RESEARCH PAPER

Pharmacokinetics and Pharmacodynamics of Chinese Herbal Medicine: Understanding Its Mechanisms and Efficacy

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Abstract

Chinese Herbal Medicine (CHM) has been widely used for centuries and remains an important component of healthcare systems worldwide. The increasing integration of Chinese herbal medicine into modern medicine has intensified interest in understanding its pharmacokinetic and pharmacodynamic characteristics and their contributions to therapeutic efficacy. This review aims to summarize current knowledge regarding the pharmacokinetics, pharmacodynamics, mechanisms of action, therapeutic applications, and safety considerations of Chinese Herbal Medicine. A comprehensive literature review was conducted using peer-reviewed articles retrieved from major scientific databases, including Scopus, Web of Science, ScienceDirect, and Google Scholar. Relevant studies addressing absorption, distribution, metabolism, excretion, pharmacological mechanisms, herb–drug interactions, and advanced analytical approaches were evaluated and organized into thematic categories. Evidence indicates that Chinese Herbal Medicine exerts therapeutic effects through complex multi-component and multi-target interactions. Pharmacokinetic processes influence the bioavailability and disposition of herbal constituents, whereas pharmacodynamic mechanisms involve modulation of receptors, enzymes, signaling pathways, and gene expression. Emerging approaches such as network pharmacology, chinmedomics, and pharmacometabolomics have improved the understanding of the molecular basis of Chinese Herbal Medicine efficacy. However, challenges related to standardization, quality control, and herb–drug interactions remain significant. Integration of pharmacokinetic and pharmacodynamic evidence provides a scientific foundation for understanding the efficacy and safety of Chinese Herbal Medicine. Future advances in systems biology, artificial intelligence, and precision medicine may facilitate the development of more effective and personalized herbal therapies.

Keywords: Chinese Herbal Medicine; Pharmacokinetics; Pharmacodynamics; Herb–Drug Interactions; Network Pharmacology.

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1. Introduction

Chinese Herbal Medicine (CHM) is one of the oldest still practiced healthcare systems in the world and has been around for thousands of years. Based on the theoretical concept of Traditional Chinese Medicine (TCM), CHM has been widely used for disease prevention, health maintenance, and treatment. The ancient medical literature records the medicinal uses of many herbs and principles about how several herbs can be used together to balance the physiology. Conventionally, every drug has a single active compound and a single biological target, but in CHM, complex drug mixtures have multiple pathways of action. The principle of herbal compatibility, which is used to select and combine medicinal ingredients, is fundamental to the practice of TCM, and is substantiated by recent pharmaceutical research on the synergism and complementariness of herbal components (Zhou et al., 2017). In the latter half of the 20th century, analytical chemistry, molecular pharmacology and systems biology have developed to the point of allowing the use of modern scientific methods in the study of CHM, which helps to integrate TK into current biomedical research.

Since then, the utilization of CHM has grown to a significant extent outside East Asia and is now acknowledged as a significant part of complementary and integrative medicine globally. It is gaining acceptance in both the developed and developing world owing to its rising popularity as a result of the growing interest from the public in natural products, personalized healthcare approaches and management of chronic diseases. Herbal medicines are used fairly regularly for cardiovascular diseases, metabolic diseases, inflammation-related diseases, neurological diseases and supportive care for cancer. Various herbal compounds, such as puerarin, anthraquinones and Z-ligustilide, have been shown to have a wide range of pharmacological effects and therapeutic potential through preclinical and clinical studies (Zhang, 2019; Wang et al., 2021; Xie et al., 2020). Moreover, CHM is integrated into the treatment more and more with conventional medicine. There is, however, growing clinical application of herbal products, with concerns

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that they may be ineffective, not standardized, not safe and may interact with prescription medications, making it important to have them scientifically evaluated thoroughly (Singh & Zhao, 2017).

