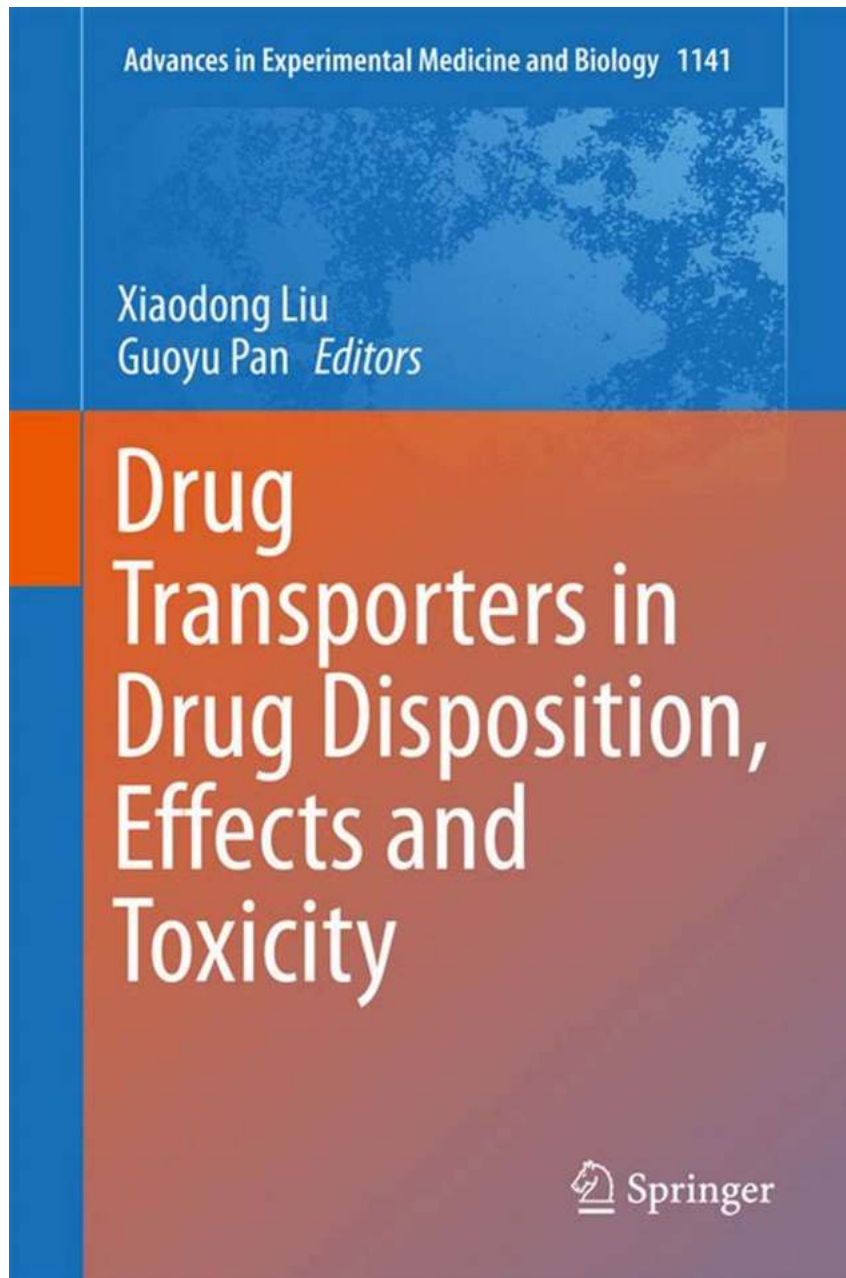


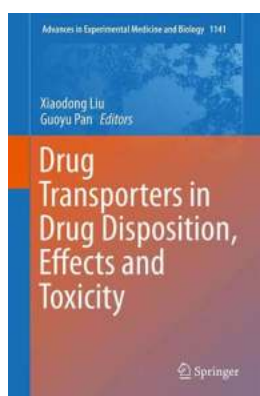
Drug Transporters in Drug Disposition Effects and Toxicity: Advances in Understanding and Implications for Therapy



About Drug Transporters

Drug transporters play a crucial role in the disposition and elimination of drugs from the body. These membrane-bound proteins are responsible for the uptake and efflux of drugs in various tissues and organs, influencing their bioavailability, distribution, and elimination kinetics.

