Herbal Drug Interactions: Investigating Safety and Efficacy in Asian Traditional Medicine

Md Shahadat Hossan[1], Mohammed Rahmatullah[2*], Rownak Jahan [2]

Abstract

Asia and South Asia have long been the centers of traditional medicine in the field of healthcare, with a key role for herbal treatments in recovery and well-being. But as modern pharmaceuticals develop, there's reason for concern about possible drug interactions between herbal remedies and contemporary medications. In order to improve patient safety and treatment efficacy, this abstract highlights the necessity of looking into and comprehending these interactions. Herbal medicine has long been used throughout Asia and South Asia, where it is widely accepted as a standard component of both cultural and medical practices. The natural and comprehensive approach to healing that these herbal treatments are said to provide makes them highly sought after. However, using these herbal remedies in addition to conventional medications raises questions regarding possible interactions that could jeopardize patient safety and therapeutic results. Investigating the complex network of herbal-drug interactions, this review focuses on herbs that are widely utilized in South and Southeast Asia. By examining the effects of these interactions on the effectiveness and safety of traditional medications, the study seeks to clarify the nature of these interactions. The review aims to pinpoint particular herbs and herbal combinations that have either antagonistic or synergistic effects with contemporary medications This information will be crucial for creating treatment programs that minimize risks and optimize therapeutic benefits, eventually enhancing patient safety and wellbeing. Both practitioners of traditional medicine and the contemporary healthcare system should gain from the study's findings, which will support an integrated approach to patient treatment. Healthcare providers can choose the best course of action for their patients by raising understanding about herbal medicine interactions and the possible side effects. This review also describes how to persuade regulatory agencies to create rules and regulations that guarantee the safe coadministration of conventional medications and herbal remedies. To sum up, research on herbal medication interactions in the framework of Asian traditional medicine is essential to improving patient safety and therapeutic effectiveness.

Keywords: Herbal drug interactions, Asian traditional medicine, safety, efficacy, conventional pharmaceuticals, Asia, South Asia.

Significance | Asia's rich tradition of herbal medicine intersects with modern pharmaceuticals, prompting research into herbal-drug interactions for enhanced safety and efficacy.

*Correspondence. Mohammed Rahmatullah, Department of Biotechnology & Genetic Engineering, University of Development Alternative, Dhaka, Bangladesh.
E-mail: rahmatm@uoda.edu.bd

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Introduction

A long-standing practice of using herbal therapy has been fostered for ages by the many cultures of Asia and South Asia. Herbal medicines have been widely used in Traditional Chinese Medicine (TCM), Indian Ayurveda, and other traditional healing systems in these regions. Communities and their healthcare decisions have developed a strong bond as a result of the traditional value and historical significance of these herbal remedies (World Health Organization, 2002). Herbal medicines, s ometimes known as

Author Affiliation.
[1] School of Pharmacy, University of Nottingham, UK
[2] Department of Biotechnology & Genetic Engineering, University of Development Alternative, Dhaka, Bangladesh

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traditional or botanical medicines, are a broad category of medicinal remedies derived from plants. Plant leaves, roots, stalks, flowers, and other natural substances are a few examples of these sources. These medicines can be used topically, orally, or by other means to treat a variety of medical conditions. In many Asian and South Asian societies, these treatments are an integral element of healthcare procedures, having their roots in traditional knowledge systems that have been passed down through the generations (Chopra et al., 1956).Asian nations have a long history of using herbal treatments; historical records go all the way back to ancient times. Herbal medicines like ginseng and ginkgo biloba have been utilized for thousands of years in traditional Chinese medicine (TCM) (Dhar et al., 2015). Ayurveda is a comprehensive medical approach that originated in South Asia. To balance the body and mind, a variety of botanical components are used (Rastogi et al., 2015). The region's healthcare decisions are still influenced by these customs.In Asia, the use of herbal medicines is still very common. Herbal remedies are extensively utilized in India, particularly in rural regions where they are frequently the main source of healthcare, according to a study by Shinde et al. (2016). Similar to this, TCM is still used in China in addition to modern treatment, and prescriptions for herbal medicines are common (Xu et al., 2013). These behaviors show that herbal therapy is still a significant component of the local healthcare system.Potential interactions are a problem when herbal and conventional medicine combine. Izzo et al. (2016) stress that in order to prevent negative impacts, it is important to look into these interactions. For instance, it has been demonstrated that the popular herbal medicine St. John's Wort interacts with a number of prescription drugs, potentially reducing their effectiveness (Nemer et al., 2017).