To assess the therapeutic efficacy of CHM, a thorough pharmacokinetics (PK) and pharmacodynamics (PD) assessment is crucial. Pharmacokinetics refers to the absorption, distribution, metabolism and excretion of herbal constituents, while pharmacodynamics is related to the biological and physiological response that occurs as a result of the absorption of the constituent. PK and PD studies are complementary and give important insight into the optimization of dosage and assessment of efficacy, safety, and elucidation of mechanism. The investigations of herbal constituents like anthraquinones and Z-ligustilide have exhibited that the different pharmacokinetic actions can significantly impact therapeutic efficacy and toxicity (Li et al., 2017; Wang et al., 2021; Xie et al., 2020). Furthermore, plasma protein binding and drug interactions with other active components in the herbs can impact the tissue distribution, bioavailability and target-site exposure, which can lead to changes in pharmacologic activity (Jiao et al., 2018). The incorporation of PK and PD data is then critical for providing scientific evidence for the clinical use of herbal medicines.

Even though considerable research has been conducted in the field of herbal medicine, there are still a number of challenges to understand the complexity of the CHM. Herbal medicine products often contain many different active ingredients (decad, hundreds, and more) that can either interact synergistically, additively, or antagonistically, unlike synthetic drugs that usually contain only one single active ingredient. The interactions make the discovery of active compounds, therapeutic targets and mechanisms of action more complicated. Moreover, differences in plant species, growing conditions, harvesting, processing and formulation may also give rise to a high degree of variability in chemical composition and pharmacological activity. Another major challenge is the herb–drug interactions as many herbs contain constituents that can affect the pharmacokinetics of concurrently administered drugs by altering drug-metabolizing enzymes and transport proteins (Singh & Zhao 2017). In recent years, there has been an attempt to enhance the bioavailability and therapeutic index of herbal formulations with the emergence of new nanotechnology and herbal nanomedicine, which, when applied to herbal medicine, involve additional complexities in formulation design, pharmacokinetic behavior and long-term safety (Kumar & Sharma, 2018).

With the emerging popularity of CHM in the world and the rising interest in evidence-based herbal medicine, it is appropriate to comprehensively investigate the pharmacokinetic and pharmacodynamic properties of CHM. The goal of this review is to provide a summary of existing information on absorption, distribution, metabolism, excretion and pharmacological effects of CHMs. Special focus is given to multi-component interactions, herb–drug interactions, compatibility theory, new delivery systems, and new ways to study therapeutic mechanisms. This review aims to elucidate the therapeutic mechanisms of action of CHM based on contemporary pharmacokinetic/pharmacodynamic evidence, as well as suggesting potential areas of future research and clinical use.

2. Methodology

This study aims to review the pharmacokinetic and pharmacodynamic features of CHM and give a comprehensive understanding of the mechanisms of action and therapeutic efficiency. Literature related to the subject was gathered from peer-reviewed journals, scholarly books, review articles and reliable scientific publications, as well as important seminal publications that have paved the way for pharmacokinetic and pharmacodynamic studies of TCM. Articles were searched using the major scientific databases: ScienceDirect, Web of Science, Scopus, DOAJ, and Google Scholar. Various keywords were used in combination to conduct the searches, including CHM, TCM, pharmacokinetics, pharmacodynamics, ADME, bioavailability, herb–drug interactions, network pharmacology, systems pharmacology, metabolomics, multi-component herbal formulations, and therapeutic efficacy. Other studies were found by citation tracking of relevant articles and review papers. The sources were selected based on their relevance regarding the absorption, distribution, metabolism and excretion profile of herbals constituents, their pharmacodynamic profile, their molecular targets, therapeutic effects, safety profile and clinical applications. Special attention was given to research focusing on multi-component herbal formulations, herb–drug interactions, network pharmacology approaches, and new analytical technologies that are utilized for the evaluation of CHMs. The literature was subsequently sorted into thematic sections including pharmacokinetics process, pharmacodynamics mechanism, bioactive compounds, herb-drug interactions, network pharmacology, therapeutic uses and safety measures. The thematic organization enabled a thorough synthesis of what was already known and it was possible to discuss the mechanisms of effectiveness of CHMs critically.

