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Pharmacokinetics/ADME of Small Molecules

Vangala V. Subrahmanyam and Alfred P. Tonelli

Preclinical Drug Evaluation, Johnson & Johnson Pharmaceutical Research and Development, Raritan, New Jersey, U.S.A.

1. INTRODUCTION

A major objective of the drug development process is to establish that the investigational new drug candidate is both efficacious and safe for human use. Besides pharmacological properties, the efficacy and toxicity of a drug depends upon its pharmacokinetic (PK) properties. Pharmacokinetics can be simply defined as the science that describes the time course of drug disposition including its absorption, distribution, metabolism, and excretion (ADME) properties, following administration of drug.

Pharmacokinetics can be considered a biomarker of drug exposure as well as a marker of efficacy and safety of drugs. It has been estimated that about 40% of drugs fail during development due to inappropriate pharmacokinetics (PK) in humans (1–3). This is very critical because a drug with poor PK properties can be terminated early in development before significant futile investments are made. Therefore, extensive efforts have been devoted to predict human pharmacokinetics earlier during preclinical drug discovery and development, to reduce the occurrence of failures after the drugs are introduced into humans. Efforts have focused on in vitro and in vivo allometric scaling (Chapter 2) as well as specific comparisons of the individual physiological systems (4,5). Although some progress has been