

Review Article

Pharmacokinetics Advances: Understanding Drug Absorption, Distribution, Metabolism, Excretion

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A B S T R A C T

Pharmacokinetics, the study of how medications are metabolized by the body, is a core area of study in the subject of pharmacology and is essential for maximizing drug efficacy and safety. This review article explores contemporary pharmacokinetics developments with a particular emphasis on drug absorption, distribution, metabolism, excretion (ADME). We examine cutting-edge methods, tactics, discoveries that have fundamentally altered our comprehension of how medications interact with the body, enabling more intelligent drug development and individualized treatment plans.

Recent developments in drug delivery technologies, like as nanoparticles, liposomes, micelles, have significantly improved medication absorption profiles and created new opportunities for targeted therapy. Additionally, tailored drug delivery techniques and oral bioavailability optimization have been made possible by predictive models and simulations that use computational tools, offering more effective and patient-friendly treatments.

Researchers have developed customized dosing regimens by using cutting-edge imaging techniques, such as positron emission tomography (PET) and magnetic resonance imaging (MRI), to get previously unattainable insights into medication distribution inside tissues. The complex functions of cytochrome P450 enzymes and their genetic diversity in drug metabolism have also been discovered, enabling the development of tailored medicines based on unique genetic profiles, thereby reducing the possibility of side effects.

Our understanding of drug removal mechanisms has improved as a result of developments in renal and hepatic clearance investigations. To enable more precise predictions of drug-drug interactions, novel biomarkers and non-invasive approaches collect useful information on how drugs interact with transporters and clearance systems.

Keywords: Pharmacokinetics, Drug Distribution, Biotransformation, Personalized Medicine, Systems Pharmacology

Introduction

Modern pharmacology is built on the dynamic study of pharmacokinetics, or how medications interact with the body. Pharmacokinetics helps to create safer and more effective treatments and offers essential insights into personalized medicine by unraveling the complex mechanisms governing drug absorption, distribution, metabolism, excretion (ADME). This review article explores the most recent developments in pharmacokinetics, which have sparked a paradigm change in clinical practice and drug research, illuminating the path taken by medications through the body and revealing their ultimate therapeutic effects.

The goal of improving drug bioavailability has propelled significant advancements in drug delivery technologies over the years. By altering physicochemical features and focusing on particular locations of action, nanotechnology-driven inventions such as liposomes, micelles, nanoparticles have completely changed how drugs are absorbed. By improving drug absorption and reducing side effects, these developments have the potential to completely transform how many different diseases are treated.

The landscape of pharmacokinetics has been significantly broadened by the development of computational modeling and simulations. Researchers can improve medication regimens, forecast pharmacokinetic characteristics, foresee potential interactions by modelling drug behavior in a variety of physiological settings. This speeds up the drug development process and reduces the likelihood of clinical trial failures.¹

Precision pharmacokinetics has entered a new age thanks to improvements in imaging techniques. Real-time observation of medication distribution within the body is made possible by methods like positron emission tomography (PET) and magnetic resonance imaging (MRI), which enables scientists to identify tissue-specific accumulation patterns and improve dosage regimens. The ability to adapt treatments for particular individuals and lower toxicity are made possible by this greater understanding of medication localization.

The involvement of cytochrome P450 enzymes and associated genetic variants emerges as a crucial component regulating medication response variability as our understanding of drug metabolism advances. Pharmacogenomics research has paved the path for personalized medicine, which can tailor a patient's care based on their genetic composition, reducing the risk of side effects and enhancing therapeutic results.