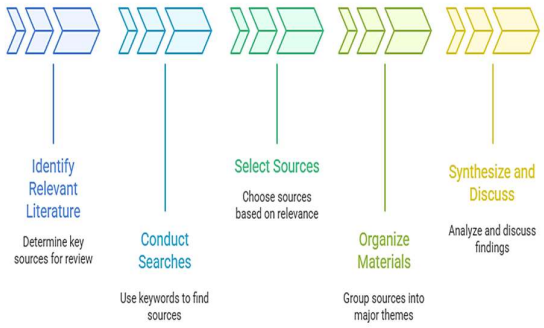

Figure 1. Overview of the Comprehensive Review Process

This study has followed the entire review process as represented in Figure 1. This comprised literature searches of the relevant information related to CHM, systematic searches of database by pre-determined keywords, selection of literature considering scientific relevance and quality, classification of collected literatures in main pharmacokinetic and pharmacodynamic topics, and integration of literature to evaluate the mechanisms, efficacy and clinical significance of CHMs. This methodological approach enabled integrating the current evidence and highlighting the areas of progress, problem areas, and future directions in CHM research.

3. Results

3.1 Fundamentals of Pharmacokinetics in CHM

The pharmacokinetics plays an important role in the understanding of therapeutic activities and safety of CHM. It states the absorption, distribution, metabolism and excretion (ADME) processes which dictates the fate of bioactive components following administration. CHM formulations consist of several ingredients which can interact and display intricate pharmacokinetic interactions, compared to single compounds used in conventional drugs. In recent years, the analytical methods have improved, and the composition of herb has been characterized and the metabolites have been identified which has enhanced the knowledge about the bioavailability and systemic exposure of herbs (Shi et al., 2018; Yan et al., 2018; Zhang et al., 2017). Moreover, the multi-component pharmacokinetic study has shown that the constituents in herbal formulas have dynamic interactions that impact therapeutic effects and safety (Xie et al., 2018; Li et al., 2022). The principle pharmacokinetic events associated with CHM are listed in Table 1.

Table 1. Major Pharmacokinetic Processes and Their Functions

Process	Description	Importance in CHM	Reference
Absorption	Uptake of herbal constituents from the gastrointestinal tract into systemic circulation	Determines bioavailability and therapeutic potential	Shi et al. (2018); Sun et al. (2019)
Distribution	Transport of absorbed compounds to tissues and organs	Influences target-site exposure and efficacy	Yan et al. (2018); Zhang et al. (2017)
Metabolism	Biotransformation of herbal compounds by enzymes and gut microbiota	Generates active or inactive metabolites affecting efficacy and safety	Li et al. (2022); Jia et al. (2022)
Excretion	Removal of compounds and metabolites through urine, bile, or feces	Determines residence time and toxicity risk	Yan et al. (2018); Zhang et al. (2017)

As illustrated in Table 1, each kinetic process is responsible for a large part of the overall therapeutic effect of CHM. The knowledge of these processes is crucial to optimize dosage, investigate herb–drug interactions, and ensure clinical use of TCMs (Jia et al., 2022; Shi et al., 2018).

3.2 Absorption, Distribution, and Bioavailability of Herbal Constituents

The therapeutic effectiveness of CHM is to a great extent dependent on the absorption and distribution of its bioactive components. Oral route of CHM is the most preferred but some herbal compounds are poorly soluble and low permeability, resulting in low bioavailability. There are several factors that influence the absorption efficiency, such as molecular structure, first-pass metabolism and intestinal transporters, and formulation strategies (Sun et al., 2019; Shi et al., 2018). The constituents of the herbs are absorbed, then distributed to different tissues and have pharmacological effects. Tissue affinity, plasma protein binding and the capacity of crossing physiological barriers like the blood-brain barrier (BBB) are responsible for their therapeutic potential (Yan et al., 2018; Zhang et al., 2017). The pharmacokinetics of CHM drugs are complex, and many drugs such as berberine, baicalin, ginsenosides and puerarin in CHM have been shown to have high inter-individual differences in bioavailability and tissue distribution (Zhang, 2019; Zhu et al., 2021). Currently, the important actors in the absorption and distribution process are presented in Table 2.

