Journal of Health Sciences, Medicine, Biotechnology, and Pharmaceutical Research
Volume. 1 Nomor. 2 April 2025
e-ISSN : 3090-8264; p-ISSN : - , Hal. 81-97
DOI: https://doi.org/10.63142/jhsmbp.v1i2.263
Available online at: https://journal.yayasancgi.com/index.php/jhsmbp

Herb–Drug Interactions Between Common Indonesian Medicinal Plants and Cardiovascular Medications: A Narrative Review

Aditya Sindu Sakti[1*], Gumilar Adhi Nugroho[2], Febrika Wediasari[3], Muhammad Adil Khan[4], Muhammad Subhan A. Sibadu[5]

[1] Department of Natural Product Pharmacy, Faculty of Medicine and Health Sciences, Universitas Khairun, Ternate, North Maluku, Indonesia
[2] Department of Pharmacognosy and Phytochemistry, Faculty of Pharmacy, Universitas Pancasila, Jakarta, Indonesia
[3] Graha Sehat, Central General Hospital Dr. Mohammad Hoesin, Palembang, South Sumatra, Indonesia.
[4] Department of Allied Medical and Health Sciences, Sir Syed Case Institute of Technology, Islamabad, Pakistan
[5] Pharmacy Study Program, Faculty of Medicine and Health Sciences, Universitas Khairun, Ternate, North Maluku, Indonesia

Correspondence Author's : aditya@unkhair.ac.id

Abstract*. The simultaneous use of herbal medicines and cardiovascular drugs is prevalent in Indonesia, a country rich in ethnomedicinal diversity. However, such combinations may lead to clinically significant herb–drug interactions, potentially compromising therapeutic efficacy and safety. This narrative review aims to summarize and evaluate the pharmacokinetic and pharmacodynamic interactions between commonly used Indonesian medicinal herbs and cardiovascular agents. A comprehensive literature search was conducted using PubMed, Scopus, ScienceDirect, and Google Scholar. The included studies reported interactions involving cytochrome P450 modulation, P-glycoprotein activity, and receptor-level mechanisms. Medicinal plants such as Panax ginseng, Allium sativum, Ginkgo biloba, Glycyrrhiza glabra, Zingiber officinale, and Cassia species were found to affect drug absorption, metabolism, and bioavailability. These interactions, primarily through CYP3A4 and P-gp modulation, altered the pharmacokinetic profiles of drugs such as warfarin, digoxin, verapamil, and simvastatin. Some herbs also exert synergistic or antagonistic pharmacodynamic effects, particularly against anticoagulants and antihypertensives. Given the chronic nature of cardiovascular therapy, herb–drug interactions pose serious clinical concerns. Enhanced awareness and monitoring are essential to prevent adverse events and therapeutic failure. Further research is needed to establish safe and evidence-based integration of herbal medicines into cardiovascular care.*
Keywords: *Cardiovascular drugs; Herb–drug interaction; Indonesian medicinal plants; Pharmacodynamics; Pharmacokinetics*

Abstrak. Penggunaan obat herbal secara bersamaan dengan obat-obatan kardiovaskular merupakan praktik yang lazim di Indonesia, negara dengan keanekaragaman hayati dan tradisi etnomedisin yang kaya. Namun, kombinasi ini berpotensi menimbulkan interaksi obat-herbal yang signifikan secara klinis dan dapat mengganggu efektivitas serta keamanan terapi. Kajian naratif ini bertujuan untuk merangkum dan mengevaluasi interaksi farmakokinetik dan farmakodinamik antara tanaman obat Indonesia yang umum digunakan dengan obat kardiovaskular. Pencarian literatur dilakukan secara menyeluruh melalui basis data PubMed, Scopus, ScienceDirect, dan Google Scholar. Studi yang dianalisis mencakup interaksi yang melibatkan modulasi enzim sitokrom P450, aktivitas P-glikoprotein, dan mekanisme pada tingkat reseptor. Tanaman obat seperti *Panax ginseng*, *Allium sativum* (bawang putih), *Ginkgo biloba*, *Glycyrrhiza glabra* (akar manis), *Zingiber officinale* (jahe), dan spesies *Cassia* terbukti memengaruhi penyerapan, metabolisme, dan bioavailabilitas obat. Interaksi ini terjadi terutama melalui modulasi CYP3A4 dan P-gp, yang berdampak pada profil farmakokinetik obat seperti warfarin, digoksin, verapamil, dan simvastatin. Beberapa herbal juga menunjukkan efek farmakodinamik sinergis atau antagonis, terutama terhadap obat antikoagulan dan antihipertensi. Mengingat terapi kardiovaskular bersifat jangka panjang, interaksi obat-herbal menjadi perhatian klinis yang serius. Diperlukan peningkatan kewaspadaan dan pemantauan untuk mencegah efek samping maupun kegagalan terapi. Penelitian lanjutan dibutuhkan guna merumuskan pedoman integrasi herbal yang aman dan berbasis bukti dalam praktik terapi kardiovaskular.
Kata Kunci: Obat Kardiovaskular; Interaksi Obat-Herbal; Tanaman Obat Indonesia; Farmakodinamik; Farmakokinetik.