This review makes its way through the complexities of pharmacokinetics, including both traditional ideas and recent innovations. By combining these developments,

pharmacokinetics not only enlightens the scientific field but also directs the course of pharmaceutical innovation. Pharmacokinetics has a significant influence on how medicine will be practiced in the future, which is highlighted by our understanding of how medications interact with the body at the molecular level.²

Advances in Drug Absorption

Drug absorption is a critical step in the pharmacokinetic process that affects the bioavailability and efficiency of pharmaceuticals. Significant progress has been achieved in recent years in the knowledge and control of drug absorption, the advancement of drug delivery systems, the optimization of therapeutic results. This section explores the most recent developments in drug absorption, illuminating novel formulations, technological breakthroughs, personalized strategies that have drastically altered the field of pharmacokinetics.³

Formulation Innovations

Drug solubility and permeability issues have long been a source of innovation in formulation development. The capacity to improve solubility, dissolving rates, eventually bioavailability has made solid dispersion methods, cyclodextrin inclusion complexes, lipid-based formulations popular. These formulations address persistent problems and increase the likelihood that delivered medications will reach their intended targets.

Nanotechnology and Targeted Delivery:

Drug absorption has been transformed by nanotechnology, which allows for precise distribution and regulated release. Liposomes, polymeric micelles, nanocrystals are examples of nanoparticles that offer a variety of advantages, including improved drug stability, longer circulation durations, tailored accumulation at certain locations of action. This strategy redefines the therapeutic environment by optimizing drug absorption while minimizing systemic negative effects.⁴

Advanced In Vitro Models

In vitro models more closely resemble physiological settings, making it easier to estimate medication absorption patterns. Researchers can examine drug permeability, metabolism, interactions in a controlled setting using intestinal organoids and microphysiological systems that mimic complex tissue structures. These models expedite the screening and development of prospective drug candidates by bridging the gap between conventional cell culture and animal investigations.⁵

Prodrug Strategies and Pro-Nanodrugs

Prodrugs have become popular for improving drug absorption since they are made to be converted enzymatically to the active form after administration.

Similar to prodrugs, pro-nanodrugs improve solubility, stability, targeted distribution by fusing prodrug benefits with nanotechnology. These methods increase medication assimilation and systemic accessibility, showing promise for difficult molecules with low bioavailability.⁷

Personalized Approaches and Gut Microbiota

Pharmacogenomics has drawn attention to the role that individual differences play in drug absorption. Medication transporters and metabolizing enzymes have genetic variations that affect medication absorption rates and therapeutic outcomes. Additionally, new study demonstrates how the gut flora affects drug metabolism and absorption, opening up new possibilities for tailored therapeutic approaches.

Unveiling Drug Distribution Mechanisms

Drug access to target tissues and organs is determined by the distribution of the drug inside the body, which has an impact on both treatment effectiveness and potential side effects. Recent developments in imaging techniques, transporter research, tissue-specific targeting have given us previously unheard-of insights into drug delivery systems. This section explains how these discoveries have transformed our knowledge of medication distribution and made it possible for more targeted and efficient treatment approaches.⁸

Imaging Techniques for Real-Time Visualization:

Our capacity to observe drug distribution in real time has changed as a result of the development of improved imaging techniques like positron emission tomography (PET), single-photon emission computed tomography (SPECT), magnetic resonance imaging (MRI). These tools help scientists better understand pharmacokinetics and facilitate the creation of targeted drug delivery systems by enabling them to track drug accumulation, penetration, clearance in various tissues.

Transporter Studies and Efflux Mechanisms

Drug distribution across numerous biological barriers, including the blood-brain barrier and the placental barrier, is greatly influenced by drug transporters. The individual transporters responsible for drug influx and efflux, which affects drug access to particular organs, have been identified by recent study. Modifying these transporters can improve drug delivery to target areas, providing novel treatment options for disorders for which there are few available medications.⁹

Nanotechnology and Tissue-Specific Targeting

A potent technique to improve tissue-specific medication distribution has emerged: nanoparticles designed with precise targeting ligands. These ligands are able to identify

and bind to receptors or markers on the surface of target cells, ensuring that medications are only accumulated in diseased tissues while exposing healthy tissues to the least amount of medication possible. This strategy decreases systemic toxicity while also improving treatment efficacy.¹⁰

Physiological Variability and Personalized Distribution

Drug distribution is greatly influenced by individual diversity in physiological parameters such as blood flow, tissue composition, disease condition. In order to ensure that therapeutic levels are reached in the target tissues, personalized pharmacokinetics takes these variances into account when optimizing dosage schedules for specific individuals. This specialized strategy enhances therapeutic results while reducing side effects.¹¹