Table 2. Factors Influencing Absorption and Distribution of Herbal Compounds

Factor	Role	Impact on Pharmacokinetics	Reference
Solubility	Determines dissolution in gastrointestinal fluids	Low solubility reduces bioavailability	Sun et al. (2019); Shi et al. (2018)
Intestinal Transporters	Facilitate or restrict intestinal uptake	Influence absorption efficiency	Yan et al. (2018)
First-Pass Metabolism	Metabolic transformation before systemic circulation	Decreases active compound availability	Jia et al. (2022)
Tissue Distribution	Movement into target organs	Affects therapeutic efficacy	Zhang et al. (2017)
Plasma Protein Binding	Binding to serum proteins	Modulates free drug concentration	Jiao et al. (2018)

Blood-Brain Barrier Penetration	Entry into central nervous system	Determines neurological activity	Zhu et al. (2021); Zhang (2019)

The factors listed in Table 2 suggest that the absorption and distribution is highly dynamic and is dependent on physicochemical and biological factors. To improve the bioavailability and therapeutic effect of CHMs (Sun et al., 2019; Jia et al., 2022), it is crucial to optimize these factors.

3.3 Metabolism and Elimination of CHMs

Pharmacological activity and safety of CHM are crucial dependent upon metabolism and elimination. Herbal components are intensively metabolized (Phase I and Phase II reactions) after absorption. Phase II reactions, which are mainly catalyzed by glucuronidation and sulfation, are conjugation reactions that promote drug excretion, while Phase I reactions are oxidation, reduction, and hydrolysis reactions, most of which are mediated by the enzymes of the cytochrome P450 (CYP450) family (Jia et al., 2022; Zhang et al., 2017). Besides hepatic metabolism, the gut microbiota also has a significant role in metabolizing herbal constituents into bioactive or inactive metabolites, which impacts therapeutic effects (Li et al., 2022; Yan et al., 2018). The primary route of elimination is renal and biliary, and some compounds may remain in the body for longer via enterohepatic circulation (Shi et al., 2018). The major metabolic and elimination pathways of herbal constituents are summarized in Table 3.

Table 3. Major Metabolic and Elimination Pathways of Herbal Constituents

Pathway	Function	Pharmacokinetic Significance	Reference
Phase I Metabolism	Oxidation, reduction, and hydrolysis	Generates active or intermediate metabolites	Jia et al. (2022); Zhang et al. (2017)
Phase II Metabolism	Conjugation reactions	Enhances solubility and excretion	Yan et al. (2018)
CYP450 Enzymes	Enzymatic biotransformation	Major determinant of herb metabolism and interactions	Jia et al. (2022); Rombolà et al. (2020)
Gut Microbiota Metabolism	Microbial transformation of compounds	Produces bioactive metabolites and affects efficacy	Li et al. (2022)
Renal Excretion	Urinary elimination of metabolites	Major route of compound clearance	Shi et al. (2018)
Biliary Excretion	Elimination through the bile	Facilitates the removal of larger metabolites	Yan et al. (2018)
Enterohepatic Circulation	Reabsorption after biliary secretion	Prolongs systemic exposure	Zhang et al. (2017)

As indicated in Table 3, metabolism and elimination have a profound impact on the length, effectiveness and safety of herbal treatments. It is necessary to know these pathways to be able to predict herb–drug interactions, to optimize the dosage regimens, and to improve the clinical application of CHM (Jia et al., 2022; Shi et al., 2018).

