

Preface



Drug metabolism and pharmacokinetic studies have evolved to play major roles in drug discovery and development, and are substantial components of regulatory marketing submission. With the dramatic increase in the number of new chemical entities (NCEs) arising from combinatorial chemistry and high-throughput biological screening, there is an urgent need for the determination of the absorption, distribution, metabolism and elimination characteristics of NCEs to facilitate the selection of "ideal" drug candidates for further development. To meet this demand, drug metabolism scientists have developed novel approaches, including cassette dosing, "humanized" in vitro based cell systems, automation and higher-throughput screens and assays, ultrasensitive analytical technologies, and computational models for accelerating drug metabolism examination of NCEs. Current Drug Metabolism aims to cover all these latest and outstanding developments in drug metabolism and disposition.

The present issue of Current Drug Metabolism consists of five invited review articles prepared by some of the experts in their fields.

The first review presents the roles of electrophilic sulfate ester metabolites in the metabolic activation of xenobiotics. Although sulfate conjugation is generally considered as a detoxification pathway producing water-soluble metabolites, sulfation of certain class of compounds such as hydroxymethyl polycyclic hydrocarbons, allylic alcohols, N-hydroxy-arylamines and heterocyclic amines produce reactive metabolites that can covalently bind to cellular macromolecules, DNA and RNA. The second review describes the usefulness of prodrugs entrapped liposomes for drug metabolism studies.

The third review describes the kinetic and molecular characterization of long-chain fatty acid Coenzyme A ligase, implicated in the metabolism of xenobiotic carboxylic acids. With increasing recognition of the importance of fatty acyl-CoA esters as physiological regulators of cell function, the review also discusses the metabolic fate and toxicity of xenobiotic acyl-CoA esters.

Cytochrome P-450 (CYP), a family of heme-containing proteins, is the most important enzyme system that plays a dominant role in the elimination of drugs from the body by their oxidation to hydrophilic metabolites. The fourth review describes the significance of understanding the chemical mechanisms by which methylenedioxy compounds interact with CYPs. The last review describes the turnover studies on cardiac natriuretic peptides.

I would like to thank all the authors for taking the time and trouble to write informative and authoritative reviews. I believe that these reviews offer the reader up-to-the-minute information on some of the latest findings affecting metabolism, pharmacokinetics and toxicology related to drug discovery and development as we enter into the new century .

Finally, as the Editor-in-Chief of Current Drug Metabolism, I would like to look ahead and invite contributions for future issues.

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