Conclusions: Trans-ancestry PGS and DDS provide complementary information for BMI prediction across diverse populations. Our findings demonstrate that the systematic integration of modifiable environmental factors alongside genetic information significantly outperforms single-predictor approaches. These results highlight the importance of considering population-specific gene-diet interactions to improve metabolic risk stratification.

Funding Sources: National Institute of Health

Current Developments in Nutrition 10 (2026) 109221
https://doi.org/10.1016/j.cdnut.2026.109221

P41-16-26 Biomarkers of Dietary Blueberry Intake: Insights From an Untargeted Metabolomics Study of Human Urine Using Dual-Column UHPLC-MS

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Objectives: We aim to discover metabolites that demonstrate high sensitivity and specificity for blueberry consumption.

Methods: A randomized, controlled, cross-over feeding study was conducted in 20 healthy young adults. After a standardized run-in phase (2 days), participants consumed fresh blueberries. Fasting, postprandial and follow-up (day5 and 6) urine samples were collected. We employed a dual-column (Amide and T3) ultra-high performance liquid chromatography spectrometry (UHPLC-MS) untargeted metabolomics strategy coupled with a multi-stage statistical and plausibility selection pipeline to discover candidate urinary BFIs, involving the analysis of fruit and *in vitro* digested samples. The predictive capacity of the candidate biomarkers and panels was tested using XGBoost machine learning models, and specificity was evaluated against consumption data from other commonly consumed fruits.

Results: A total of 28 compounds were identified as candidate urinary BFIs of blueberry, including novel metabolites such as 4-hydroxy-3-prenylbenzaldehyde and kirenol. A three-compound multi-biomarker panel (4-hydroxy-3-prenylbenzaldehyde, kirenol, and *p*-coumaric acid glucoside) achieved superior predictive performance (accuracy 0.87, AUC 0.81), outperforming all single biomarkers (accuracy 0.22-0.76). This predictive panel showed low predictive accuracy for other fruits (AUC < 0.6), demonstrating good specificity.

Conclusions: This study established a highly specific and predictive multi-biomarker panel for recent blueberry intake in a controlled setting. These findings provide a critical foundation for developing specific blueberry BFIs to complement dietary assessment and further validation in larger population.

Funding Sources: The current study was supported by the National Natural Science Foundation of China.

Current Developments in Nutrition 10 (2026) 109222
https://doi.org/10.1016/j.cdnut.2026.109222

P41-17-26 Genetic Variability Determines Cardiometabolic Response to Orange Juice and Hesperidin Intake

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Objectives: Several clinical studies have suggested that intake of orange juice and/or hesperidin has a positive effect on health outcomes. However, large interindividual variability in response has been described, which could be attributed to different factors, including genetic polymorphisms described in one study. The aim of our study was to evaluate the effect of orange juice and hesperidin intake on cardiometabolic parameters and assess the association between genetic polymorphisms of key genes (identified as target genes of orange juice (OJ) and hesperidin (HESP) based on the integration of gene expression analyses and GWAS) and the response of these parameters (blood pressure, arterial stiffness, blood lipids, and markers of vascular function).

Methods: A randomized, 3-arm, crossover study, was conducted in 37 men, 40-65 y old, BMI $\leq$30 kg/m^2, waist circumference $>$94 cm, and otherwise healthy, who daily consumed A) orange juice (providing 200 mg hesperidin/day); B) sugary drink (placebo); C) sugary drink + 200 mg HESP, for 6 weeks. Cardiometabolic parameters were measured and genetic polymorphisms of 21 genes were assessed. SNP association analyses were performed using SNPStats in volunteers presenting higher than median polyphenol excretion level.

Results: No significant changes in cardiometabolic parameters were observed following OJ and HESP intake. However, significant associations were observed between target SNPs and individual responses. For example, a significant association between SNPs and ICAM1 level, total cholesterol, and systolic blood pressure after HESP intake was observed. rs10224002 in PRKAG2 gene was associated with ICAM1, SNP identified to impact vascular function. Similarly, significant associations were observed between SNPs and selectin, pulse pressure, and diastolic blood pressure after OJ intake. Subgroup analysis showed a significant effect on these parameters for both OJ and HESP depending on the genotype of these SNPs.

Conclusions: The positive health effects of OJ and HESP can be affected by genetic polymorphisms of target genes, providing novel data for future precision nutrition.

Funding Sources: European Association of Fruit Juice (AIJN)

Current Developments in Nutrition 10 (2026) 109223
https://doi.org/10.1016/j.cdnut.2026.109223