3.4 Pharmacodynamic Mechanisms of CHM

The pharmacodynamic activity of CHM is due to the action of multiple bioactive components on various biological targets. CHM can work through receptor modulation, enzyme regulation, signal transduction pathways and gene expression changes – all of which are mechanisms by which conventional single-target drugs cannot work. Due to their anti-inflammatory, antioxidant, neuroprotective and immunomodulatory properties, these mechanisms have led to the potential pharmacodynamic targets and the effects of CHM. use of these compounds in the treatment of a wide range of diseases (Zhu et al., 2021; Liu & Liang, 2017). A large number of herbal compounds have multiple effects on several signaling cascades, which means they have more widespread effects and less potential for target resistance. Additionally, the synergistic effects of the multiple constituents in herbs are well illustrated in the pharmacodynamic effects, which is in accordance with the holistic therapeutic principle of TCM (Li et al., 2017; Zhou et al., 2017). Table 4 shows that the main

Table 4. Pharmacodynamic Targets and Biological Effects

Target/Mechanism	Biological Function	Therapeutic Effect	Reference
Receptor Modulation	Interaction with cellular receptors	Regulation of physiological responses	Zhu et al. (2021)
Enzyme Regulation	Activation or inhibition of enzymes	Control of metabolic and inflammatory processes	Liu & Liang (2017)
Signal Transduction Pathways	Modulation of intracellular signaling	Cellular protection and disease regulation	Zhu et al. (2021)
Gene Expression Regulation	Influence on transcriptional activity	Long-term therapeutic adaptation	Han et al. (2020)
Anti-inflammatory Activity	Suppression of inflammatory mediators	Reduction of tissue injury and disease progression	Zhu et al. (2021)

Antioxidant Activity	Neutralization of reactive oxygen species	Protection against oxidative stress	Li et al. (2017)

Table 4 shows that all the pharmacodynamic mechanisms of CHM are interconnected. This poly-targeted mode of action is one of the reasons for the effectiveness of herbal remedies in complex diseases that involve several disease pathways (Zhu et al., 2021; Han et al., 2020).

3.5 Multi-Component and Multi-Target Actions of Herbal Formulas

One of the unique features of CHM is its multi-component and multi-target therapeutic action. In herbal formulas, she's likely to find a number of bioactive compounds, which work together to control multiple biological pathways at once. This synergistic effect not only improves therapeutic effectiveness but may also help to limit side effects when compared with single-compound therapies (Li et al., 2022; Du et al., 2021). TCM principle: match like with like, to enhance the and their effects. beneficial effects of the herbs, optimize their absorption, and reduce toxicity. The contemporary pharmacological analysis of herbs has identified that their preparations can have an impact on interconnected molecular networks that play a role in regulating inflammation, oxidative stress, metabolism, and immunity (Zhou et al., 2017; Liu & Liang, 2017). The concept that herbal formulas work by modulating a series of targets is further supported by systems-level pharmacology. Table 5 shows some examples of synergistic herbal products

Table 5. Examples of Synergistic Herbal Formulations and Their Mechanisms

Herbal Formula/Approach	Mechanism of Action	Therapeutic Significance	Reference
Baoyuan Decoction	Multi-component regulation of metabolic pathways	Protection against cardiac hypertrophy	Du et al. (2021)
Multi-Herb TCM Formulas	Synergistic enhancement of bioactive constituents	Improved efficacy and reduced toxicity	Li et al. (2022)
Compatibility-Based Prescriptions	Optimization of herb combinations	Enhanced pharmacological outcomes	Zhou et al. (2017)
CHM–Western Medicine Combinations	Complementary pharmacodynamic actions	Improved clinical effectiveness	Liu & Liang (2017)
Systems Pharmacology Models	Network-level target regulation	Comprehensive disease management	Li et al. (2022)

The effectiveness of CHM formulations is mainly due to synergisms between several compounds and multiple targets, as presented in Table 5. The results reflect the holistic therapeutic conception of TCM, and also demonstrate the significance of system-based approaches to the effectiveness of herbal medicine (Du et al., 2021; Zhou et al., 2017).

3.6 Herb–Drug Interactions and Clinical Implications

One important consideration for the clinical use of CHM is herb–drug interactions especially for those taking conventional pharmaceuticals. Such interactions may be pharmacokinetic, which is a change in the way the drug is absorbed, metabolized, distributed or excreted, or pharmacodynamic, which is an additive, synergistic or antagonistic therapeutic effect (Jia et al., 2022; Rombolà et al., 2020). Plasma levels and the therapeutic effect of drugs may be altered by many herbal constituents, which affect the activity of cytochrome P450 enzymes and/or drug transporters. Significant interactions with anticoagulants, antiplatelet agents and anticancer medications have been reported (Singh & Zhao, 2017; Cheng et al., 2018). These interactions must be known to make sure the treatment is safe and reduce side effects, as well as improve medication combinations with herbs and conventional drugs. Table 6 summarizes the major herb–drug interactions reported in the literature.