Understanding the intricate mechanisms of drug transporters is essential for optimizing drug therapy as well as predicting and minimizing drug-drug interactions and adverse effects.



Drug Transporters in Drug Disposition, Effects and Toxicity (Advances in Experimental Medicine and Biology Book 1141)

by Alvin W. Orbaek (1st ed. 2019 Edition, Kindle Edition)

★★★★☆ 4.5 out of 5

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File size : 11384 KB

Text-to-Speech : Enabled

Screen Reader : Supported

Enhanced typesetting : Enabled

Print length : 1111 pages



Drug Disposition and Toxicity

The disposition of drugs in the body determines their therapeutic efficacy and potential for toxicity. Drug transporters regulate the movement of drugs across cell membranes, affecting their concentration gradients and ultimately impacting drug disposition.

By modulating drug transport, these proteins can influence drug absorption, distribution, metabolism, and excretion (ADME). Drug transporters are particularly

abundant in organs involved in drug elimination, such as the liver, kidneys, intestines, and brain.

Transporters can affect drug disposition and toxicity in several ways:

1. **Drug Absorption:** Transporters in the intestine and liver play a significant role in drug absorption from the gastrointestinal tract. They can promote uptake or efflux of drugs, influencing their bioavailability.
2. **Drug Distribution:** Transporters in blood-brain barriers and placental barriers regulate the entry of drugs into the brain and fetus, affecting their distribution and potential neurotoxicity.
3. **Drug Metabolism:** Transporters in the liver and intestine can transport drugs into hepatocytes and enterocytes, facilitating their metabolism or preventing their elimination. This process can contribute to drug-drug interactions or alter drug efficacy.
4. **Drug Excretion:** Transporters in the kidneys and liver actively eliminate drugs from the body by transporting them into urine or bile. Dysfunction of these transporters can lead to drug accumulation and toxicity.

Advances in Understanding Drug Transporters

Research on drug transporters has advanced significantly over the years, leading to a better understanding of their roles in drug disposition and toxicity. This knowledge has a profound impact on drug development, individualized therapy, and managing drug-induced toxicity.

Some of the recent advancements include:

Identification and Characterization of Transporter Substrates

Scientists have identified numerous drugs and xenobiotics that are substrates for various drug transporters. This knowledge helps predict the likelihood of drug-drug interactions and adverse effects.

For example, an investigational drug that inhibits a transporter responsible for the elimination of a commonly used medication may lead to increased plasma concentrations of the latter, potentially causing toxicity.

Transporter Polymorphisms and Personalized Medicine

Genetic variations in drug transporters can alter their activity, leading to inter-individual variability in drug response and toxicity. Understanding these polymorphisms allows for personalized medicine approaches.

Genotyping patients for transporter polymorphisms can help predict their response to specific drugs and guide dose modifications. This approach enables tailored therapy, optimizing treatment outcomes and minimizing adverse effects.

Influence of Drug Transporters on Drug-Drug Interactions

Drug transporters play a crucial role in drug-drug interactions. Co-administration of drugs that compete for the same transporter can lead to altered pharmacokinetics, leading to potential adverse effects or therapeutic failure.

Understanding the interplay between drug transporters and drug metabolizing enzymes is essential for predicting and managing drug-drug interactions effectively.

Implications for Therapy

The knowledge of drug transporters and their impact on drug disposition and toxicity has significant implications for therapy. It allows for:

- **Optimizing Drug Efficacy:** By considering the influence of transporters on drug disposition, clinicians can develop strategies to maximize drug efficacy.
- **Minimizing Drug-Drug Interactions:** Understanding the involvement of transporters in drug-drug interactions aids in avoiding potential adverse effects or therapeutic failures.
- **Individualized Therapy:** Genetic testing for transporter polymorphisms enables tailored therapy, ensuring optimal drug response and minimizing toxicity.
- **Reducing Drug-Induced Toxicity:** Identifying drugs that are substrates for transporters associated with toxicity allows for more precise assessment of potential adverse effects and implementing appropriate mitigation measures.

The role of drug transporters in drug disposition and toxicity is an area of immense importance in pharmacology and therapeutics. Advances in understanding these transporters provide valuable insights into optimizing drug therapy and minimizing adverse effects.