Received: March 15, 2025; Revised: June 23, 2025; Accepted: June 24, 2025;
Online Available: June 25, 2025; Published: June 25, 2025;

1. INTRODUCTION

The global use of herbal medicines continues to rise, driven by growing interest in natural and traditional therapies for both disease prevention and health maintenance. According to the World Health Organization (WHO), herbal medicines are defined as finished, labeled medicinal products that contain active ingredients derived from plant materials, either in their raw form or as preparations (Parveen, Parveen, Parveen, & Ahmad, 2015). In Indonesia, these are classified as Obat Tradisional by the Badan Pengawasan Obat dan Makanan (BPOM), encompassing remedies composed of plant, animal, or mineral ingredients used across generations based on sociocultural and empirical traditions (Sumarya, Suarda, Sudaryati, & Sitepu, 2020).

Indonesia, recognized as one of the world's most biodiverse countries, hosts thousands of indigenous medicinal plant species, many of which are integral to traditional health practices such as jamu, a Javanese-based formulation using plant-derived ingredients (Elfahmi, Woerdenbag, & Kayser, 2014). The growing commercialization of jamu and increased public reliance on traditional medicine have led to a parallel rise in scientific research investigating their pharmacological properties, safety profiles, and clinical relevance (Astutik, Pretzsch, & Ndzifon Kimengsi, 2019; Purwono et al., 2023).

A critical issue emerging from this trend is the co-administration of herbal remedies with conventional pharmaceuticals, particularly in the management of chronic conditions such as cardiovascular diseases (CVDs) (Shaito et al., 2020). CVDs remain the leading cause of morbidity and mortality worldwide, and their treatment often involves complex, long-term pharmacotherapy (Netala, Teertam, Li, & Zhang, 2024). The concurrent use of herbal medicines often perceived as “natural and safe” with cardiovascular drugs raises concerns about potential herb–drug interactions (HDIs) that may compromise therapeutic outcomes or increase the risk of adverse events (Moreira, Teixeira, Monteiro, De-Oliveira, & Paumgartten, 2014).

Herbal preparations typically contain multiple phytoconstituents capable of modulating cytochrome P450 enzymes, drug transporters, and other metabolic pathways, thereby altering the pharmacokinetics or pharmacodynamics of cardiovascular agents (Czigle, Nagy, Mladěnka, & Tóth, 2023). Notable consequences include changes in drug absorption, enhanced or reduced plasma concentrations, and altered therapeutic efficacy, which may lead to complications such as bleeding, arrhythmias, hypotension, or drug toxicity (Vaou et al., 2022; Wang et al., 2023). Despite the clinical relevance, herb–drug interactions remain underreported

and poorly understood in many healthcare settings, especially in regions where traditional medicine use is widespread.

Given the increasing prevalence of herbal medicine use in Indonesia and the global burden of cardiovascular diseases, there is a pressing need to examine and synthesize available evidence on potential interactions between commonly used Indonesian medicinal plants and cardiovascular medications. This narrative review aims to provide a comprehensive overview of clinically relevant herb–drug interactions in the cardiovascular context, with a focus on common Indonesian herbs. The objective is to support pharmacists, clinicians, and healthcare policy-makers in optimizing patient safety and therapeutic outcomes through informed clinical decision-making.

