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Editorial

Xenobiotic Metabolism

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Abstract

The combination of mass spectrometry, chemometrics, genetically engineered mice, and improved ultraperformance liquid chromatography offers an alluring array of instruments with which to study the metabolism of xenobiotics. Here, the metabolism of the suspected carcinogen areca alkaloids (arecoline, arecaidine, and arecoline 1-oxide), the hormone supplement melatonin, the food mutagen PhIP (2-amino-1-methyl-6-phenylimidazo [4,5b]pyridine), and the experimental cancer treatment aminoflavone are reexamined. The xenobiotics' metabolic maps in every instance were greatly expanded, offering fresh perspectives on their toxicity. The use of transgenic mice allowed for the clear attribution of particular metabolic pathways, frequently unique, to specific enzymes. Finally, a potential direction for xenobiotic metabolomics is presented, along with its effects on the metabolome.

Keywords: Drug metabolism, Metabolomics, Mass spectrometry, Chemo metrics

INTRODUCTION

The word "xenobiotic" refers to chemical compounds that are unnatural to animal life. Examples include plant components, medications, insecticides, cosmetics, flavourings, scents, food additives, industrial chemicals, and environmental contaminants. Humans are thought to come into contact with between 1-3 million xenobiotics throughout the course of their lifespan (Soldin et al., 2005). The majority of these chemicals, which enter the body through ingestion of food, air, water, medicine administration, and lifestyle decisions, go through a variety of detoxication processes that, in general, make them less poisonous, more polar, and easily excretable. Lower animals' detoxication responses may have an effect on human health as well. The degree of human exposure to environmental toxins, such as mycotoxins consumed by agricultural animals and hepatotoxic microcystins from algal blooms, may be determined by the degree of incomplete detoxication in creatures in the food chain (Chan et al., 2009). While the fundamentals of xenobiotic detoxication were established long ago, it was also understood that the metabolism of xenobiotics might alter the pharmacological effects of medications or even activate inert compounds into physiologically reactive species. The

first medications that were expressly created to undergo xenobiotic metabolism and activation in the human body to generate pharmacologically active species were the cancer chemotherapy agents stilboestrol diphosphate and cyclophosphamide. It is obvious that in order to acquire insight into the mechanistic components of toxicity profiles, it is crucial to comprehend both the qualitative and quantitative features of xenobiotic metabolism in both Man and lower animals (Carel et al., 2009).

The gut microbiome has a part in the bioavailability and metabolism of many medications, according to recent studies. Since the bulk of medications are taken orally and are mostly absorbed in our guts and intestines, the gut microbiota will inevitably play a role in regulating the bioavailability, effectiveness, and toxicity of medications. It is known that microbes in different environments have mechanisms they use to metabolise xenobiotic substances by altering and converting them to active/inactive/toxic metabolites. Studies have also shown that microorganisms can produce chemicals that could influence how much the host's drug-modifying enzymes, including cytochrome P450, are expressed (Elmlinger et al., 2005). Most xenobiotic alterations and/or metabolic processes rely on reduction, hydrolysis, mono- and di-oxygenation, cleavage, and coupling reactions as their primary mechanisms. According to recent studies, the gut microbiota's metabolic capacity and ability are comparable to those of the liver. Thus, the gut microbiome appears to have a significant impact on physiological processes, such as xenobiotic metabolism, in addition to its function in a variety of illnesses and disorders (Davis et al., 2006).

The advancement of analytical chemistry as a technological subject has been crucial to the study of xenobiotic metabolism over the years. Since its inception in the middle of the 1800s, xenobiotic metabolism has been studied mostly by the separation, purification, and basic chemical analysis of urine components. A significant increase in activity in the sector was sparked by the development of UV/visible and fluorescence spectroscopy, radiolabelled chemicals, and partition chromatography. However, the introduction of biomedical mass spectrometry-first with GC-MS, then with a variety of LC-MS and NMR technologies that are now commonplace—was the single most significant advancement that has benefited the research of xenobiotic metabolism. Drug metabolomics may now be used to study how drugs are metabolised. In its brief history, metabolomics has often been viewed as a technique for cataloguing metabolic pathways in health and illness or for identifying cellular responses to external stimuli such the injection of toxicants. Metabolomics may be used to examine xenobiotic metabolites, the cellular metabolic traces left on xenobiotic compounds, in addition to studying endogenous molecular changes in response to stimuli (Owen et al., 2010).

CONCLUSIONS

There is no question that xenobiotic metabolism directly contributes to the metabolome, both in terms of quantity (e.g., PhIP exposure results in 19 detectable urinary metabolites) and relative abundance (e.g., xenobiotics are some of the most highly concentrated metabolites), as has been expertly addressed. The success of the metabolomic methods included in this study can be attributed to these factors. While this review has mainly focused on xenobiotic metabolism, endogenous metabolism can also be influenced by xenobiotic metabolism. By removing drugs and drugs' metabolites from the dataset and running a new chemometric analysis, it is possible to gain more information about changes in host metabolism. This method has recently been shown to help understand how fenofibrate affects people.

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