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Coffee Beyond Caffeine: Human Pharmacokinetics of Coffee-Specific Biomarkers and Their Association with Acute Immunomodulatory Responses

ABSTRACT

Coffee consumption has consistently been associated with a lower risk of cardiometabolic diseases, yet the biological mechanisms responsible for these benefits remain incompletely understood. Our work combines findings from two randomized human intervention studies investigating both the biological activity and the pharmacokinetics of coffee-specific compounds. In a randomized crossover trial, healthy volunteers received coffee, an aqueous caffeine solution, or water. Serial blood sampling demonstrated that coffee and caffeine differentially modulated circulating cytokines. Pure caffeine induced a stronger suppression of several pro-inflammatory cytokines, whereas coffee produced a distinct immune response, indicating that the coffee matrix substantially modifies caffeine-mediated effects. These findings provide novel evidence that bioactive compounds beyond caffeine contribute to the acute immunological effects of coffee.

In a complementary intervention study, targeted UHPLC-MS/MS analysis characterized the pharmacokinetics of coffee-derived atractyligenin metabolites. Atractyligenin and its 19-O- β -D-glucuronide were rapidly absorbed, remained detectable in plasma for up to 24 hours, and proved to be robust biomarkers of Arabica coffee intake independent of brewing method. These biomarkers offer objective tools for assessing coffee exposure in nutritional and epidemiological studies.

Our research demonstrates that coffee exerts biological effects extending beyond caffeine alone while providing validated biomarkers for objective exposure assessment. Combining pharmacokinetic profiling with functional immune phenotyping contributes to a more comprehensive mechanistic understanding of the health effects associated with habitual coffee consumption.

Keywords: Coffee, caffeine, atractyligenin, biomarkers, immunomodulation, pharmacokinetics

BIOGRAPHY

Thomas Skurk is Professor of Nutritional Medicine and Head of the Core Facility Human Studies at the ZIEL Institute for Food & Health, Technical University of Munich (TUM), Germany. His research focuses on human nutrition, metabolic diseases, and clinical nutrition, with particular emphasis on diabetes, obesity, and precision nutrition. He leads translational human intervention studies integrating advanced metabolic phenotyping, biomarkers, and nutritional interventions to investigate diet–health interactions. Prof. Skurk studied medicine at the Universities of Regensburg and Würzburg and completed his habilitation in Nutritional Medicine at TUM. He has authored more than 350 scientific publications and serves on several national expert committees in nutritional medicine.