2. METHODOLOGY

This narrative review was conducted to systematically compile and synthesize scientific evidence on herb–drug interactions between widely used Indonesian medicinal herbs and conventional cardiovascular medications. The review adhered to established methodological standards for literature-based synthesis in pharmacology and ethnomedicine. A comprehensive literature search was carried out using four major electronic databases: PubMed, Scopus, ScienceDirect, and Google Scholar. The search employed Boolean combinations of relevant keywords, including “herb–drug interaction,” “cardiovascular drugs,” “Indonesian herbal medicine,” “CYP450 interactions,” and “P-glycoprotein modulation.” Articles published in both English and Bahasa Indonesia were considered, without limitation on publication year, to ensure comprehensive coverage. However, only peer-reviewed studies presenting original data or scientifically grounded analyses relevant to herb–drug interactions were included.

Eligibility criteria were defined to include studies that (1) reported either pharmacokinetic or pharmacodynamic interactions between medicinal herbs and cardiovascular drugs, (2) utilized clinical trials, observational studies, in vivo or in vitro experiments, or pharmacological reviews as study designs, and (3) examined herbal species with documented traditional or commercial use in Indonesia. The initial search yielded 314 records. After removing duplicates and screening titles and abstracts, 76 articles were selected for full-text review. Following detailed eligibility assessment, 36 articles published between 2014 and 2025 were included in the final analysis.

From each eligible study, key data were extracted, including the herbal species involved, the cardiovascular drug(s) studied, the type and mechanism of interaction (e.g., cytochrome P450 modulation, P-glycoprotein inhibition or induction), and reported pharmacological or clinical outcomes. These findings were systematically organized and summarized in tabular

form (Table 1). To enhance transparency in the study selection process, a PRISMA-style flow diagram was incorporated (Figure 1), although such diagrams are not mandatory for narrative reviews. Overall, this methodological approach was designed to provide clinically meaningful insights into herb–drug interactions that may inform healthcare practice, patient counseling, and future pharmacological research in the context of cardiovascular therapy.

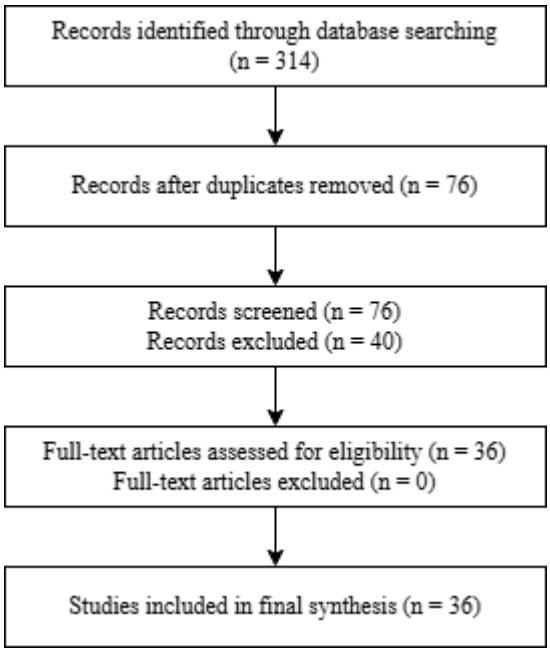

Figure 1. PRISMA diagram of study selection on herb–drug interactions involving Indonesian medicinal herbs and cardiovascular drugs.

3. RESULTS AND DISCUSSION

Cardiovascular Disease Treatment and the Role of Herb–Drug Interactions

Cardiovascular disease (CVD) comprises a spectrum of conditions, including coronary artery disease, cerebrovascular disease, peripheral arterial disease, congenital heart anomalies, and venous thromboembolism (Sakti, Nityasa, & Saputri, 2020). From a pathophysiological standpoint, CVD is often associated with persistent acidemia and elevated circulating free fatty acids. These molecules contribute to the formation of fatty micelles and acidic vesicles that adhere to the vascular endothelium, thereby initiating atherosclerotic changes (Reis, 2016). If left unaddressed, these processes may culminate in acute clinical events such as myocardial infarction and stroke (Madaudo, Coppola, Parlati, & Corrado, 2024).

