THE ROLE OF THE PHARMACIST IN THE ASSESSMENT OF HERB–DRUG INTERACTIONS AND THE SAFETY OF HERBAL MEDICINES

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Abstract

In recent decades, there has been a significant increase in the global use of herbal medicines and phytotherapeutic products, driven by the widespread perception that "natural" products are inherently safer than synthetic pharmacotherapy, as well as by their broad availability and long-standing traditional use. However, this trend raises important clinical, pharmacological, and regulatory concerns, particularly in the context of the concomitant use of herbal and conventional medicines without appropriate consultation with healthcare professionals. This research aims to analyze herb–drug interactions, with a particular focus on their pharmacokinetic and pharmacodynamic mechanisms, and to evaluate the safety of herbal products in clinical practice. Key risks include adverse effects such as hepatotoxicity, nephrotoxicity, and allergic and neurological reactions, as well as contamination, variability in composition, adulteration, and lack of standardization. Challenges related to limited clinical evidence and underdeveloped pharmacovigilance systems are also addressed.Global regulatory inconsistencies represent a major barrier to ensuring consistent quality, safety, and efficacy of herbal products. Therefore, the need for an integrated approach that combines scientific research, regulatory frameworks, and clinical practice is emphasized.Particular attention is given to the role of the pharmacist as a key clinical expert in identifying and preventing interactions, optimizing therapy, educating patients, and contributing to pharmacovigilance.
In summary, the safe and rational use of herbal medicines requires a multidisciplinary, evidence-based approach, active pharmacist involvement, and improved patient health literacy, reinforcing the principle that "natural does not always mean safe," particularly in the context of polypharmacy.

Keywords: herbal medicines, interactions, pharmacovigilance, pharmacist, safety.

Introduction

In recent decades, the global use of herbal medicines and phytotherapeutic products has increased substantially, representing a major trend in contemporary healthcare. This expansion is driven by sociocultural, economic, and medical factors, including the perception that natural products are inherently safer than synthetic drugs, growing interest in holistic medicine, and their widespread availability (Ekor, 2014; World Health Organization, 2019). In many low- and middle-income countries, herbal medicines remain a primary source of healthcare, while in developed countries they are increasingly used as complementary therapies. Despite their traditional use, herbal medicines are pharmacologically active and contain diverse bioactive compounds capable of producing significant biological effects. Their use is therefore not without risk. A major concern is the frequent lack of patient disclosure, particularly when herbal products are used alongside prescribed pharmacotherapy, increasing the risk of clinically relevant herb–drug interactions (Izzo & Ernst, 2009; Posadzki et al., 2013). These interactions may alter the pharmacokinetics and pharmacodynamics of conventional drugs, leading to reduced efficacy or increased toxicity, especially in vulnerable populations such as elderly patients and those undergoing polypharmacy (Routledge et al., 2004). The complexity and variability of herbal products, influenced by factors such as plant origin, processing, and

storage, further complicate their safe use (Jordan et al., 2010; Bent, 2008). In addition, inconsistent regulatory frameworks and classification differences across regions contribute to challenges in standardization, quality assurance, and safety monitoring (European Medicines Agency, 2021). Given these challenges, a systematic, evidence-based approach is essential. In this context, pharmacists play a key role in identifying interactions, educating patients, and supporting pharmacovigilance. This research therefore aims to analyze herb–drug interactions and the safety of herbal medicines, with particular emphasis on their clinical implications and the role of the pharmacist in ensuring their rational use.

Herbal Medicines: Definition and Characteristics

Herbal medicines are defined as therapeutic products derived from plant materials, including whole plants, plant parts, extracts, or isolated phytochemicals, used for the prevention and treatment of various diseases (World Health Organization, 2019; European Medicines Agency, 2021). These products represent a complex group of medicinal agents characterized by multiple bioactive constituents, such as alkaloids, flavonoids, terpenoids, glycosides, and phenolic compounds, which contribute to their pharmacological activity (Jordan et al., 2010). A key distinction between herbal medicines and conventional drugs lies in their compositional complexity. While synthetic drugs typically contain a single well-defined active ingredient, herbal medicines are multicomponent systems in which constituents may act synergistically, additively, or antagonistically. This complexity may enhance therapeutic effects but also introduces variability and unpredictability in clinical outcomes (Bent, 2008; Ekor, 2014). The pharmacological activity of herbal medicines is often attributed to the combined action of their constituents rather than a single dominant compound. This "entourage effect" complicates the identification of active principles and the establishment of dose–response relationships, making the evaluation of efficacy and safety more challenging than for conventional drugs (Jordan et al., 2010). Another major limitation is the lack of standardization. Variability in composition may result from factors such as plant species, geographical origin, environmental conditions, harvesting, and processing. Differences in extraction and formulation can further affect the concentration and bioavailability of active compounds (Ekor, 2014). Quality control is also challenged by contamination and adulteration. Herbal products may contain heavy metals, pesticide residues, microbial contaminants, or undeclared synthetic substances, posing significant safety risks (Jordan et al., 2010). In addition, the pharmacokinetic properties of many phytochemicals remain insufficiently characterized. Limited data on absorption, distribution, metabolism, and excretion (ADME) hinder accurate prediction of interactions with conventional drugs (Brantley et al., 2014). Finally, the perception of herbal medicines as inherently safe often leads to unsupervised use, increasing the risk of adverse effects and interactions. Overall, while herbal medicines offer potential therapeutic benefits, their complexity, variability, and limited standardization present important challenges for their safe and effective use, highlighting the need for evidence-based evaluation and clinical integration.

