

EDITORIAL

The development of new and novel techniques and technologies such as combinatorial chemistry, high throughput screening, molecular and cell biology, medical imaging and decoding or sequencing of the human genomes in pharmaceutical research has given discovery scientists the ability to deliver large numbers of new chemical entities (NCE). However, the success rate of NCEs entering the market place is unacceptably low with estimate of 1 in 5000 compounds. The major reasons for failure of NCEs are poor clinical efficacy, serious undesired side effects, adverse drug reactions and unfavorable drug metabolism and pharmacokinetics (DMPK). Therefore, it has been recognized that in addition of good pharmacological activity (potency and selectivity), safety and pharmacokinetics are crucial determinants of the ultimate clinical success of a drug candidate. The early refinement of these properties has been regarded as essential features of the drug candidate selection process and it has compelled the pharmaceutical industry to integrate more greatly DMPK functions into the early stages of drug discovery. Such DMPK integration should allow the selection of a drug candidate that has good oral absorption and bioavailability, optimum half-life, favorable clearance, and acceptable metabolic and toxicological profiles in patients.

To predict the PK, metabolic profiles and safety of NCEs in humans, drug metabolism scientists have developed novel techniques such as *in vitro* assays using animals and human liver microsomes, hepatocytes or recombinant enzymes, Cell-based such as the Caco-2 screen and parallel artificial membrane permeability assays, transporter assays, *in vivo* studies using a range of experimental animal models and *in silico* models. Recently, the use of microdose strategy to assess the full pharmacokinetics profiles of drug candidates in animals and humans has been reported.

Metabolic drug interactions have received considerable attention in pharmaceutical industries because in recent years several prominent drugs have been withdrawn from the market in the US and Europe due to serious events as a result of significant drug-drug interactions. These drug interactions often result by alteration of the pharmacokinetics of one drug by another co-administered drug. A variety of approaches, *in vitro*, *in silico*, and preclinical species are being used to predict these interactions at early stage of drug discovery.

Drug Metabolism Letters (DML) aims to cover all these latest and outstanding scientific advances in all areas of drug metabolism and disposition such as *in vitro* systems including CYP-450; enzyme induction and inhibition; drug-drug interactions and enzyme kinetics; pharmacokinetics, toxicokinetics, species scaling and extrapolations; P-glycoprotein and transport carriers; target organ toxicity and interindividual variability; drug metabolism and disposition studies; extrahepatic metabolism; phase I and phase II metabolism; identification of drug metabolites, reactive intermediate and glutathione conjugates.

I would like to thank all the authors for taking the time to write informative and interesting articles for this first issue of **Drug Metabolism Letters**.

As the Editor-in-Chief, I wish **Drug Metabolism Letters** to become a forum for in-depth discussion of those areas, which we all feel are crucial for the expansion of the field. The journal will be an essential reading to both researchers and clinicians who wish to keep abreast of the latest developments in the field.

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