Table 6. Clinically Relevant Herb–Drug Interactions

Drug/Class	Type of Interaction	Clinical Consequence	Reference
Warfarin	Pharmacokinetic and pharmacodynamic	Increased bleeding risk and altered anticoagulant activity	Choi et al. (2017)
Anticancer Drugs	Altered metabolism and drug disposition	Modified efficacy and toxicity profiles	Cheng et al. (2018)
Clopidogrel	Effects on platelet aggregation and metabolism	Changes in antiplatelet response	Hu & Wang (2019)
CYP450 Substrate Drugs	Enzyme induction or inhibition	Altered plasma drug concentrations	Jia et al. (2022); Rombolà et al. (2020)
Multiple Prescription Drugs	Transporter-mediated interactions	Unpredictable therapeutic outcomes	Singh & Zhao (2017)

Herb–drug interactions are relevant to clinical practice in today's medical environment, as emphasized in Table 6. A careful consideration of these interactions is essential for enhancing patient safety and for rationalizing the use of CHM in traditional treatments (Rombolà et al., 2020; Jia et al., 2022).

3.7 Advanced Approaches for Understanding CHM Mechanisms

The last decade saw tremendous advances in technology that increased the knowledge and understanding of the intricate pharmacological processes of CHM. Compared with traditional reductionist methods, the multi-component herbal formulations require a more comprehensive analysis approach due to their complexity, which becomes more and more significant by systems-based methods like network pharmacology, chinmedomics, pharmacometabolomics, and multi-omics integration (Han et al., 2020; Lai et al., 2020). These strategies allow for detection of active compounds, molecular targets, metabolic pathways, and biomarker responses to be detected concurrently. With the aid of the network pharmacology, the multi-target property of CHM can be clarified; Chinmedomics combines metabolomics with therapeutic evaluation and can be used to find efficacy-related biomarkers (Han et al., 2020). Likewise, pharmacometabolomics has shed light on the synergistic mechanism of action and the effects of herbal preparations on metabolically related networks of disease (Du et al., 2021). These are the dominant analytical methodologies being used in CHM research today and are outlined in Table 7.

Table 7. Modern Analytical Approaches in CHM Research

Approach	Primary Application	Research Significance	Reference
Network Pharmacology	Identification of compound–target interactions	Reveals multi-target therapeutic mechanisms	Lai et al. (2020)
Chinmedomics	Biomarker discovery and efficacy evaluation	Links metabolic changes with therapeutic outcomes	Han et al. (2020)
Pharmacometabolomics	Analysis of metabolic responses to treatment	Explains synergistic mechanisms of herbal formulas	Du et al. (2021)
Multi-Omics Integration	Integration of genomics, proteomics, and metabolomics	Provides comprehensive systems-level understanding	Han et al. (2020)
Poly-Pharmacokinetic Analysis	Simultaneous evaluation of multiple constituents	Characterizes complex herbal formulations	Xie et al. (2018)
Quality Marker (Q-Marker) Analysis	Identification of efficacy-related compounds	Supports quality control and standardization	He et al. (2018)

Table 7 illustrate that the advanced analytical technologies offer strong capabilities in understanding the complex mechanisms of CHM. These methods allow for the evaluation of the effectiveness of these products, quality control and modernization of the research of traditional herbal medicine through evidence-based methods (Han et al., 2020; He et al., 2018).

