic, ferulic acids and rutin.