Editorial

In Vitro Approaches to Evaluate Absorption, Metabolism, Drug- Drug Interactions and Toxicity (AMD-dT) During Drug Discovery and Development

To understanding a disease and bringing a safe and effective new treatment to patients, this whole process takes an average of 10-15 years. There is no doubt that AMD-dT drug properties, are properties crucial to the final clinical success of a drug candidate. 50% of drugs fail because of unacceptable efficacy in the initial stages of drug development. About 40% of drug candidates have failed because of safety issues. In addition to the relatively large number of drug candidates that fail during clinical trials and after getting launched in market. FDA withdraws the following drugs from the market due to toxicity Soruvidine, mibefradil (posicor), Terfenadine troglitazone, Raptiva, Zelnorm and Pergolide (novratis product). Reduction in the time gap is the need of the hour and the time gap can be reduced by High Throughput Screening (HTS) of the drugs by the use of scientific concept and practice of human based, *in vitro* AMD-dT screening approaches.

Absorption studies are made by using in vitro models such as Caco-2, HT-29 cells, MDCK cells, IAM Chromatography, PAMP assay. Screening for metabolic stability involves the following two major human-based *in vitro* experimental systems: Human liver microsomes and Human hepatocytes. It is now well known that a drug can affect the metabolic stability of another drug, a concept known as Pharmacokinetic drug–drug interactions. Drug drug interactions may be due to potent inhibition of Drug metabolizing enzymes or Induction of Drug metabolizing enzymes. Models used for screening the Drug drug interactions CYP3A4, CYP2A6 and CYP2C9 (Cytochrome P450 enzymes) substrates.

Drug toxicity is a major problem in drug development. A large number of drugs, in spite of extensively preclinical animal safety studies and clinical human trials, have been found to cause severe human toxicity, leading to market withdrawal or severe use limitations. The following cell systems may be used for specific human organ toxicity studies: Primary human hepatocytes for hepatotoxicity, Primary human cardiomyotcytes for cardiotoxicity, Primary human kidney tubule cells for nephrotoxicity by using the toxicity assays viz: ATP measurement, Enzyme release, Neutral red uptake, Macromolecular synthesis, Glutathione measurement.The use of the above approaches in HTS will inevitably save time and costs in drug discovery and development by enhancing the probability of the success of drug candidates in clinical trials.
.

Mrs.F.S.Dasankoppa
Associate Editor, IJNDD

*Department of Pharmaceutics,
K.L.E.University's College of Pharmacy, Hubli,
INDIA*