World Journal of Pharmacology and Toxicology

Mantel, World J Pharmacol Toxicol 2023, 6:3

Mini Review Open Access

Kidney Transporters Medication Discovery, Development, and Safety

Hilary Mantel*

Development and Medical Institute, Drug Safety, USA

Abstract

The kidney is an excretory organ having influx transporters on the basolateral membrane of proximal tubular cells and efflux transporters on the apical membrane. Cross-species changes in kidney transporter expression, function, location, and homology are crucial factors. DIKI is caused mostly by intracellular drug accumulation or metabolites and is accompanied with kidney histological abnormalities and a rise in serum creatinine (Scr). It is critical to determine whether a rise in Scr is caused by DIKI or by indirect transporter inhibition, which results in reversible and transitory drug-induced Scr increase [DICI] without histopathological abnormalities. Finally, in vitro and in vivo animal models can anticipate unexpected changes in systemic exposure and the effect of kidney transporters.

Keywords: Kidney transporters; Medication discovery; Medication development; Drug-drug interactions

Introduction

In today's world, pharmaceutical drugs play a crucial role in treating various diseases and improving the quality of life for millions of people. However, along with their undeniable benefits, drugs also carry inherent risks. Ensuring drug safety is paramount to protect public health and promote responsible medication use. This article explores the importance of drug safety, the regulatory framework in place, and ongoing efforts to enhance drug monitoring and surveillance. Drug safety refers to the assessment and management of the risks associated with pharmaceutical products throughout their lifecycle [1]. It involves evaluating the potential benefits and risks of a drug before it is approved for use, monitoring its safety once it enters the market, and taking appropriate actions to mitigate any identified risks. In recent years, there have been significant advancements in drug safety surveillance and monitoring Pharmaceutical companies also have a vital role to play in ensuring drug safety. They are expected to conduct robust post-marketing surveillance and promptly report any emerging safety concerns to regulatory authorities. The kidneys play a vital role in maintaining the body's homeostasis by regulating the filtration, reabsorption, and excretion of various substances [2]. The transporters located in the kidney cells are crucial for these functions and have gained significant attention in the field of medication discovery and development. Understanding the role of kidney transporters in drug metabolism, their impact on medication efficacy, and ensuring their safety is essential for optimizing therapeutic outcomes. This article explores the significance of kidney transporters in medication development, the challenges faced, and the strategies employed to ensure their safety [3].

Importance of kidney transporters in medication development: Kidney transporters, located in the renal tubules, facilitate the uptake and efflux of numerous substances, including medications. These transporters influence the pharmacokinetics of drugs by affecting their absorption, distribution, metabolism, and excretion (ADME). They play a critical role in determining drug concentration in the kidney, influencing therapeutic efficacy, and potential adverse effects.

Transporter-mediated drug-drug interactions: Transporters in the kidney can be responsible for drug-drug interactions (DDIs) that affect medication efficacy and safety. Certain drugs may inhibit or induce these transporters, leading to altered drug concentrations in the kidneys. Understanding these interactions is crucial for clinicians to make informed decisions regarding dosing regimens and potential drug combinations to avoid adverse outcomes or therapeutic failure.

Drug discovery and development: The discovery and development of medications that interact with kidney transporters present opportunities for optimizing drug therapy. By targeting specific transporters, drugs can be designed to enhance renal excretion of harmful substances or increase the tubular reabsorption of essential compounds. This approach has been particularly valuable in treating conditions such as hypertension, heart failure, and kidney diseases.

Safety considerations: While kidney transporters offer promising avenues for medication development, ensuring their safety is paramount. Potential risks associated with kidney transporter modulation include altered drug disposition, accumulation of toxic metabolites, and compromised renal function. Therefore, it is crucial to thoroughly evaluate the safety profile of drugs targeting these transporters during preclinical and clinical studies.

Preclinical assessment: In preclinical studies, the interaction of drugs with kidney transporters can be evaluated using in vitro cell models and animal studies. These investigations assess the potential for transporter-mediated DDIs, drug accumulation, and any adverse effects on renal function. Additionally, predictive models and computational simulations aid in understanding the drug's behavior in the kidney and provide insights into its safety.

Clinical evaluation: Clinical studies play a crucial role in assessing the safety of drugs interacting with kidney transporters. Pharmacokinetic studies with human subjects can identify potential DDIs and evaluate the drug's impact on renal function. Additionally, monitoring renal biomarkers, such as serum creatinine and estimated glomerular filtration rate, helps detect any signs of impaired kidney function.

