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Molecular Pharmacokinetics: Mechanisms of Drug Absorption, Distribution, Metabolism, and Excretion

Ruthann Siam*

Pharmacokinetic, Nanotechnology and Gene Therapy Group, Faculty of Pharmacy, University of the Basque Country UPV/EHU, Spain

Abstract

Molecular pharmacokinetics is a branch of pharmacology that investigates the fate of drugs within the human body. Understanding how drugs are absorbed, distributed, metabolized, and excreted (ADME) is essential for predicting drug behavior and efficacy. This field integrates molecular biology, biochemistry, and physiology to study the processes that govern drug interactions at the cellular and molecular levels. By examining the mechanistic pathways of drug transport, enzymatic conversion, and elimination, molecular pharmacokinetics provides insights into drug efficacy, toxicity, and potential drug-drug interactions. Advanced techniques in molecular imaging, genetic profiling, and computational modeling are increasingly being applied to enhance drug development, optimize therapeutic strategies, and personalize medicine. This review highlights the key mechanisms involved in drug ADME processes and explores their implications for drug design, clinical applications, and future pharmacological research.

Keywords: Molecular pharmacokinetics; Drug absorption; Drug distribution; Drug metabolism; ADME processes; Drug transporters; Enzyme kinetics; Personalized medicine

Introduction

Pharmacokinetics is the study of the time course of a drug's absorption, distribution, metabolism, and excretion (ADME) within the body. While traditional pharmacokinetics focuses on the physiological parameters governing drug movement, molecular pharmacokinetics delves deeper into the molecular mechanisms that regulate these processes. The understanding of how drugs interact with molecular targets, transport systems, and metabolic enzymes is crucial for optimizing therapeutic outcomes and minimizing adverse effects [1]. Drug absorption begins at the site of administration, where drugs pass through biological membranes, typically aided by transporters or passive diffusion. Once absorbed, drugs are distributed through the bloodstream, where their bioavailability can be influenced by protein binding, tissue permeability, and organ-specific transporters [2]. Metabolism primarily occurs in the liver, where phase I and II enzymes transform drugs into more water-soluble metabolites for easier excretion. Excretion occurs primarily through the kidneys, although alternative pathways such as bile or the lungs are also involved [3]. Recent advances in molecular biology and biotechnology have enabled the identification of genetic variations that affect drug metabolism, transport, and response. This has paved the way for personalized medicine, where drug therapy is tailored to an individual's genetic makeup to enhance efficacy and reduce side effects. Additionally, drug-drug interactions, which can significantly alter pharmacokinetic profiles, are a growing concern in clinical practice and drug development [4]. By understanding the intricate molecular details of ADME processes, researchers and clinicians can better predict drug behavior, design safer drugs, and improve therapeutic outcomes for patients. This review aims to explore the molecular mechanisms that govern each phase of pharmacokinetics and examine how they influence drug efficacy, toxicity, and individual variability in drug response.

Discussion

Molecular pharmacokinetics offers a deeper understanding of how drugs interact with the body at a cellular and molecular level, significantly influencing their absorption, distribution, metabolism, and excretion (ADME). Each phase of pharmacokinetics is influenced by a variety of factors, including the chemical properties of the drug, its interaction with biological membranes, and genetic factors affecting drug transporters and metabolizing enzymes [5]. The ability to study these mechanisms at a molecular level has profound implications for drug development, personalized medicine, and clinical pharmacology. Absorption is a crucial first step in determining a drug's bioavailability. The mechanisms of drug transport across biological membranes are mediated by a combination of passive diffusion, active transport, and endocytosis [6]. Key factors such as the physicochemical properties of the drug (e.g., lipophilicity, molecular size) and the presence of specific drug transporters significantly influence the rate and extent of absorption. In addition, the gastrointestinal environment, including pH levels and enzyme activity, can also impact drug uptake. Distribution involves the movement of the drug from the bloodstream to target tissues [7]. The role of plasma protein binding, tissue permeability, and organ-specific transporters is central to determining the concentration of the drug at its site of action. Genetic variations in drug transporters (e.g., P-glycoprotein, organic anion transporters) can lead to interindividual variability in drug distribution, potentially affecting both efficacy and toxicity. Metabolism, primarily occurring in the liver, is another critical step in determining a drug's pharmacokinetic profile [8]. Phase I (oxidation, reduction, and hydrolysis) and Phase II (conjugation) reactions are carried out by cytochrome P450 enzymes and other metabolic systems. Genetic polymorphisms in these enzymes can lead to variations in drug metabolism rates, influencing drug efficacy and safety. Poor metabolizers may experience drug toxicity due to prolonged drug exposure, while ultra-rapid metabolizers may face

***Corresponding author:** Ruthann Siam, Pharmacokinetic, Nanotechnology and Gene Therapy Group, Faculty of Pharmacy, University of the Basque Country UPV/EHU, Spain, E-mail: siamthann@gmail.com

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suboptimal therapeutic effects due to the rapid clearance of the drug.

Excretion**,** primarily via the kidneys, is the final step in the pharmacokinetic process. Renal elimination depends on glomerular filtration, tubular secretion, and reabsorption. Variability in renal function due to age, disease, or genetic factors can impact drug clearance, making dose adjustments essential in certain patient populations. Furthermore, drug-drug interactions can significantly alter pharmacokinetics [9]. These interactions may affect absorption, distribution, metabolism, or excretion, leading to altered drug efficacy or increased toxicity. Understanding the molecular mechanisms of these interactions is essential for optimizing drug therapy and preventing adverse effects. As our understanding of molecular pharmacokinetics advances, the role of personalized medicine becomes more evident [10]. Genomic data are increasingly used to predict how individuals will respond to drugs, enabling the tailoring of treatments based on an individual's genetic makeup, metabolic capacity, and drug transporter profiles. This shift toward personalized approaches can improve treatment outcomes, minimize adverse effects, and enhance the safety of drug therapies.

Conclusion

Molecular pharmacokinetics provides a sophisticated and integrated approach to understanding the fate of drugs in the body. By exploring the molecular mechanisms underlying absorption, distribution, metabolism, and excretion, we gain valuable insights into how drugs interact with biological systems. The advancements in genomics and molecular technologies are propelling the field toward more personalized, efficient, and safe drug therapies. The study of molecular pharmacokinetics is not only critical for improving drug development but also for optimizing clinical practices. As new pharmacogenomic tools and techniques emerge, they hold the potential to revolutionize the way drugs are prescribed, ensuring that each patient receives the most effective and safest therapy based on their unique biological profile. Future research in molecular pharmacokinetics will continue to focus on understanding complex drug interactions, genetic variability, and the development of novel therapeutic strategies to meet the evolving challenges of modern medicine.

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Conflict of Interest

None

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