Although there are many advantages to using herbal remedies in Asian and South Asian cultures, there are drawbacks as well. Variations in efficacy and safety can result from a lack of standardization and quality control, particularly in traditional formulations. Regulatory agencies such as the China Food and Drug Administration (CFDA) and the Indian Pharmacopoeia Commission (IPC) are actively drafting quality assurance standards in response to these concerns (Liu et al., 2016; Garg et al., 2014).There is also ongoing research into the medicinal potential of herbal remedies. Promising fields have been brought to light by recent research, including the usage of Asian ginseng (Panax ginseng) for potential anticancer effects and turmeric (Curcuma longa) for treating inflammatory diseases (Basnet & Skalko-Basnet, 2011). (Yun & Choi, 2013). These investigations add to an expanding corpus of research that emphasizes the validity of herbal medicine use from a scientific standpoint.These interactions emphasize how crucial it is to make well-informed healthcare decisions when combining pharmaceutical and herbal treatments at the same time.It is essential to guarantee the efficacy and safety of herbal remedies. The Indian Ministry of Ayurveda, Yoga, Naturopathy, Unani, Siddha, and Homoeopathy (AYUSH) and the Chinese State Food and Drug Administration (SFDA) are two regulatory authorities that are essential to the standardization of herbal goods (Panda et al., 2019). According to Ekor (2013), scientific study validates herbal medicines with evidence, which increases their safety and legitimacy. Protecting patient health requires both encouraging appropriate use and maintaining quality control.The close cultural ties between Asian and South Asian cultures are among the main benefits of herbal treatments. Because of their cultural familiarity and beliefs, patients frequently favor these traditional medicines. According to Verma et al. (2016), this preference may have a positive effect on treatment results overall and patient compliance. Healthcare professionals must respect patients' cultural preferences while making sure they are informed and aware of any possible interactions with prescription drugs.The possibility of drug interactions with prescription pharmaceuticals is a pertinent safety concern related to the use of herbal remedies (Ernst et al., 2000). This matter is particularly crucial when it comes to medications like digoxin and warfarin that have a limited therapeutic index (Izzo et al., 2004).

According to recent studies, up to 16% of people who take prescription drugs also take herbal supplements. Herbal cures are frequently promoted on the Internet with deceptive and unverified promises, which exacerbates the issue. People still mistake "natural" for safe despite constant cautions. Healthcare providers need to be more aware of potential difficulties as the use of herbal treatments increases and reports of negative effects keep coming in. There are several goods on the market right now that have been connected to poisoning. This article's goal is to draw attention to the clinical interactions that exist between prescription medications and herbal treatments. Now, we provide details on the many methods used to investigate the interactions between herbs and medications that involve drug metabolism transporters and enzymes. Theoretical interactions between herbs and drugs, derived from in vitro investigations, animal research, and there are further sources of hypothetical empirical evidence (Marechal1 et al., 2008). Herbal medicines in Asian and South Asian cultures have a rich history and continue to be widely used. To maximize their benefits and minimize risks, it is imperative to investigate interactions with conventional pharmaceuticals and ensure

safety and efficacy. As these traditional practices intersect with modern healthcare, a holistic approach, guided by scientific research and regulatory oversight, is essential.

Understanding the Role of Herbal Medicines in Asia

For millennia, Asian traditional medical systems have used herbal medicine as a crucial component. The cultural, historical, and philosophical views of many Asian countries are strongly ingrained

in the usage of medicinal herbs and natural cures. Three main facets of the use of herbal medicines in Asia are examined in this review are the function of Traditional Chinese Medicine (TCM), Ayurveda, and other local herbal medicine systems; and the holistic ideas that support these systems, emphasizing harmony and balance. We hope to clarify the role that herbal remedies play in fostering health and healing in Asia through this review.