Pharmacological interventions for CVD aim to mitigate these risks through the long-term use of antiplatelet agents, antithrombotic therapies, lipid-lowering drugs, and antihypertensives (Altreuther et al., 2024). However, the concurrent use of herbal remedies widely adopted in

traditional and complementary medicine raises significant concerns regarding herb–drug interactions. Such interactions can compromise therapeutic efficacy or lead to adverse drug events, particularly when herbal constituents modulate drug absorption, distribution, metabolism, or excretion (Gamil et al., 2025).

Pharmacokinetic and Pharmacodynamic Dimensions of Herb–Drug Interactions

Herb–drug interactions are broadly classified as either pharmacokinetic or pharmacodynamic (Surana, Agrawal, Kumbhare, & Gaikwad, 2021). Pharmacokinetic interactions affect the concentration of a drug within the body and typically involve alterations in the processes of absorption, distribution, metabolism, or excretion (Saha, 2018). These interactions may arise from the inhibition or induction of drug-metabolizing enzymes most notably the cytochrome P450 (CYP) family or from interference with membrane-bound drug transporters such as P-glycoprotein (P-gp) (Guengerich, 2022).

A wide range of cardiovascular drugs are metabolized via CYP pathways. When herbs act as inhibitors, they may reduce drug clearance and increase systemic concentrations, potentially leading to toxicity (Rombolà et al., 2020). Conversely, CYP inducers may accelerate drug metabolism, reducing plasma levels and therapeutic efficacy. Similarly, modulation of P-gp activity can affect the oral bioavailability and systemic retention of cardiovascular agents. (Del Re et al., 2025)

Pharmacodynamic interactions, on the other hand, occur when herbal compounds modify the physiological effects of drugs at their site of action. These can be synergistic, antagonistic, or additive, depending on whether the herb potentiates or dampens the drug's intended effects (Chaachouay, 2025). Such interactions are particularly important when herbs share overlapping mechanisms of action with cardiovascular drugs, such as those influencing platelet aggregation, vascular tone, or coagulation (Shaito et al., 2020).

Clinical Relevance and Evidence from Indonesian Herbal Medicines

A comprehensive review of the literature (summarized in Table 1) reveals that several herbs commonly used in Indonesia—including *Panax ginseng*, *Allium sativum*, *Ginkgo biloba*, *Glycyrrhiza glabra*, *Zingiber officinale*, *Camellia sinensis*, and Cassia species exhibit both pharmacokinetic and pharmacodynamic interactions with cardiovascular drugs. These interactions influence key parameters such as area under the curve (AUC), maximum plasma concentration (Cmax), half-life (t½), and international normalized ratio (INR).

For instance, St. John's wort significantly reduces the bioavailability of drugs such as digoxin, ivabradine, and warfarin via induction of CYP3A4 and P-gp, while Ginkgo biloba may elevate the effects of calcium channel blockers by inhibiting their metabolism (Grimstein

& Huang, 2018). Ginseng and ginger have been reported to potentiate bleeding when combined with anticoagulants like warfarin due to their antiplatelet effects (Abebe, 2019; Chua, Ang, Zhong, & Khoo, 2015a). These findings underscore the clinical importance of evaluating herb–drug interactions, particularly among patients on chronic cardiovascular therapy. Healthcare professionals should maintain a high level of vigilance and obtain detailed medication histories that include herbal product use.

Table 1. Herb–Drug Interactions with Cardiovascular Medicines

Herb	Drug	Results of Interaction	Mechanism	Source
St. John's Wort (*Hypericum perforatum*)	Digoxin	Decreases AUC and Cmax of digoxin	Induces intestinal P-gp, reducing absorption and enhancing elimination	(Coumau & Csajka, 2025)
	Ivabradine	Decreasing AUC and Cmax of ivabradine	Induces intestinal and hepatic CYP3A4 metabolism	(Chrubasik-Hausmann, Vlachojannis, & McLachlan, 2019)
	Warfarin	Reducing warfarin activity resulting in INR and AUC decrease	Increases clearance via CYP2C9 metabolism	(Di Minno et al., 2017)
	Verapamil	Decreases the bioavailability of verapamil	Induces first-pass metabolism via CYP3A4	(Shang et al., 2021; Soleymani, Bahramsoltani, Rahimi, & Abdollahi, 2017)
	Nifedipine	Decreases AUC of nifedipine	Induces CYP3A4 metabolism	(Costache et al., 2019)
	Simvastatin	Decreases simvastatin plasma concentration	Induces CYP3A4 and P-gp	(Likhodii, Chin, & Baskin, 2024; Nicolussi, Drewe, Butterweck, & Meyer zu Schwabedissen, 2020)
	Talinolol	Decreases AUC of talinolol	Induces intestinal P-gp	(Morris & Ren, 2022)
Ginseng (*Panax ginseng*)	Warfarin	Ginseng can reduce the INR ratio	Antiplatelet activity inhibits platelet aggregation and thromboxane formation	(J. Li, Liang, & Sun, 2019)