Herb–Drug Interactions

Herb–drug interactions represent a significant and complex clinical challenge associated with the use of herbal medicines, arising when bioactive constituents alter the pharmacokinetic or pharmacodynamic profile of co-administered drugs, potentially leading to reduced efficacy or

increased toxicity (Izzo & Ernst, 2009; Posadzki et al., 2013). Their clinical relevance is often underestimated due to underreporting, variability in herbal composition, and limited pharmacovigilance data, although they are particularly important in patients undergoing long-term therapy or polypharmacy (Awortwe & Bruckmueller, 2017).

Pharmacokinetic interactions involve changes in absorption, distribution, metabolism, or excretion, most commonly through modulation of cytochrome P450 enzymes and drug transporters such as P-glycoprotein. For example, *Hypericum perforatum* induces CYP3A4, reducing drug efficacy, while certain plant constituents, including those in grapefruit, inhibit CYP3A4 and increase drug toxicity. Pharmacodynamic interactions, on the other hand, occur when herbal products influence the same physiological pathways as drugs, producing additive, synergistic, or antagonistic effects. Clinically relevant examples include increased bleeding risk when anticoagulant drugs are combined with *Ginkgo biloba* or garlic, and enhanced sedation when valerian is used with central nervous system depressants. The clinical consequences of these interactions range from mild to life-threatening and depend on factors such as dosage, duration of use, patient characteristics, and drug properties. Risk assessment is further complicated by variability in herbal products and insufficient patient disclosure. Despite growing research, important knowledge gaps remain due to limited clinical validation and the complexity of multicomponent systems. Overall, improved clinical studies, enhanced pharmacovigilance, and better integration of herbal medicine data are essential for understanding and managing herb–drug interactions effectively.

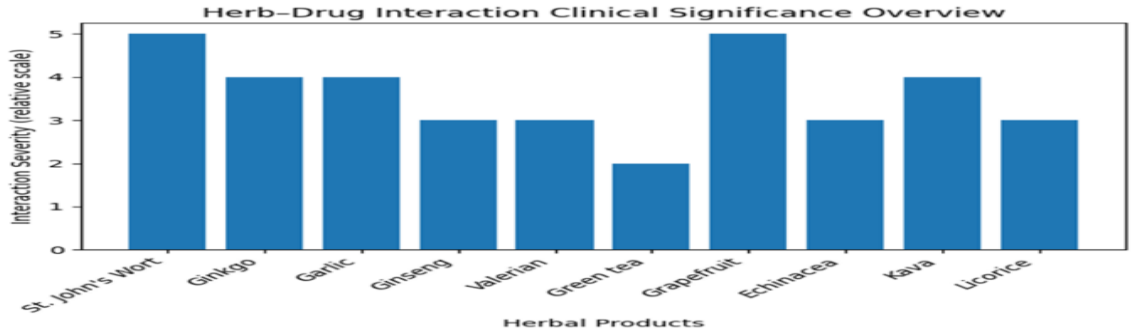

Figure 1. Overview of clinically relevant herb–drug interactions based on relative severity and clinical significance. The figure highlights commonly reported interactions involving widely used herbal products, emphasizing their potential impact on pharmacotherapy.

Safety Issues of Herbal Medicines

Despite their widespread use and perception as safe therapeutic agents, herbal medicines are associated with significant safety concerns that require careful consideration in clinical practice. These risks arise from their intrinsic pharmacological activity, as herbal products contain multiple bioactive constituents capable of producing both therapeutic and adverse effects (Ekor, 2014). Reported adverse reactions include hepatotoxicity, nephrotoxicity, allergic responses, and neurological disturbances, ranging from mild to life-threatening, and are influenced by factors such as dosage, duration of use, patient characteristics, and concomitant pharmacotherapy (Stickel & Shouval, 2015). In addition to intrinsic toxicity, safety concerns are closely related to quality issues. Herbal products may be contaminated with heavy metals, pesticide residues, or microbial agents due to environmental exposure or inadequate manufacturing practices. Intentional adulteration with synthetic pharmaceutical compounds further increases risk by exposing patients to undeclared substances that may cause

unexpected pharmacological effects and interactions (Jordan et al., 2010). Variability in composition, influenced by plant species, cultivation conditions, processing, and storage, also contributes to inconsistent chemical profiles, unpredictable therapeutic outcomes, and challenges in safety assessment (Bent, 2008). Certain populations, including elderly individuals, pregnant and breastfeeding women, patients with chronic diseases, and those undergoing polypharmacy, are particularly vulnerable, as even minor pharmacokinetic or pharmacodynamic changes may result in significant clinical consequences (Routledge et al., 2004). Pharmacovigilance systems for herbal medicines remain limited due to underreporting, lack of standardized monitoring, and difficulties in establishing causality, further complicated by the multicomponent nature of these products. Overall, ensuring the safe use of herbal medicines requires a multidisciplinary approach that integrates improved pharmacovigilance, stricter quality control, and active involvement of healthcare professionals, particularly pharmacists, in risk identification, patient education, and clinical management.