TCM, or traditional Chinese medicine, is an age-old practice with strong roots in holistic ideas. The idea of Qi, or life energy, and the balance between Yin and Yang energies are central to it. TCM uses a wide range of herbs in its pharmacopeia to bring this equilibrium back. In a clinical trial published in 2017, Wu et al. Showed how well TCM herbal treatments worked for a wide range of ailments, including chronic pain, gastrointestinal issues, and cardiovascular problems.TCM includes herbal treatment as well as techniques like moxibustion, acupuncture, and acupressure that are all intended to balance the body's energy flow.Another traditional and all-encompassing herbal medical system is Ayurveda, which has its roots in India. The equilibrium of the three doshas Vata, Pitta, and Kapha lays the groundwork for it. Herbal remedies are customized by Ayurveda to address each person's particular imbalances and constitution. Studies conducted by Sharma and Gupta (2018) have demonstrated the effectiveness of Ayurvedic herbal formulations in the treatment of inflammatory diseases, diabetes, and skin ailments.In Asia, there are several different traditional herbal treatment systems in addition to Ayurveda. Two prominent instances, each profoundly ingrained in their respective historical traditions and cultural contexts, are Hanbang in Korea and Kampo in Japan. Kampo has been shown to have potential in treating respiratory disorders by Kim et al. (2019), while Hanbang herbal formulations have been utilized to treat a variety of medical ailments.

These herbal medicine systems have one thing in common: they emphasize the search of harmony and balance as a holistic approach to health. These methods take into account not just the physical symptoms but also the patient's emotional and mental health. In their 2020 study, Zhang et al. addressed the use of Traditional Chinese Medicine in the holistic nursing care of cancer patients, utilizing herbal remedies to ease physical discomfort and enhance mental and emotional health.In addition, these holistic methods support dietary changes, exercise, and meditation as vital lifestyle choices that help one attain and preserve a condition of harmonious health.In conclusion, herbal medicines in Asia, exemplified by TCM, Ayurveda, and various regional systems, are rich and integral parts of the region's healthcare practices. Their holistic philosophies and the emphasis on balance and harmony offer unique perspectives on health and healing. Extensive research consistently affirms the efficacy of herbal treatments within these systems, reaffirming their relevance in modern healthcare.

Chemicals present in herbal products

There is a common misperception among consumers of herbal goods that, due to their natural source, herbal treatments are safe for human health. The fact that these "all natural" extracts are essentially a mixture of potentially biologically active components that present in these marketed products in unknown levels is not well understood or appreciated by the general public. The last ten years have seen a sharp increase in the usage of herbal products in the US as a result of patients looking for a "all natural" substitute for traditional western medicine. Many of the structurally varied compounds found in herbal remedies that are marketed either have inherent pharmacological activity or even exhibit potential toxicity. Among the more widely used herbal remedies Two well-known herbal remedies that are sold to cure depression and liver problems, respectively, are milk thistle and St. John's wort (Jacobs et al., 2002, Rodriguez et al., 2003, Chavez et al., 2006). When treating mild to severe depression, St. John's wort may be more beneficial than conventional medication, according to a number of clinical trials and case reports (Linde et al., 1996, Wheatley et al., 1997, Hussain et al., 2009). Research both in vivo and in vitro have demonstrated that components of St. John's wort prevent neurotransmitters associated with depression in people from being reabsorbed (Nathan et al., 1999).An extract of Hypericum perforatum's blooming part, known as St. John's wort, is a complex mixture of many chemicals that are both biologically active and complicated (Figure 1). Hypericin, or napthodianthrone, comes in capsule form and is used as about the advertised product's standardization.

One of the most popular unconventional remedies, especially in Germany, is milk thistle extract (Silybum marianum (L.) (Family: Asteraceae). In clinical settings, milk thistle has been used to treat a range of liver conditions and is currently being researched as a therapy for prostate cancer. Numerous flavonolignans, which are substances created in plants by the radical coupling of a flavonoid and a phenylpropanoid, have been found to be present in milk thistle (Dewick et al., 1997). According to Wagner et al. (1986), silymarin, a combination of various flavonolignans, is mostly made up of silybin (about 50–70%), silychristin, silydianin, and other closely related flavonolignans (Figure 2). At least 70% silymarin is included in a standardized milk thistle extract (Foster et al., 1999, Schulz et al., 2001). The information above makes it evident that herbal extracts contain a variety of structurally distinct chemical ingredients. The kidneys or the liver must be used to remove these substances from the body.