Emerging Therapeutic Areas

New opportunities in fields like oncology and neurology have been made possible by improvements in drug distribution research. Innovative medicines have been created by better understanding how pharmaceuticals spread within tumor microenvironments or penetrate the blood-brain barrier. For previously difficult disorders, techniques like blood-brain barrier disruption and localized drug administration show promise.¹²

Metabolism Insights and Cytochrome P450 Enzymes

A medicine's pharmacokinetic profile and therapeutic efficacy are greatly influenced by the complex process of drug metabolism, which is principally controlled by a family of enzymes known as cytochrome P450 (CYP). The discipline of pharmacology has undergone a revolution as a result of recent advances in knowledge on the genetic diversity of CYP enzymes, their interactions, their effects on drug metabolism. This section explores the most recent findings and developments in metabolic research, emphasizing how these advancements inform the creation of individualized therapeutic solutions.

Cytochrome P450 Enzymes: An Overview

A wide range of enzymes that catalyze the oxidation, reduction, hydrolysis of medications and endogenous chemicals make up the CYP superfamily. The CYP3A4, CYP2D6, CYP2C9 enzymes, which are involved in the metabolism of a wide variety of drugs, are particularly significant. Enzymology, structural biology, computer modeling innovations have recently shed light on the intricate substrate selectivity and catalytic processes of CYP enzymes.

Genetic Variability and Pharmacogenomics

Inter-individual variation in drug metabolism rates is caused by genetic variations within the CYP genes.

Pharmacogenomic research has pinpointed particular genetic markers linked to altered enzyme activity, which affects medication reactions and toxicity. Personalized medicine strategies use this genetic data to modify treatment regimens for specific individuals, reducing unwanted effects and improving therapeutic results.

Drug-Drug Interactions and CYP Enzymes

The potential for one medicine to activate or inhibit CYP enzymes, changing the metabolism of co-administered drugs, is the cause of many drug interactions. Improved prescribing techniques and drug safety profiles have resulted from recent breakthroughs in anticipating and understanding these interactions. Assessment of possible interactions during medication development and clinical practice is aided by in vitro testing and in silico modelling.¹³

Beyond CYP Enzymes: Phase II Metabolism and Conjugation

Phase I metabolism depends heavily on CYP enzymes, but Phase II metabolism incorporates conjugation processes that further alter drug molecules. The functions of enzymes like UDP-glucuronosyltransferases (UGTs), sulfotransferases (SULTs), glutathione S-transferases (GSTs) have recently come to light, allowing us to better understand the biotransformation of drugs and identify prospective targets for individualized therapies.

Emerging Technologies in Metabolism Studies

Comprehensive profiling of drug metabolites is now possible thanks to improvements in analytical techniques like liquid chromatography-mass spectrometry (LC-MS) and high-resolution metabolomics. The discovery of metabolic pathways, intermediates, potential toxicity is made easier with the help of these techniques, which offer thorough insights into the metabolic fate of medications.

Exploration of Excretion Pathways

For determining drug clearance from the body, limiting buildup, guaranteeing therapeutic efficacy while reducing potential toxicities, it is essential to understand the drug elimination pathways. Recent developments in the study of drug excretion pathways have illuminated the complex methods by which medications are removed, offering insightful knowledge that may be used to optimize prescription regimens and prevent hazardous interactions. This section examines the most recent advances in the study of excretion pathways, demonstrating how these discoveries are changing pharmacokinetics and patient treatment.¹⁴

Renal Excretion: Filtration and Secretion

The kidneys play a pivotal role in eliminating water-soluble drugs through renal excretion. Advances in understanding

renal transporters, such as organic anion transporters (OATs) and organic cation transporters (OCTs), have unraveled the complex interplay between drug secretion and reabsorption. This knowledge aids in predicting and preventing drug-drug interactions that impact renal clearance and overall drug disposition.