	Debrisoquine	Reducing the urinary recovery ratio of Debrisoquine	Inhibits CYP2D6	(Liang et al., 2022)
Ginkgo (*Ginkgo biloba*)	Diltiazem	Increases AUC and Cmax, and affect at t½ diltiazem	Inhibits intestinal and hepatic CYP3A	(Moeinipour, Akaberi, & Sobhani, 2024)
	Nifedipine	Increases heart rate	Interacts with CYP3A substrates	(Nyulas et al., 2024)
	Propanolol	Reduces plasma concentration, also increases AUC and Cmax	Induces CYP1A2; interacts with CYP2B1, CYP2B2, CYP3A1	(Qiang, Li, Xu, Lin, & Wang, 2020)
	Warfarin	Increases AUC, Cmax, and t½ of warfarin	Inhibits hepatic CYP2C9	(Soyata, Nur Hasanah, & Rusdiana, 2020)
Garlic (*Allium sativum*)	Propranolol	Increases bioavailability and t½ of warfarin	Induces CYP3A4	(Leite, Martins, & Castilho, 2016)
	Nifedipine	Increase plasma concentration	Reduces calcium influx to smooth muscle	(Kansara & Jani, 2017)
	Captopril	Combination with captopril has a synergistic effect	Inhibits ACE, increases bradykinin, promotes vasodilation	(Hemaiswarya, Prabhakar, & Doble, 2022)
Licorice (*Glycyrrhiza glabra*)	Digoxin	Inhibited CYP3A4/5 activity	18β-glycyrrhetic acid inhibits CYP3A4/5	(Cheng, Xia, Wu, & Li, 2023; X. Li et al., 2014)
	Diuretics	Increases risk for hypokalemia	Synergistic hypokalemia effect with diuretics	(Almaghrabi, Alghamdi, Alfadel, & Alharbi, 2021)
	Warfarin	Reduces anticoagulant effect of warfarin	Induces CYP3A4 and CYP2D6	(Zhuang et al., 2021)
Aloe vera (Lidah Buaya)	Digitalis	Increases risk for digitalis toxicity and arrhythmia	Causes hypokalemia and inhibits CYP3A4/2D6 affecting drug concentrations	(Djuv & Nilsen, 2012)
	Cardiac glycoside and antiarrhythmic drugs	Hypokalemia increases plasma concentration of cardiac drugs	Laxative-induced hypokalemia increases drug plasma concentration	(Khan & Khan, 2020)
Angelica sinensis	Warfarin	Increases bleeding risk, reduces drug effectiveness	Coumarins increase INR and induce CYP3A4 via pregnane X receptor	(Sultan et al., 2017)

Capsicum (Cabe)	Antihypertensive drugs	May interfere with antihypertensives	Decreases CGRP synthesis and release	(Szallasi, 2023)
Fenugreek (*Trigonella foenum-graecum*)	Warfarin, anticoagulant and antiplatelet	Increases bleeding risk	Coumarins affect blood coagulation	(Abebe, 2019)
Ginger (*Zingiber officinale*)	Warfarin	Increases bleeding risk	Inhibits thromboxane and platelet function	(Marx et al., 2015; Shadrack, Faraj, Alex, & Kenneth, 2019)
	Phenprocoumon	Over-anticoagulation	Inhibits thromboxane synthase, prostacyclin agonist	(Alshimemeri, Al-Mishari, Shoukry, Ali, & Metawe, 2024; Chua, Ang, Zhong, & Khoo, 2015b)
Green tea (*Camellia sinensis*)	Warfarin	Reduces anticoagulant effect	Contains vitamin K which reduces warfarin efficacy	(Talasaz et al., 2024; Tan & Lee, 2021)
Turmeric (*Curcuma longa*)	Antiplatelets and anticoagulants	Increases bleeding risk	Inhibits CYP3A4 and CYP1A12, enhances CYP2A6	(Thikekar, Thomas, & Chitlange, 2021)
Papaya (*Carica papaya*)	Warfarin, heparin, enoxaparin	Long acting antiplatelet effect	Inhibits CYP3A4	(Asare, Koffuor, Nyansah, Gyanfosu, & Abruquah, 2015)
Cassia species	Digoxin, warfarin, heparin, enoxaparin	Synergism activity	Decreases deoxycholic acid and biliary cholesterol saturation	(Shaikh, Thomas, & Chitlange, 2020)