Biological description of Cytochrome P450

Human CYP enzymes that are involved in drug metabolism are mostly expressed in the liver. But it's also found in the brain, lungs, and intestines—both small and large. These proteins are insoluble and have intricate structural and mechanistic characteristics. They are attached to the endoplasmic reticulum. But since the first crystal

structures of the mammalian CYP enzymes, CYP2C5, CYP2B4, CYP2C9, and CYP3A4, were recently discovered (Paul et al., 1996, Meunier et al., 2004), significant advancements in this field can be anticipated soon.It is estimated that 15–20 distinct CYP enzymes are involved in the liver's role in drug metabolism in humans. The most significant CYP enzymes among them, however, are thought to be 1A2, 2C9, 2C19, 2D6, 2E1, and 3A4 (Werck et al., 2000, Degtyarenko et al., 1995, Guengerich et al., 2006, Guengerich et al., 1997). They can metabolize a wide variety of xenobiotics and have distinct but complementary substrate specificities. More than 50% of medicines are known to be metabolized in the liver by CYP3A4, which works on most lipophilic substrates (Munasinghe et al., 2002). In contrast, CYP2D6 prefers positively charged compounds, typically those that contain basic nitrogen.

Weakly anionic compounds are metabolized by CYP2C9, poly-aromatic hydrocarbons by CYP1A2, and tiny, soluble organics by CYP2E1. Therefore, practically any organic xenobiotic can be metabolized by the CYP systems. Medications have the ability to change the activity of one or more CYP enzymes, which modifies how quickly the drug is broken down and eliminated from the body. This has two possible outcomes. When a medication activates a CYP protein, the drug may become ineffective due to CYP's rapid excretion from the body. On the other hand, CYP may not be able to stop a drug from building up to hazardous levels when it inhibits a CYP protein, even to the point where an overdose occurs. Among CYP, CYP1, CYP2, CYP3, and CYP4 are the most crucial for drug biotransformation.Most common in the body, CYP3A4 is known to metabolize a number of medications (Glue et al., 1999, Robertson et al., 2005,Warrington et al,2005).

Herbal Drugs Interaction (HDI)

When food, alcohol, or other substances are present along with one or more drugs, the effects of the drugs are said to interact. [Stockley and others, 2002]. An interaction with potential clinical significance occurs when a therapy combination has the potential to cause an unanticipated change in the patient's state. The overall result of the combination could be the generation of idiosyncratic effects, antagonistic or adverse effects of one or more medications, or synergism or additive impact of one or more pharmaceuticals (Grenier et al. 2003).An effect that one drug has on another is known as a drug-drug interaction. Drug-drug interactions are not limited to the senior population and can be either pharmacokinetic or pharmacodynamic in character (Nebert et al., 2002, Christians et al., 2005). Pharmacokinetics, or the way the body processes drugs, includes the impact of one medication on another's distribution, excretion, metabolism, or absorption. These exchanges may lead to variations in serum medication concentrations that could impact the clinical outcomePharmacodynamics, or the effects of a drug on the body, is related to the pharmacological activity of interacting drugs; the result is an amplification or decrease in the therapeutic effects or side-effects of a particular drug. The most common pharmacokinetic drug–drug interactions involve several isoenzymes of the hepatic cytochrome P450 (CYP) and drug transporters such as the P-glycoprotein and organic anion transporters (Bista et al., 2006, Lee and Stockley, 2003).

Mechanism of herbal-drug interactions

Herbal remedies adhere to contemporary pharmaceutical theories. Hence, pharmacokinetic (PK) or pharmacodynamic (PD) mechanisms may be used to describe herb–drug interactions. More research has been done on pharmacokinetic interactions. In vitro and in vivo studies suggest that the altered drug concentration caused by co-administered herbs may be related to the induction or inhibition of drug transporters like P-glycoprotein and/or hepatic and intestinal drug-metabolizing enzymes, especially Cytochrome P-450 (CYP) (Boullata et al., 2005, Hussain et al., 1999). The most significant Phase I drug-metabolizing enzyme system, the CYP, is in charge of many different medications' metabolism. Numerous plants (like St. John's wort) and naturally occurring substances that have been extracted from plants (including flavonoids, coumarins, furanocoumarins, anthraquinones, and caffeine) and terpenes) have been found to either activate or inhibit certain CYP enzymes as substrates (Dietary Supplement-A- 2005). In particular, research has demonstrated that prolonged (2 weeks) treatment of St. John's wort considerably increased CYP3A4 in the colon and liver, as well as perhaps additional CYP enzymes, are involved in the metabolism of medicines. Additionally, a clinical trial conducted on 12 healthy individuals revealed that echinacea influenced CYP3A's catalytic activity at intestinal and hepatic locations (inhibition of intestinal CYP3A4 and activation of hepatic CYP3A4). Pglycoprotein in the intestine, liver, and kidney may play a significant role in the absorption, distribution, or excretion of drugs. Pglycoprotein appears to limit the cellular transport from intestinal lumen into epithelial cells and also enhances the excretion of drugs out via hepatocytes and renal tubules into the adjacent luminal space. In contrast, a number of herbal medicines, including Green tea, Ginkgo garlic, Saw palmetto, and Siberian ginseng, do not affect CYP3A4 and CYP2D6 activities in normal volunteers.St. John's wort contains a compound called hyperforin, which binds to the orphan pregnane X receptor and causes a sequence of intracellular processes that cause P-glycoprotein and CYP3A4 to be expressed. Additionally, a few pharmacodynamic interactions have been documented. Pharmacodynamic interactions can be antagonistic, in which the herbal medicine lessens the effectiveness of synthetic drugs (e.g., kava possesses dopaminergic antagonistic properties and hence reduces the pharmacological activity of the anti-Parkinson drug levodopa), or additive (or synergetic), in which the herbal drug potentiates the action of synthetic drugs (e.g., interaction between the anticoagulant warfarin with antiplatelet herb) (Izzo et al., 2005).