Hepatic Excretion and Biliary Clearance

Drugs are transported from the blood into the bile during hepatic excretion, then they are finally eliminated through the feces. The importance of hepatic transporters, particularly the bile salt export pump (BSEP) and multidrug resistance-associated proteins (MRPs), in drug clearance has come to light in recent studies. Impaired drug elimination and cholestatic liver damage are also possible consequences of these transporters' dysregulation.¹⁵

Enterohepatic Circulation: Recycling and Delayed Elimination

Drugs can be discharged into the bile, enter the intestines, then be reabsorbed back into the bloodstream through a phenomenon known as the enterohepatic circulation. Understanding this process better has crucial ramifications for dosage intervals since it can lengthen the time a drug is present in the body, which can impair its therapeutic benefits and perhaps cause toxicity.

Gastrointestinal Elimination and Microbiota Interactions

Additionally, the gastrointestinal system plays a role in drug disposal, especially when it comes to substances with low absorption rates. Recent studies have revealed how the gut microbiota plays a part in drug metabolism. Microbial enzymes can change drug molecules, impacting how well they are absorbed and then eliminated. This complex relationship between medications and the gut bacteria opens up new possibilities for customized treatments.¹⁶

Emerging Biomarkers and Predictive Tools

The study of biomarkers linked to excretion routes is becoming more popular. Renal elimination capacity can be evaluated using biomarkers like creatinine clearance and renal function indicators. Furthermore, improvements in non-invasive approaches, such urinary metabolomics and imaging, provide insights into the kinetics of drug clearance and potential toxicity.

Integration of Systems Pharmacology

Understanding how medications interact with the body to have therapeutic effects requires a thorough understanding of both pharmacokinetics (PK) and pharmacodynamics (PD). Systems pharmacology is an interdisciplinary approach that combines disease biology with PK and PD data to provide a comprehensive understanding of how drugs work. Systems

pharmacology is now at the forefront of drug discovery and development thanks to recent developments in computer modeling, high-throughput screening, network analysis. The potential of systems pharmacology to transform customized medicine is examined in this section.¹⁷

Computational Modeling for Drug Response Prediction

The prediction of drug reactions in various physiological and pathological circumstances is made easier by computational models that incorporate PK and PD factors. Physiologically-based pharmacokinetic (PBPK) models simulate drug behavior by taking into account the unique patient features and medication properties. This helps with dosage optimization and the identification of potential drug interactions.

High-Throughput Screening and Omics Data Integration

Multiple thousands of drug candidates can be tested simultaneously in intricate biological systems because to improvements in high-throughput screening. Integration of omics data, including as genomic, transcriptomic, proteomic, metabolomic information, reveals the molecular pathways that medications affect and sheds light on how those drugs work.

Network Analysis and Pathway Mapping

The complicated interactions between medications, proteins, biological pathways can be seen using network-based techniques. Researchers can find prospective drug targets, off-target effects, pathways important to drug response and toxicity by creating drug-target interaction networks and pathway maps.

Pharmacokinetic-Pharmacodynamic Modeling

It is easier to grasp how drug exposure and therapeutic effects relate when PK and PD data are combined in mathematical models. This makes it possible to determine the best dose schedules, reduces under- or overdosing, provides information for clinical practice and drug development decisions.

Systems Pharmacology in Disease Modeling

Beyond drug discovery, disease modeling is included in systems pharmacology. It is possible to simulate illness progression, examine medication effects, explore prospective therapeutic treatments in silico by combining PK and PD data with disease-specific genetic information.¹⁸

Personalized Medicine and Therapeutic Design

Systems pharmacology is essential for customizing therapies for each patient. Computational models can forecast drug reactions and direct treatment decisions by taking into account patient-specific aspects including genetics, age,

comorbidities. This improves therapeutic outcomes and minimizes side effects.

Challenges and Future Directions

Pharmacokinetics (PK), the study of how medications are metabolized by the body, is the cornerstone of sane drug formulation, dosing protocols, therapeutic efficacy evaluation. New difficulties and opportunities arise as pharmacokinetics develops, shaping the course of drug development and patient treatment. This article examines the difficulties that pharmacokinetics research is now experiencing and speculates on possible future directions that could improve drug discovery, development, individualized treatment plans.

