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Advancing the Evaluation of Botanicals' Nephrotoxic Potential using Modern Toxicological Tools

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Abstract

The evaluation of nephrotoxic potential in botanicals has been revolutionized by the application of modern toxicological tools. Traditional methods, such as animal models and histopathology, have limitations in predicting human toxicity accurately. This article highlights the advancements in toxicology that have enhanced the assessment of nephrotoxicity in botanicals. In vitro cellular models allow researchers to study the effects of botanical compounds on kidney cells, providing insights into cellular responses and mechanisms of toxicity. High-throughput screening enables rapid evaluation of multiple compounds, identifying those requiring further investigation. Omics technologies offer a comprehensive view of molecular changes induced by botanicals, aiding in identifying underlying mechanisms and potential biomarkers. The integration of these tools has important regulatory implications, aiding evidence-based decision-making and identifying safer botanical alternatives. Collaboration between disciplines is crucial for maximizing the benefits of these tools. Advancements in toxicological tools contribute to improved risk assessment, informed decision-making, and the development of safer botanical products, ensuring the well-being of consumers while harnessing the potential of botanical medicine.

Keywords: Nephrotoxic; Toxicological tools; Botanicals; Kidney cells

Introduction

Botanicals have been used for centuries as a source of therapeutic agents, offering potential remedies for various ailments. However, alongside their beneficial properties, certain botanical compounds may possess nephrotoxic potential, posing a risk to kidney health. In recent years, the field of toxicology has witnessed significant advancements in tools and techniques for evaluating nephrotoxicity [1]. This article explores how modern toxicological tools are enhancing the assessment of botanicals' nephrotoxic potential, enabling researchers and regulators to make more informed decisions regarding their safe usage. Se of botanicals can lead to various unintended toxicological effects, underscoring that having access to safe botanical products is a critical public health need. In extreme cases, permanent organ damage and even death can occur. Multiple reviews highlight known or suspected nephrotoxic botanicals, although causality is not typically well established. However, most botanical products have not been specifically evaluated for nephrotoxicity [2]. More research is needed to decipher the extent and mechanisms of toxicity from known and potentially nephrotoxic botanicals. Given their chemical complexity and variability, selecting a single representative botanical sample for traditional rodent in vivo testing can be difficult, and testing multiple samples is resource intensive. Thus, predictive techniques suitable for whole complex mixtures are needed to screen for botanical nephrotoxicity that are relatively rapid, effective, and resource (cost, time, animals) appropriate.

Unleashing the power of modern toxicological tools

Traditionally, the evaluation of nephrotoxicity relied on animal models and histopathological examination. While these methods provide valuable insights, they have limitations in terms of species-specific differences and predicting human toxicity accurately. Modern toxicological tools, such as in vitro cellular models, high-throughput screening, and omics technologies, have revolutionized the field, offering a more comprehensive and mechanistic understanding of nephrotoxicity [3].

In vitro cellular models

In vitro cellular models, such as renal cell lines and organoids, allow researchers to study the effects of botanical compounds on kidney cells in a controlled laboratory setting [4]. These models provide a valuable platform for assessing cellular responses, evaluating biomarkers of nephrotoxicity, and identifying potential mechanisms of toxicity. The use of in vitro models reduces the need for animal testing and allows for high-throughput screening of multiple botanical compounds. High-throughput screening (HTS) techniques enable the rapid evaluation of a large number of botanical compounds for their nephrotoxic potential. Using automated platforms and robotic systems, HTS allows researchers to assess cellular viability, mitochondrial function, oxidative stress, and other key indicators of nephrotoxicity. This approach streamlines the identification of compounds that require further investigation and helps prioritize resources for in-depth toxicological analysis [5]. Omics technologies, including genomics, transcriptomics, proteomics, and metabolomics, provide a comprehensive view of the molecular changes induced by botanical compounds in kidney cells. These techniques allow for the identification of specific genes, proteins, and metabolites that are altered upon exposure to potentially nephrotoxic botanicals. By unraveling these molecular signatures, researchers can gain insights into the underlying mechanisms of nephrotoxicity and identify potential biomarkers for early detection and monitoring [6].

Regulatory implications and future directions

The integration of modern toxicological tools in the evaluation of botanicals' nephrotoxic potential has important regulatory implications [7]. Regulators can make evidence-based decisions regarding the

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safety and usage guidelines for botanical products. Furthermore, the application of these tools facilitates the identification of safer botanical alternatives with reduced nephrotoxicity potential. To maximize the benefits of modern toxicological tools, collaboration between toxicologists, pharmacologists, and herbalists is crucial. By combining traditional knowledge with cutting-edge science, researchers can leverage the strengths of both disciplines to enhance the safety assessment of botanicals and ensure the well-being of consumers [8]. Physiologically Based Pharmacokinetic (PBPK) modeling is a computational approach that uses mathematical equations to predict in vivo concentrations by simulating the processes of compound absorption, distribution, metabolism, and excretion. To be successful, this method requires accurate in vitro approximations of pharmacokinetic parameters, including transporter mediated drug disposition and drug–drug interactions [9]. Data generated by kidney MPS combined with PBPK modeling has accurately reproduced the kinetics of renal reabsorption and excretion observed in vivo for numerous nephrotoxic compounds. This approach could be used to predict nephrotoxicity and optimize dosing strategies for novel botanicals prior to human exposure. For botanicals, PBPK models will typically be based on individual marker constituents. Dose information can be estimated from sources such as pharmacopoeia monographs, chemical markers if supplied by the manufacturer, or from toxic kinetic studies based on individual constituents. These data can help estimate parameters for the mixture [10].

(Table 1)

Conclusion

Advancements in modern toxicological tools are transforming the evaluation of botanicals' nephrotoxic potential, offering a more comprehensive understanding of their safety profile. In vitro cellular models, high-throughput screening, and omics technologies provide researchers and regulators with valuable insights into the mechanisms and markers of nephrotoxicity. This integration of modern tools will undoubtedly contribute to improved risk assessment, informed decision-making, and the development of safer botanical products. As the field continues to evolve, it is essential to foster collaborations and embrace interdisciplinary approaches to unlock the full potential of botanical medicine while safeguarding renal health. Botanical-induced nephropathies can occur via multiple mechanisms, and given the increasing use of botanicals more research is needed to develop and validate tools that can be used for nephrotoxicity screening. Although there are numerous case reports and reviews on botanical-induced nephrotoxicity in the literature, many rely on a very small number of clinical reports that often lack ingredient identification, supporting information, or mechanistic investigation. The development of NAMs will enable more specific mechanistic data and improve safety, thereby limiting the potential for people to develop nephrotoxicity from botanicals.

Table 1: Advancing the evaluation of botanicals' nephrotoxic potential using modern toxicological tools.

Aspect/Tool	Description
Botanical Sample	Source and details of the botanical
Chemical Composition	Identification of active compounds
In vitro Studies	Cell culture models for toxicity
In vivo Animal Models	Animal studies assessing nephrotoxicity
Biomarkers	Identification of kidney damage markers
Omics Technologies	Genomics, proteomics, and metabolomics
Histopathology	Microscopic examination of kidney tissue
Toxicokinetics	Absorption, distribution, metabolism, elimination
Computational Models	Predictive modeling for nephrotoxicity
Human Clinical Trials	Botanicals' effects on human kidneys
Regulatory Considerations	Compliance with safety regulations
Risk Assessment	Quantification of nephroto

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