3.8 Therapeutic Applications, Safety, and Future Perspectives

The multi-target pharmacological activities of CHM have been shown to have therapeutic potential in a broad spectrum of diseases. Many studies have been published which showed its positive effects on cardiovascular diseases, ischemic stroke, cancer, metabolic disorders, inflammatory diseases, and osteoporosis, among others, through its antioxidant, anti-inflammatory and immunomodulatory effects (Zhu et al., 2021; Liu et al., 2017). Despite these advantages, toxicity, product variation, contamination and misuse are still major concerns. Some herbal remedies can contain substances that are toxic or may contain heavy metals, such as mercury containing remedies, which need to be monitored carefully (Zhao et al., 2022). To overcome these problems it has been suggested that herbal products can be standardized, assured for quality and optimized for clinical efficacy by implementing quality marker (Q-marker) strategies (He et al., 2018). Advanced pharmacokinetic and pharmacodynamic studies and systems biology studies are expected to enhance the scientific foundation and world-wide acceptance of CHM in the future. A summary of the main therapeutic uses, safety issues and quality control points is provided in Table 8.

Table 8. Therapeutic Applications, Safety Issues, and Quality Control Considerations

Area	Key Findings	Clinical Significance	Reference
Cardiovascular Diseases	Multi-target cardioprotective effects	Improved cardiac function and disease management	Du et al. (2021)
Ischemic Stroke	Neuroprotective and antioxidant activities	Reduction of neuronal injury	Zhu et al. (2021)
Cancer	Adjunctive therapeutic benefits	Enhanced treatment outcomes and supportive care	Cheng et al. (2018)
Metabolic Disorders	Regulation of metabolic pathways	Improved metabolic homeostasis	Li et al. (2022)

Osteoporosis	Promotion of bone health and remodeling	Prevention of bone loss	Liu et al. (2017)
Toxicity Concerns	Potential adverse effects and contamination risks	Need for safety evaluation	Fan et al. (2019); Li & Wang (2020)
Mercury-Containing Preparations	Risk of heavy metal exposure	Requires strict monitoring and regulation	Zhao et al. (2022)
Quality Markers (Q-Markers)	Identification of efficacy-related compounds	Supports standardization and quality control	He et al. (2018)

As shown in Table 8, CHM has a wide therapeutic range and has significant safety and quality control issues. Ongoing standardization, pharmacovigilance, and mechanistic studies will play a critical role in maximizing therapeutic benefits and safe integration of CHM into the conventional healthcare systems (He et al., 2018; Zhao et al., 2022).

4. Discussion

The results of this review show that the pharmacokinetic (PK) and pharmacodynamic (PD) characteristics of CHM strongly interact with each other and both are critical for therapeutic efficacy. Pharmacokinetic processes affect the amount of active components available to the target tissues, and pharmacodynamic processes affect the biological processes triggered by the compounds. The pharmacological activity of bioactive components is not enough to explain the therapeutic efficacy, as the mode of absorption, metabolism, distribution and elimination of these components also plays a crucial role (Li & Wang, 2020; Li et al., 2017; Chen et al., 2023). Thus, a combined PK–PD approach is crucial to gain insight into the mechanism of CHM efficacy and safety.

CHM's multi-component composition and multi-target mode of action are one of the defining characteristics of CHM. Herbal medicines have several bioactive compounds that can act on multibranched biological pathways, whereas traditional medicine is usually targeted at a single molecular target. This complexity can help increase the overall therapeutic benefits and decrease the likelihood of single-target failure. Herbal medicines have been shown to have therapeutic effects through synergistic multi-gene, multi-protein and multi-signaling pathway interactions in network pharmacology studies (Lai et al., 2020; Hong et al., 2017). In addition, studies have been performed on medicinal plants like Zanthoxylum bungeanum, Xanthium strumarium and Fructus Ligustri Lucidi, revealing the various pharmacological activities resulting from the synergistic interaction of their constituents (Zhang et al., 2017; Fan et al., 2019; Chen et al., 2017). They are in line with the classical view of the effectiveness of CHM as the result of the multiple action of several active molecules.