Complexity of Drug-Drug Interactions

Predicting and controlling drug-drug interactions is difficult due to the rising prevalence of polypharmacy and the possibility of unanticipated drug interactions. To better forecast and manage negative interactions, future trends in pharmacokinetics should include cutting-edge computer models, predictive algorithms, extensive drug interaction databases.

Pharmacogenomics and Personalization

Although pharmacogenomics holds the promise of personalized treatments based on unique genetic profiles, pharmacogenomics-guided dosing is still difficult to put into practice. Realizing the full potential of personalized pharmacokinetics requires getting beyond obstacles relating to regulatory issues, testing standards, physician education.

Physiologically-Based Pharmacokinetic (PBPK) Modeling Advancements

A potent method for predicting drug activity in various physiological settings is PBPK modeling. The development of PBPK models to include juvenile populations, unique patient demographics, novel drug formulations will result in safer and more efficient dosage regimens that will benefit a variety of patients.¹⁹

Biopharmaceutics and Formulation Challenges

It is still difficult to create pharmacological formulations that maximize bioavailability and targeted administration, especially for poorly soluble chemicals. Future research should focus on continuous manufacturing techniques, novel drug delivery methods, formulations driven by nanotechnology that allow for exact control of drug release and absorption.

Real-World Evidence Integration

A promising direction for pharmacokinetics research is the integration of real-world data from electronic health records, patient monitoring, clinical trials. By combining various data sources with modern analytics and machine

learning, it is possible to improve post-marketing surveillance, gain insights into actual medication usage, alter dosing.

Ethical and Regulatory Considerations

Pharmacokinetics research has ethical ramifications that need to be carefully considered, especially in vulnerable populations. It's crucial to address these issues while keeping innovation moving forward. Global regulatory standards harmonization will also accelerate the application of pharmacokinetics research to clinical practice.

Integration of Pharmacokinetics and Pharmacodynamics (PK/PD)

In order to create comprehensive models that clearly explain the connection between drug exposure, target engagement, therapeutic effects, future developments in pharmacokinetics should better combine PK with pharmacodynamics. For maximum efficacy, these integrated models will direct the choice of suitable drug doses and dosing regimens.²⁰

Discussion

It is crucial for developing drug development and patient-centered therapy in the field of pharmacokinetics to address present issues and map out the way forward. To predict and manage negative effects, drug-drug interactions are becoming more complicated, necessitating powerful computational models and extensive datasets. Overcoming regulatory obstacles and educating healthcare personnel are necessary for using pharmacogenomics into dosage procedures. Modern advances in physiologically-based pharmacokinetic modeling have the potential to improve drug regimens for a variety of patient demographics, supporting individualized care. Drug delivery systems must be improved through biopharmaceutics and formulation improvements, increasing bioavailability and enabling tailored therapy. Beyond clinical trials, patients gain from incorporating real-world evidence into research since it makes it easier for them to make educated decisions. Responsible advancement depends on a harmonization of international regulations and ethical issues. The best dose and therapeutic results are guaranteed by the integration of pharmacokinetics and pharmacodynamics. A pharmacokinetics landscape that maximizes medication efficacy, safety, customized medicine will take shape as a result of embracing these difficulties and future directions.²¹

Conclusion

To advance drug discovery and improve patient care, it is critical to navigate hurdles and embrace new approaches in the changing world of pharmacokinetics. The area is ready for revolutionary transformation, from tackling complex medication interactions to utilizing pharmacogenomics for

individualized dosage. The development of physiologically based modeling offers personalized treatments, while advances in formulation technology improve the accuracy of medication distribution. Responsible advancement is ensured by integrating real-world facts and harmonizing ethical factors. The best dose regimens are ensured by the interaction of pharmacokinetics and pharmacodynamics. At the nexus of technology and therapeutics, cross-disciplinary collaboration will lead us to a future in which pharmacokinetics not only supports drug development but also facilitates individualized treatments, ultimately reshaping the practice of medicine for better patient outcomes.

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