Regulatory guidelines and pharmacovigilance: Regulatory agencies, such as the FDA and EMA, have provided guidelines to

***Corresponding author:** Hilary Mantel, Development and Medical Institute, Drug Safety, USA, E-mail: hilary345@gmail.com

Received: 01-May-2023, Manuscript No: wjpt-23-102173; **Editor assigned:** 03-May-2023, Pre QC No: wjpt-23-102173 (PQ); **Reviewed:** 17-May-2023, QC No: wjpt-23-102173; **Revised:** 24-May-2023, Manuscript No: wjpt-23-102173 (R); **Published:** 31-May-2023, DOI: 10.4172/wjpt.1000186

Citation: Mantel H (2023) Kidney Transporters Medication Discovery, Development, and Safety. World J Pharmacol Toxicol 6: 186.

assess and mitigate the risks associated with drugs targeting kidney transporters. These guidelines emphasize the evaluation of transporter-mediated DDIs during drug development and recommend post-marketing surveillance to monitor the long-term safety and effectiveness of medications [4-6].

Discussion

The study of kidney transporters in medication discovery, development, and safety is a topic of great significance in the field of pharmacology. Understanding the role of kidney transporters in drug metabolism and their impact on medication efficacy and safety is crucial for optimizing therapeutic outcomes. This discussion will delve into the importance of kidney transporters in medication development, the challenges faced in this area, and the strategies employed to ensure their safety. Kidney transporters play a pivotal role in the absorption, distribution, metabolism, and excretion of drugs. They are responsible for the uptake and efflux of various substances, including medications, within renal tubules. By influencing drug disposition in the kidneys, these transporters have a direct impact on drug concentrations, therapeutic efficacy, and potential adverse effects. One key aspect to consider is the potential for transporter-mediated drug-drug interactions (DDIs). Some medications can interact with kidney transporters, either inhibiting or inducing their activity. These interactions can lead to altered drug concentrations in the kidneys, affecting therapeutic outcomes. Understanding these DDIs is crucial for healthcare professionals to make informed decisions regarding dosing regimens and potential drug combinations, aiming to avoid adverse effects or therapeutic failure. The discovery and development of medications that target kidney transporters present opportunities for optimizing drug therapy. By specifically targeting these transporters, drugs can be designed to enhance the renal excretion of harmful substances or increase the reabsorption of essential compounds. This approach has proven valuable in the treatment of conditions such as hypertension, heart failure, and kidney diseases. However, ensuring the safety of drugs that interact with kidney transporters is of paramount importance. Modulating these transporters can have potential risks, including altered drug disposition, accumulation of toxic metabolites, and compromised renal function. Therefore, it is essential to thoroughly evaluate the safety profile of drugs targeting kidney transporters during preclinical and clinical studies. Preclinical assessments are crucial in understanding the interactions between drugs and kidney transporters. In vitro cell models and animal studies help assess the potential for transporter-mediated DDIs, drug accumulation, and any adverse effects on renal function. Predictive models and computational simulations also aid in understanding how drugs behave in the kidney and provide insights into their safety profiles. Clinical evaluation plays a vital role in assessing the safety of drugs that interact with kidney transporters. Pharmacokinetic studies involving human subjects can identify potential DDIs and evaluate the drug's impact on renal function. Monitoring renal biomarkers, such as serum creatinine and estimated glomerular filtration rate, is essential in detecting any signs of impaired kidney function.

Regulatory guidelines established by agencies such as the FDA and EMA provide recommendations for assessing and mitigating the risks associated with drugs targeting kidney transporters. These guidelines emphasize the evaluation of transporter-mediated DDIs during drug development and highlight the importance of post-marketing surveillance to monitor the long-term safety and effectiveness of medications. In drug research and development programmes, efflux and influx kidney transporters can influence drug disposition, DDIs, DIKI, and overall kidney safety and risk assessment. Cross-species changes in kidney transporter expression, function, location, and homology must be considered. DICI must be distinguished from direct DIKI. Tools for kidney transporters, including as in vitro models, gene deletion and transgenic animal models, can aid in the prediction of unanticipated alterations. Membrane transporters, through substrate selectivity and varied tissue distributions, regulate endogenous chemical and nutrient concentrations in tissues. These transporters are also important in the disposition of medicinal drugs, influencing their efficacy and safety profile. A transporter-mediated tissue targeting strategy is developing as an effective approach in drug discovery, in which the structural properties recognised by the transporters are included into the therapeutic molecule. We explore these phenomena and highlight current occurrences in the design of liver and kidney targeting medicinal compounds in this digest. However, ensuring the safety of drugs that interact with kidney transporters is a key consideration. Modulating these transporters can present risks such as altered drug disposition, accumulation of toxic metabolites, and compromised renal function. Therefore, thorough evaluation of the safety profile of drugs targeting kidney transporters is crucial during preclinical and clinical studies. Preclinical assessments, including in vitro cell models and animal studies, help understand the potential interactions between drugs and kidney transporters [7-11].

