Applying an untargeted metabolomics approach using two complementary platforms for the discovery and validation of banana intake biomarkers

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Published: 15 November 2018 by **MDPI AG** in 3rd International Electronic Conference on Metabolomics session Precision Nutrition and Food Specific Profiles

MDPI AG, 10.3390/iecm-3-05849

Abstract:

Background: Accurate assessment of dietary intake is crucial for nutritional and health research. However, the dietary assessment tools currently used, such as dietary records or food frequency questionnaires, are subject to different factors that result in inaccurate information. The use of biomarkers of intake to determine dietary exposure offers more objective and potentially more precise information compared to the currently used dietary assessment tools. The identification of biomarkers of intake for highly consumed foods i.e. banana, may promote further research on their impact on human health. Banana is a widely consumed fruit in different countries. However, it has been widely neglected by the research community. Thus, identifying the biomarkers of intake of this fruit may promote further investigation on its impact on human health.

Objective: To discover and validate urinary intake biomarkers of banana by applying an untargeted metabolomics approach using two different platforms, UPLC-QTOF-MS and GC×GC-MS, to analyze urine samples from two different study designs.

Methods: In order to discover new biomarkers of banana intake, n=12 healthy subjects were recruited for a three arm, crossover, randomized, controlled meal study. The dietary interventions consisted of: 1) 240 g of banana, 2) 300 g of tomato and 3) 250 ml of control drink; each intervention phase was separated by a washout period of 3 days minimum. Urine samples obtained from the meal intervention study were analyzed by UPLC-QTOF-MS and GC×GC-MS. Following data-analysis, the identification of the relevant features was performed with MS/MS experiments in an Orbitrap-LTQ-XL MS instrument. To confirm the identity of the compounds in both systems, standards were acquired and conjugated when needed. In addition, banana samples were analyzed to look for compounds recovered in urine profiles. Finally, to validate the candidate biomarkers of banana, n=78 samples from an observational study, The Karlsruhe Metabolomics and Nutrition Study (KarMeN), were selected based on the volunteers' declared amount of banana consumption using 24 h dietary recalls. Samples were grouped based on recorded intakes (1)high consumers of banana, 2) low consumers of banana and 3) non consumers of banana) and analysed on both platforms.

Results: The discriminating compounds identified by both platforms in the meal intervention were cross-validated in the observational study. Among the highly discriminant compounds biogenic amine metabolites, methoxyphenols as well as tryptophan and carbohydrate metabolites were observed. The combination of two metabolites, *methoxyeugenol glucuronide and 6-hydroxy-1-methyl-1,2,3,4-tetrahydro-b-carboline-sulfate*, were validated as a parsimonious biomarker of banana intake with excellent ability to predict the intake of banana, exhibiting a ROC curve AUC (CV) of 0.92 ($p<0.001$). In addition, from the analysis by the GC×GC-MS system three metabolites (*5-hydroxyindole-acetic-acid, dopamine and the putatively identified deoxypentitol)* were detected in significantly higher concentrations ($p <0.001$, $p= 0.001$, $p=0.01$ respectively) in the urine samples of the high and low-consumers of banana compared to non-consumers.

Conclusion: This collaborative work led to the identification and validation of new candidate biomarkers for the intake of banana. This information may be useful to further investigate the effect of this fruit in human health.