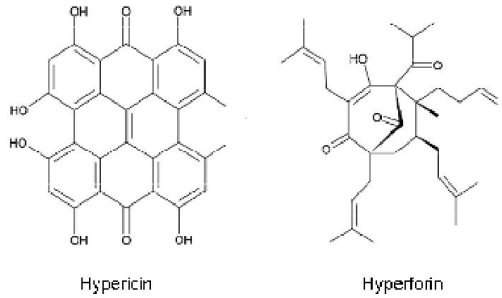

Figure 1. Chemical structures of hypericin and hyperforin, biologically active constituents of St John'swort

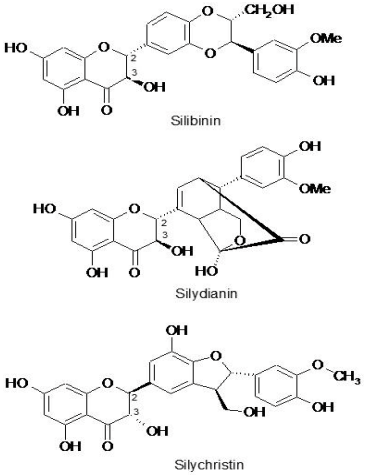

Figure 2. Chemical structures of silybin, silychristin, silydianin, biologically active constituents of Milk thistle

Table 1. Some clinically significant drug-herb interactions

Herbal drugs	Biological source	Interaction reported or suspected
Ginkgo	Ginkgo biloba	Concurrent use of ginkgo and nonsteroidal antiinflammatory agents may result in an increased risk of bleeding and with warfarin causes bleeding. (Meisel et al., 2003).
Garlic	Allium sativum	Concurrent use of garlic and anticoagulants result in increased risk of bleeding. (Legnani et al., 1993)
Ginger	Zingibar officinale	Concurrent use of ginger and anticoagulants may result in increased risk of bleeding, sulfa guanidine enhance absorption. (Kruth et al., 2004)
Ginseng	Panax ginseng	Concurrent use of ginseng and antidiabetic agents may result in increased risk of hypoglycemia. (Vuksan et al., 2000
St. John's wort	Hypericum perforatum	Concurrent use of digoxin and St John's wort may result in reduced digoxin efficacy. (Hennessy et al., 2003)
St. John's wort	Hypericum perforatum	Warfarin (cause bleeding); serotonin-uptake inhibitors (cause mild serotonin syndrome); indinavir (decreased bioavailability); digitoxin, theophylline, cyclosporin, phenprocoumon and oral contraceptives reduces bioavailability. (Cupp et al., 1999)
Rhubarb	Rheum officinale	Cardiac glycosides and anti-arrhythmic agents potentiates by reducing potassium via laxative effect. (Westendorf, 1993)
Astragalus	Astragalus membranaceus	Cyclosporine, azathioprine, methotrexate impair immunosuppressive effects.
Licorice	Glycyrrhiza uralensis	Corticosteroids and thiazide diuretics potentiating; digitalis or other cardiac glycosides increases sensitivity (Mu et al.,2006)

List of herbal drug interactions

A list of herbal drugs is shown in Table 1.