Role of the Pharmacist

The increasing use of herbal medicines alongside conventional pharmacotherapy has positioned the pharmacist as a key contributor to safe and effective patient care. As medication experts with in-depth knowledge of pharmacokinetics, pharmacodynamics, and potential interactions, pharmacists are uniquely qualified to identify, assess, and manage herb–drug interactions in clinical practice (Awortwe & Bruckmueller, 2017). A central responsibility of pharmacists is the early identification and prevention of potential interactions through comprehensive medication review, which includes prescribed drugs, over-the-counter products, and herbal preparations. This process involves evaluating patient history, comorbidities, and interaction risk, and is particularly important given that patients often fail to disclose herbal product use. Pharmacists also play a critical role in assessing the safety and efficacy of herbal medicines by evaluating scientific evidence, product quality, and potential contraindications. In addition, they contribute to optimizing pharmacotherapy by adjusting treatment regimens, recommending safer alternatives, and monitoring therapeutic outcomes, especially in patients undergoing polypharmacy. Patient education is another key component of pharmaceutical care. Pharmacists inform patients about potential risks, emphasize the importance of full disclosure, and provide guidance on appropriate use, dosage, and duration of therapy, thereby improving health literacy and reducing adverse outcomes. Furthermore, pharmacists contribute significantly to pharmacovigilance by detecting, documenting, and reporting adverse effects and interactions associated with herbal products. Their collaboration with physicians and other healthcare professionals supports a multidisciplinary approach to patient care and improves therapeutic outcomes. Overall, the pharmacist's role has evolved into a patient-centered clinical function, serving as a vital link between traditional and modern medicine. Their involvement is essential for the safe, rational, and evidence-based integration of herbal medicines into clinical practice.

Regulatory Aspects

The regulation of herbal medicines represents a complex and heterogeneous field that varies significantly across regions due to cultural, traditional, and healthcare differences. Despite their widespread use, herbal products are not uniformly regulated worldwide, creating challenges in

ensuring their quality, safety, and efficacy (World Health Organization, 2019). While the World Health Organization provides guidelines for standardization and pharmacovigilance, the European Medicines Agency establishes a regulatory framework based on well-established and traditional use, whereas in the United States these products are often classified as dietary supplements, with less stringent pre-market requirements. Key challenges include lack of standardization, variability in composition, limited clinical evidence, and underdeveloped pharmacovigilance systems, all of which complicate safety monitoring and increase the risk of adverse outcomes. Therefore, global harmonization of regulatory standards, stronger quality control, and the integration of scientific evidence into clinical practice are essential. In summary, despite ongoing improvements, current regulatory frameworks remain insufficient to fully address the complexity of herbal medicines, highlighting the need for their safe and evidence-based integration into modern healthcare systems.

Discussion

The findings of this study highlight the increasing complexity of integrating herbal medicines into modern clinical practice, primarily due to concerns related to safety, variability, and insufficient regulatory harmonization. A key issue is the discrepancy between public perception and scientific evidence, where the belief that “natural equals safe” promotes unsupervised use and increases the risk of clinically significant herb–drug interactions. Herbal medicines can significantly affect drug pharmacokinetics and pharmacodynamics, particularly in patients with chronic diseases and those undergoing polypharmacy. Their multicomponent composition and variability further complicate the prediction and management of interactions, while additional risks such as contamination, adulteration, and lack of standardization reduce their reliability. Regulatory inconsistencies and limited pharmacovigilance systems represent major barriers to ensuring safety and quality. Within this context, pharmacists play a critical role in identifying risks, educating patients, and supporting safe use through clinical practice and interprofessional collaboration. Overall, the integration of herbal medicines requires a multidisciplinary, evidence-based approach, improved regulation, and a shift in perception, recognizing that natural products are not inherently safe.

Conclusion

In conclusion, the growing use of herbal medicines presents both opportunities and challenges for modern healthcare systems. Although these products offer potential therapeutic benefits, their complex composition, variability, and lack of standardization raise important concerns regarding safety and efficacy. Herb–drug interactions remain a significant clinical issue, particularly in patients undergoing polypharmacy, where they may lead to reduced therapeutic effectiveness or increased toxicity. Additional risks, including contamination, adulteration, and limited clinical evidence, further complicate their safe use. The lack of harmonized regulatory frameworks and insufficient pharmacovigilance highlights the need for improved monitoring, standardization, and evidence-based evaluation. Within this context, pharmacists play a crucial role in ensuring safe and rational use through interaction management, patient education, and pharmacovigilance.

Overall, the integration of herbal medicines into clinical practice requires a multidisciplinary, evidence-based approach and a clear understanding that "natural" does not necessarily mean "safe."

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