Adverse pharmacokinetic and bioavailability results have long been the most significant cause of attrition in drug development, with a number of candidate compounds dropped from development due to pharmacokinetic difficulties in clinical studies. Pharmaceutical companies have therefore attempted to predict human pharmacokinetic profiles of candidate compounds through semi-quantitative screening approaches, selecting only those compounds with appropriate pharmacokinetic profiles for subsequent focus. Consequently, these factors of attrition have been dramatically reduced in drug development. With improvement in pharmacokinetic profiles achieved, poor efficacy and safety now represent the major causes of attrition in clinical studies. The situation has remained thus far, and the purpose of predicting human pharmacokinetics has changed from screening by semi-quantitative prediction to quantitative prediction. In addition, the target of pharmacokinetics has changed from screening by semi-quantitative methods for prediction of pharmacokinetic processes. This extrapolation has been conducted mainly for low-molecular-weight compounds. Pharmaceutical companies have begun to focus on new fields such as cell-based medicine, therapeutic biologics including monoclonal antibodies and nucleic acid medicine. However, the contribution of drug metabolism and pharmacokinetic scientists is limited in these new fields compared to that for low-molecular-weight drugs. In the future, drug metabolism and pharmacokinetics researchers should expand their fields of study to increase their knowledge and gain access to new evaluation technologies, familiarizing themselves with new prediction methods and mechanisms of drug metabolism and pharmacokinetics not encountered in studies of low-molecular-weight compounds.

In this editorial, the future perspectives of predicting human pharmacokinetics are discussed. Resolving these multi-faceted issues will contribute to more effective drug discovery and development.

To solve these issues of pharmacokinetic prediction, the introduction of the following tools should be considered:

- More reliable in silico approaches and PBPK models, and the introduction of systems biology for more accurate prediction
- Genetically modified or transgenic mouse models developed for drug metabolizing enzymes and transporters, and chimeric mice with humanized livers
- Bio-imaging technologies (e.g. PET and imaging mass spectrometry) for predicting distribution
- IPS cell-derived human hepatocytes for predicting pharmacokinetics related to personalized medicine
- In vitro experimental systems which accurately reflect in vivo situations (e.g. optimization of hepatocyte cultivation systems and bioreactor systems)

Research into the prediction of human pharmacokinetics has been conducted mainly for low-molecular-weight compounds. Pharmaceutical companies have begun to focus on new fields such as cell-based medicine, therapeutic biologics including monoclonal antibodies and nucleic acid medicine. However, the contribution of drug metabolism and pharmacokinetic scientists is limited in these new fields compared to that for low-molecular-weight drugs. In the future, drug metabolism and pharmacokinetics researchers should expand their fields of study to increase their knowledge and gain access to new evaluation technologies, familiarizing themselves with new prediction methods and mechanisms of drug metabolism and pharmacokinetics not encountered in studies of low-molecular-weight compounds.

In this editorial, the future perspectives of predicting human pharmacokinetics are discussed. Resolving these multi-faceted issues will contribute to more effective drug discovery and development.

**References**


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