With the increasing use of CHM in contemporary healthcare, the significance of PK/PD research for evidence-based clinical practice is emphasized. While pharmacokinetic research offers valuable insights into dosage optimization, bioavailability, and safety, pharmacodynamic studies shed light on the therapeutic mechanisms and potential clinical benefits. This type of data is relevant to the management of chronic diseases and to an integrative treatment. The use of traditional herbal medicines in scientifically proven therapies is gaining recognition in clinical pharmacology frameworks (Marshall, 2020). Furthermore, investigations of interactions between herbal medicines and antiplatelet medications like clopidogrel highlight the importance of scrutinizing PK and PD interactions in clinical practice (Hu & Wang, 2019). The better understanding of these interactions can help to make CHM use more safe and effective with traditional treatments.

Although significant progress has been made in CHM research, it is difficult to apply the research results to a routine clinical setting. Numerous studies are performed in controlled laboratory settings that may lack the complexity of the clinical environment in real practice. A considerable amount of variability exists in the composition, cultivation, processing and formulation of herbs, which may result in different PKs and therapeutic effects. Furthermore, the failure to have standardized quality control adds to the difficulty of comparing between studies and reduces the ability to repeat. Clinical translation is also challenged by safety issues of some herbal preparations, such as toxicity and contamination (Zhao et al., 2022; Fan et al., 2019). All of these factors underscore the importance of strict standardization, high-quality clinical trials and harmonization of regulations to facilitate wider acceptance of CHM in clinical practice.

There are still some constraints that hinder the establishment of solid scientific evidence for CHM. Firstly, multi-component herbal products are complicated to determine the specific active compounds, and to establish a definitive PK–PD relationship. Secondly, most published studies have been conducted with isolated constituents and not the whole herbal formula as used in clinical practice. Third, experimental designs, methods of analysis, and measures of outcomes are subject to change across experiments, which makes it difficult to compare findings across studies. In addition, toxicological information on many traditional medicines is still lacking, even though the growing awareness of the safety concerns associated with some herbs and mineral-based formulations is a growing problem (Zhao et al., 2022; Chen et al., 2023). Solving these challenges will necessitate collaboration between various disciplines, including pharmacology, clinical, toxicology and regulatory fields.

Future studies and research should be focused on the integration of advanced technologies and traditional

pharmacological strategies to gain a better understanding of CHM. AI in drug discovery provides a chance to discover new bioactive molecules and forecast potential drug targets more effectively (Singh et al., 2022). Precision herbal medicine and personalized therapy strategies that consider individual genetic, metabolic and clinical features may allow for tailored treatment strategies. Omics technologies such as genomics, proteomics, metabolomics and transcriptomics can give holistic insight into the mechanisms of action of herbal medicines (Lai et al., 2020). Moreover, physiologically based pharmacokinetic (PBPK) modeling can improve the absorption, distribution, metabolism, excretion, and herb–drug interactions predictions in various patient populations (Marshall, 2020). These developing approaches will help accelerate the modernization of CHM research, and allow its utilization in an evidence-based healthcare system without compromising its holistic principles used for centuries.

5. Conclusion

CHM turns out to be a completely new therapeutic system with multi-component composition, multi-target action and rich history of clinical use. This review concludes that the efficacy of CHM can be affected by a complex pharmacokinetic/pharmacodynamic relationship. Herbal constituents with several pharmacodynamic effects induce molecular, cellular and physiological responses, which are highly dependent on the factors of their absorption, distribution, metabolism and excretion. These processes are related to the therapeutic efficacy observed in a wide variety of diseases including cardiovascular, ischemic stroke, metabolic, inflammatory and osteoporosis. Another key point is the principle of compatibility, which is the synergic interaction of the constituents of the herbs, and is not possible with the conventional single target remedies, as reviewed above. However, there is a challenge of product standardization, quality control, herb–drug interactions and variability in clinical responses for wider acceptance and implementation. Thanks to the development of network pharmacology, omics technologies, and artificial intelligence and physiologically based pharmacokinetic modeling these are all overcome and the scientific basis of CHM is strengthened. Future studies should also focus on the integration of traditional herbal medicine and modern biomedical approaches to facilitate the more effective evaluation of efficacy, safety and the development of personalized and evidence-based herbal medicine to be used in the global healthcare system.

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