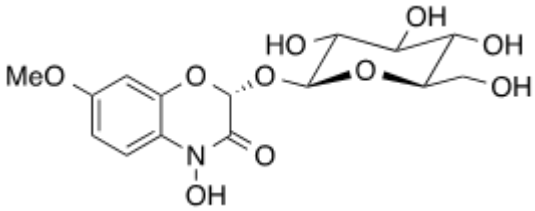
From Diet to Microbiome: Exposure, Metabolism, and Gut Interactions of Benzoxazinoids

Visconti, Johanna Laurenzia[1,2], Ricci, Rebekka[1,2], Mateo, Pierre[1], Notter, Matheus[3], Hapfelmeier, Siegfried[3], Ganal-Vonarburg, Stephanie[2], Robert, Christelle[1*]

[1] Chemical Ecology, Institute of Plant Sciences (IPS), University of Bern, Bern, Switzerland; [2] Gastrointestinal Group, Department of Biomedical Research (DBMR), University of Bern, Bern, Switzerland; 3 Institute for Infectious Diseases, University of Bern, Bern, Switzerland

*Correspondence: christelle.robert@unibe.ch

As human nutrition increasingly shifts toward plant-based diets, exposure to plant specialized metabolites (PSMs) is rising, yet their dietary occurrence, metabolic fate, and effects on the gut microbiome remain poorly understood.



Representative example for BXs: DIMBOA-Glc

This study aimed to investigate dietary exposure, host metabolization, and microbial impact of benzoxazinoids (BXs), a class of PSMs found in cereals such as wheat, rye, and maize. Metabolomic analyses of 300 plant-based food and beverage products revealed that BXs are present in 14% of the analysed samples. In mice, the dietary BX DIMBOA-Glc was rapidly metabolized into HMBOA, HMBOA-Glc, and MBOA and excreted in urine within hours. Germ-free mice also converted DIMBOA-Glc in HMBOA-Glc and HMBOA, indicating host-mediated metabolism independently of the gut microbiota. Complementary microsomal assays using mouse and human preparations confirmed that BXs can be processed by mammalian hepatic enzymes. In parallel, selected gut microbial strains (of sDMDMm2 mice) were found to metabolize DIMBOA-Glc, DIMBOA, HMBOA, and MBOA in a strain-specific manner. Notably, the intake of BXs modulated the alpha diversity, but not the composition, of the mouse gut microbiome, and ongoing in-vitro growth assays revealed strain-specific direct effects of BXs. Overall, this study provides an integrated view of dietary BX exposure, host metabolism, and gut microbial interactions, contributing to a systems-level understanding of the fate of plant-derived metabolites in the host-microbiome axis.