The data summarized in Table 1 reveal a wide spectrum of clinically relevant herb–drug interactions involving commonly used Indonesian medicinal herbs and cardiovascular medications. Notably, herbs such as St. John's Wort, *Ginkgo biloba*, Ginseng, Garlic, and Licorice demonstrate consistent pharmacokinetic interactions through modulation of cytochrome P450 enzymes (particularly CYP3A4, CYP2C9, and CYP2D6) and P-glycoprotein, leading to altered drug metabolism, absorption, or clearance. These effects may result in subtherapeutic plasma concentrations or increased toxicity of cardiovascular drugs such as digoxin, warfarin, nifedipine, and statins. On the other hand, several herbs including *Angelica sinensis*, Ginger, Turmeric, and Fenugreek exhibit pharmacodynamic interactions, notably by enhancing anticoagulant or antiplatelet activity, thereby elevating bleeding risk. These findings

underscore the importance of vigilance in co-administering herbal products with cardiovascular drugs, especially those with narrow therapeutic indices. From a clinical perspective, healthcare practitioners should consider these interaction profiles when advising patients, particularly those with complex medication regimens or those self-medicating with traditional herbal remedies. Integration of herb–drug interaction awareness into clinical decision-making can significantly enhance patient safety, optimize therapeutic outcomes, and prevent adverse cardiovascular events.

Despite the growing body of evidence summarized in this review, it is important to acknowledge that the included studies vary considerably in their methodological designs, ranging from in vitro and in vivo experimental models to limited clinical trials in humans (Sun, Gao, Hu, & Zhou, 2022). This heterogeneity may introduce potential bias in interpreting the clinical relevance of certain herb–drug interactions. For example, while the CYP3A4-inhibitory effect of *Glycyrrhiza glabra* is well-demonstrated in in vitro settings, its impact on digoxin pharmacokinetics in humans remains inconclusive. Similarly, discrepancies are observed across studies such as *Ginkgo biloba* acting as both a CYP inducer and inhibitor highlighting inconsistencies that may stem from differences in experimental conditions, herbal extract composition, or dosing regimens. A critical comparison also reveals variation in the strength and mechanism of interactions across herbs; for instance, both Ginger and Ginseng enhance anticoagulant effects, yet they do so via distinct pharmacodynamic pathways. These findings underscore the existing gaps in knowledge and the urgent need for well-designed clinical studies to clarify the magnitude and clinical significance of herb–drug interactions, particularly in the context of long-term cardiovascular therapy.

4. CONCLUSIONS

This review highlights the clinical importance of herb–drug interactions (HDIs) involving commonly used Indonesian medicinal plants and cardiovascular drugs. Key findings indicate that herbs such as *Ginkgo biloba*, *Glycyrrhiza glabra*, *Panax ginseng*, and *Zingiber officinale* can significantly alter the pharmacokinetic and pharmacodynamic profiles of cardiovascular agents through cytochrome P450 modulation and P-glycoprotein interference. These interactions may result in reduced therapeutic efficacy, increased toxicity, or heightened bleeding risk, especially in drugs with narrow therapeutic indices such as warfarin, digoxin, and nifedipine. However, the current body of evidence is limited by methodological heterogeneity, including reliance on in vitro and animal studies, which constrains the direct applicability of findings to clinical practice. Therefore, further well-designed human studies are urgently needed to elucidate the clinical relevance and magnitude of these interactions.