Promoting Safe and Informed Healthcare Choices

Encouraging patients to make safe and knowledgeable healthcare decisions is essential to patient-centered care and can greatly enhance health outcomes. This review of the literature looks at the importance of honest communication between patients and healthcare professionals, educating people about possible conflicts, and balancing innovation with tradition in the field of medicine. Making safe and well-informed healthcare decisions is contingent upon effective communication between patients and healthcare providers. Numerous research works highlight the significance of this variable in enhancing patient contentment, treatment plan compliance, and general health results (Street et al., 2003; Stewart et al., 2000). Patients are more likely to comprehend their diseases, available treatments, and associated dangers if they actively participate in their healthcare decisions. More favorable health outcomes result from this collaborative approach's ability to customize treatment to meet each patient's needs (Epstein and Street, 2007).Interactions between medications and treatments may have a serious negative impact on patient safety. Both patients and healthcare providers need to be aware of these connections. Raising awareness requires both education and the sharing of knowledge. Healthcare professionals must keep up with the most recent findings on drug interactions and educate patients about the possible hazards of combining drugs or therapies (Muth, 2008; Leape et al., 1995). In this context, electronic health records and patient education initiatives can be useful resources (Aspden et al., 2006).While it may seem that tradition and innovation in healthcare are at odds, striking a balance is essential to encouraging people to make safe and knowledgeable healthcare decisions. Although evidence-based medicine may not always coincide with traditional healthcare practices, they may have cultural and historical importance. On the other hand, innovation advances medical diagnosis and treatment, but it can also ignore the benefits of conventional methods. To ensure that patients receive the most effective and culturally sensitive care possible, striking a balance entails incorporating the best of both worlds (Greenhalgh et al., 2004). multidisciplinary care teams and integrative medicine models can help achieve this equilibrium (Jonas et al., 2003). Promoting safe and informed healthcare choices is a multifaceted endeavor that requires open communication between patients and healthcare providers, raising awareness about potential interactions, and striking a balance between tradition and innovation in healthcare. The integration of these three elements can lead to improved patient outcomes, increased patient satisfaction, and a healthcare system that respects both evidence-based practices and individual preferences. As healthcare continues to evolve, the emphasis on these factors remains essential for a patient-centered approach to healthcare decision-making.

Future recommendations and challenges

Research and Clinical Trials: To have a better understanding of the interactions between herbal treatments and conventional pharmaceuticals, more research and clinical trials are necessary. Establishing evidence-based guidelines for safe and effective use will be aided by this.Standardization of Herbal Products: Consistency in the composition and potency of herbal remedies can be ensured by developing protocols for integrating herbal remedies with modern medicines. Education and Training: Healthcare professionals, including practitioners of traditional Asian medicine, should receive thorough education and training on herbal drug interactions. This will enable them to provide patients with informed guidance. Integration of Traditional and Modern Medicine: Collaborative efforts between traditional Asian medicine and conventional healthcare systems can enhance patient safety and care.

Lack of Regulation: In certain areas, the herbal supplement sector may not be subject to tight regulations, which makes it difficult to guarantee the products' quality and safety.Restricted Research: The study of herbal-drug interactions is still in its infancy, and there is a dearth of thorough information available.Variability in Herbal goods: The composition of natural goods can vary greatly, which makes it challenging to forecast interactions with precision.Cultural Differences: Different regions and cultures have their own traditional herbal remedies, and understanding the interactions between these diverse practices and modern medicine can be complex.Patient Compliance: Patients may not always disclose their herbal remedy usage to healthcare providers, leading to potential interactions going unnoticed

In conclusion, as we delve deeper into the complex realm of herbal drug interactions in Asian medicine, it becomes increasingly evident that the ancient wisdom of traditional healing practices harmoniously merges with modern scientific insights. Our journey through this thesis has illuminated the significance of understanding the intricate interplay between herbs and drugs, offering a pathway to enhance both safety and efficacy. With each reference cited, we have woven a tapestry of knowledge that underscores the potential for a brighter, healthier future, where the timeless traditions of Asian medicine and contemporary medical science walk hand in hand towards a world where holistic well-being reigns supreme.

Author contributions

M.S.H. conceptualized and designed the study, developed the methodology, and managed the project. M.R. was responsible for data curation and conducted the formal analysis. R.J. contributed to

drafting the manuscript, developing software, validation, visualization, and editing the manuscript.

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Competing financial interests

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