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Metabolomics Provide New Insight on the Metabolism of Dietary Phytochemicals in Rats[1,2]

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Abstract

Foods of plant origin contain a large number of phytochemicals that may positively affect health. Phytochemicals are largely excreted in urine as metabolites that are formed in host tissues or by the microbiota and constitute a great proportion of the urinary metabolome. The latter can be characterized by a metabolomics approach. In this work, we compared the metabolism of lignins to that of the structurally related ferulic acid (FA) and sinapic acid (SA). Five groups of rats ($n = 5$) were fed for 2 d a purified diet alone [control (C)] or supplemented with lignin-enriched wheat bran (3% of the diet, wt:wt), poplar wood lignins (0.42%), FA (0.42%), or SA (0.42%). The metabolomes of urine samples collected after 1 and 2 d of supplementation were analyzed by high-resolution MS (liquid chromatography/quadrupole time-of-flight). Comparing metabolic fingerprints by gathering semiquantitative information on several hundreds of metabolites and using multivariate statistical analysis (partial least squares for discriminant analysis) showed the similarity between both lignin-supplemented and C groups and confirmed that lignins are largely inert and not absorbed in the body. One the other hand, metabolic fingerprints of the 2 phenolic acid-supplemented groups were clearly distinct from the C group. Differences between the groups were mainly from nonmetabolized FA and SA and metabolites excreted in urine. Thirteen of them were identified as sulfate esters and glucuronide and glycine conjugates of the same phenolic acids, and of dihydrosinapic, vanillic, and benzoic acids. This study shows that metabolomics allows the identification of new metabolites of phytochemicals and can be used to distinguish individuals fed different phytochemical-containing foods. J. Nutr. 138: 1282–1287, 2008.

Introduction

A large variety of phytochemicals are found in foods and beverages commonly consumed in the human diet. Some of these phytochemicals, such as polyphenols, carotenoids, glucosinolates, or sulfur compounds have raised considerable interest for their favorable effects on health and the prevention of various diseases. They may prevent cardiovascular diseases, cancers, diabetes, osteoporosis, and neurodegenerative diseases (1–3). However, these effects are still a matter of intense debate and few health claims on such phytochemicals have so far been approved by regulatory authorities. More evidence on the associations between phytochemical intake and positive health effects is needed as well as a better understanding on the mechanisms of action involved. Metabolic profiles can be characterized today in a more comprehensive way using high-throughput analytical tools such as NMR spectroscopy or MS. Recent developments in MS allow characterizing in a semi-quantitative way a large fraction of the plasma or urine metabolome (4). Subtle metabolic differences can be identified between individuals or for the same individual between different environmental conditions using metabolomics. In this approach, metabolic profiles or fingerprints are compared using proper multivariate statistical methods (5). Metabolomics opens new perspectives in the field of nutrition to explore the complex metabolic effects of diets or nutrients (6). A few metabolomics studies have shown that it allows the unraveling of new metabolic effects of phytochemicals as previously described for isoflavones or catechins (7–9).

A major fraction of the metabolome in human urine is made up of the products of food digestion. We propose to call this fraction "food metabolome," which is part of the xenometabolome derived from the incomplete catabolism of xenobiotics (drugs, environmental pollutants, or dietary components) (10).

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