Conclusion

In conclusion, the study of kidney transporters in medication discovery, development, and safety is of paramount importance in the field of pharmacology. These transporters play a crucial role in drug metabolism, affecting drug concentrations in the kidneys and ultimately influencing therapeutic efficacy and potential adverse effects. Understanding the potential drug-drug interactions mediated by kidney transporters is essential for optimizing medication regimens and avoiding adverse outcomes. The discovery and development of medications targeting kidney transporters offer promising opportunities for optimizing drug therapy. By specifically targeting these transporters, drugs can be designed to enhance renal excretion of harmful substances or increase the reabsorption of essential compounds, benefiting various medical conditions. Clinical evaluations involving human subjects provide insights into the impact of these drugs on renal function and identify potential drug-drug interactions. Adherence to regulatory guidelines and pharmacovigilance practices further enhance the safety of drugs targeting kidney transporters. Continued research in this area will enable the development of safer and more effective medications for both renal and non-renal conditions. By considering the role of kidney transporters, healthcare professionals and researchers can optimize therapeutic outcomes while minimizing the risks associated with drug therapy.

Acknowledgment

None

Conflict of Interest

None

References

1. Gonzalez F, Boue S, Izpisua Belmonte JC (2011) Methods for making induced pluripotent stem cells: Reprogramming a la carte. Nat Rev Genet 12:231-242.
2. Huber I, Itzhaki O, Caspi G, Arbel M, Tzukerman A, et al. (2007)Identification and selection of cardiomyocytes during human embryonic stem cell differentiation. FASEB J, 21:2551-2563.
3. Itzhaki I, Maizels L, Huber I, Gepstein A, Arbel G, et al.(2012) Modeling of

catecholaminergic polymorphic ventricular tachycardia with patient-specific human induced pluripotent stem cells. J Am Coll Cardiol 60:990-1000.

4. Jia F, Wilson KD, Sun N, Gupta DM, Huang M, et al. (2010) A nonviral minicircle vector for deriving human iPS cells. Nat Methods 7:197-199.
5. Walton KL, Johnson KE, Harrison CA (2017) Targeting TGF-beta Mediated SMAD Signaling for the Prevention of Fibrosis. Front Pharmacol 8:461.
6. Kliment CR, Oury TD (2010) Oxidative stress, extracellular matrix targets, and idiopathic pulmonary fibrosis. Free Radic Biol Med 49:707-717.
7. An L, Peng LY, Sun NY, Yang YL, Zhang XW, et al. (2019) Tanshinone IIA Activates Nuclear Factor-Erythroid 2-Related Factor 2 to Restrain Pulmonary Fibrosis via Regulation of Redox Homeostasis and Glutaminolysis. Antioxid Redox Signal 30:1831-1848.
8. Cheresh P, Kim SJ, Tulasiram S, Kamp DW (2013) Oxidative stress and pulmonary fibrosis. Biochim Biophys Acta 1832:1028-1040.
9. Loboda A, Damulewicz M, Pyza E, Jozkowicz A, Dulak J (2016) Role of Nrf2/HO-1 system in development, oxidative stress response and diseases: an evolutionarily conserved mechanism. Cell Mol Life Sci 73:3221-3247.
10. Liu R, Chen H, Bai H, Zhang W, Wang X, et al. (2013) Suppression of nuclear factor erythroid 2-related factor 2 via extracellular signal-regulated kinase contributes to bleomycin-induced oxidative stress and fibrogenesis. Toxicol Lett 220:15-25.
11. Wang K, Chen T, Ying X, Zhang Z, Shao Z, et al.(2019) Ligustilide alleviated IL-1beta induced apoptosis and extracellular matrix degradation of nucleus pulposus cells and attenuates intervertebral disc degeneration in vivo. Int Immunopharmacol 69:398-407.