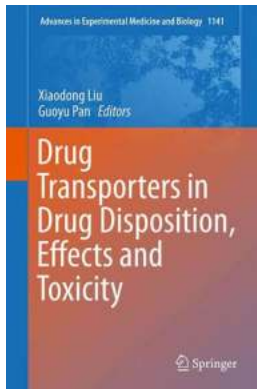
By unraveling the complex web of drug transport mechanisms, researchers can pave the way for the development of safer and more effective medications. Furthermore, personalized medicine approaches can harness the information on transporter-related polymorphisms, ensuring that patients receive tailored treatments that maximize efficacy while minimizing toxicity.

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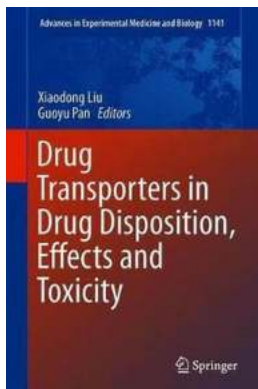
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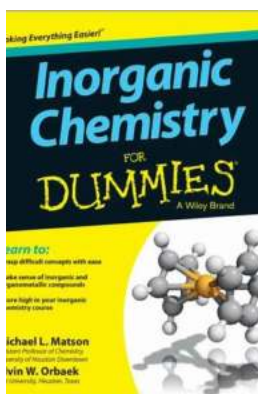


This book provides with a comprehensive overview of the role of drug transporters in drug disposition and efficacy/toxicity, as well as drug-drug interactions and recent advances in the field. Transporters are known determinants of drug disposition and efficacy/toxicity. In general, they are divided into solute carrier (SLC) and ATP binding cassette (ABC) families, and are located along cell membranes, where they mediate drug uptake into cells and export out of cells. Drug transporters are essential in maintaining cell homeostasis, and their gene mutations may cause or contribute to severe human genetic disorders, such as cystic fibrosis, neurological disease, retinal degeneration, anemia, and cholesterol and bile transport defects. Conversely, some diseases may also alter transporter functions and expressions, in turn aggravating disease process. Further, since over-expression of some ABC transporters is a potential contributor to multidrug-resistance (MDR), the book presents a number of strategies to overcome MDR, including ABC transporter inhibitors and applying epigenetic methods to modulate transporter expressions and functions. This book is useful for graduate students and professionals who are looking to refresh or expand their knowledge of this exciting field.



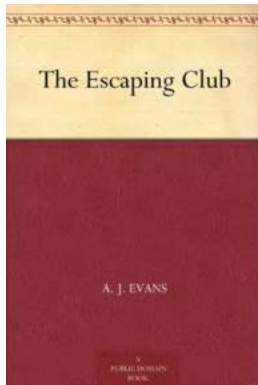
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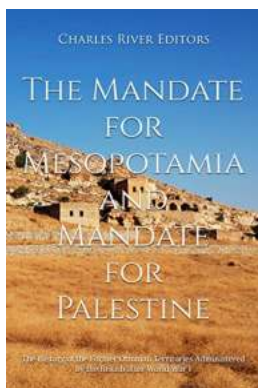
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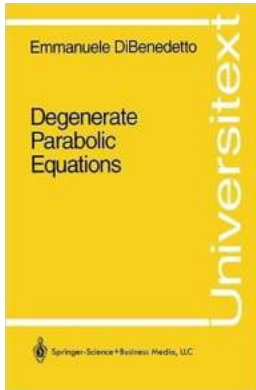
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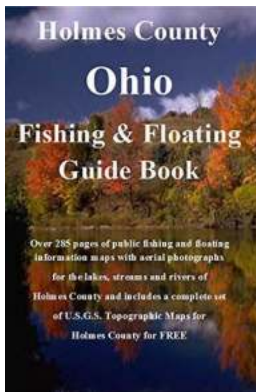
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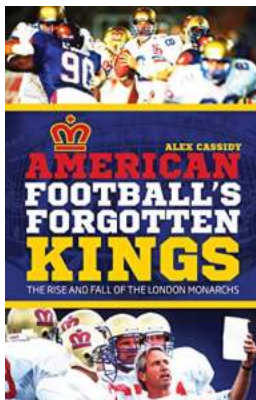
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