To mitigate the potential risks of HDIs in cardiovascular care, it is essential to implement preventive strategies across multiple levels of healthcare. Clinicians should be trained to recognize and assess herbal medicine use during routine consultations. Incorporating herb–drug interaction alerts into electronic health records and clinical decision support systems can enhance real-time risk identification. Policymakers and healthcare institutions are encouraged to support the development of integrated databases and to promote interdisciplinary collaboration in pharmacovigilance. Lastly, researchers should prioritize translational studies and develop standardized frameworks for evaluating HDIs in the Indonesian context. These measures can contribute to safer, evidence-based integration of herbal medicine into cardiovascular pharmacotherapy.

ACKNOWLEDGEMENT

The authors would like to express their sincere gratitude to the Institute for Research and Community Service (LPPM) of Universitas Khairun for the invaluable support and facilitation provided throughout the development and completion of this manuscript. This work was made possible through the institution's commitment to advancing scientific research and academic excellence.

REFERENCES

Abebe, W. (2019). Review of Herbal Medications with The Potential to Cause Bleeding: Dental Implications, and Risk Prediction and Prevention Avenues. *EPMA Journal*, *10*(1), 51–64. https://doi.org/10.1007/s13167-018-0158-2

Almaghrabi, M., Alghamdi, W., Alfadel, N., & Alharbi, F. (2021). Liquorice Interaction with Thiazide and Thiazide-Like Diuretics and the Potential Risk of Hypokalemia. *Drug Safety: An International Journal of Medical Toxicology and Drug Experience*, *44*(22), 1421. Retrieved from https://www.proquest.com/openview/809a234edd2af77cb43e6182c6376809/1?pq-origsite=gscholar&cbl=32187#:~:text=However%2C consuming large amounts of,may result in severe complications.

Alshimemeri, A., Al-Mishari, H., Shoukry, E., Ali, E., & Metawe, M. (2024). A Young Adult Male with Postoperative Bleeding Following Bariatric Surgery. *Critical Care & Shock*, *27*(3), 141. Retrieved from https://criticalcareshock.com/2024/06/12618/

Altreuther, M., Seternes, A., Saltnes, T., Myrbø, N., Vikan, K., Nilsen, L. H., & Feng, T. (2024). Antithrombotic and Lipid Lowering Therapy is Associated With Improved Survival After Vascular Surgery: A Population Based Study From Norway. *European Journal of Vascular and Endovascular Surgery*, *67*(6), 988–994. https://doi.org/10.1016/j.ejvs.2023.10.019

Asare, F., Koffuor, G., Nyansah, W., Gyanfosu, L., & Abruquah, A. (2015). Anticoagulant and Antiplatelet Properties of The Latex of Unripe Fruits of Carica papaya L. (Caricaceae). *International Journal of Basic and Clinical Pharmacology*, *4*(6), 1183–1188. https://doi.org/10.18203/2319-2003.ijbcp20151355

Astutik, S., Pretzsch, J., & Ndzifon Kimengsi, J. (2019). Asian Medicinal Plants' Production and Utilization Potentials: A Review. *Sustainability*, *11*(19), 5483. https://doi.org/10.3390/su11195483

Chaachouay, N. (2025). Synergy, Additive Effects, and Antagonism of Drugs with Plant Bioactive Compounds. *Drugs and Drug Candidates*, *4*(1), 4. https://doi.org/10.3390/ddc4010004

Cheng, W., Xia, K., Wu, S., & Li, Y. (2023). Herb-Drug Interactions and Their Impact on Pharmacokinetics: An Update. *Current Drug Metabolism*, *24*(1), 28–69. https://doi.org/10.2174/1389200224666230116113240

Chrubasik-Hausmann, S., Vlachojannis, J., & McLachlan, A. J. (2019). Understanding Drug Interactions with St John's wort (Hypericum perforatum L.): Impact of Hyperforin

Content. *Journal of Pharmacy and Pharmacology*, *71*(1), 129–138. https://doi.org/10.1111/jphp.12858

Chua, Y., Ang, X., Zhong, X., & Khoo, K. (2015a). Interaction between Warfarin and Chinese Herbal Medicines. *Singapore Medical Journal*, *56*(1), 11–18. https://doi.org/10.11622/smedj.2015004

Chua, Y., Ang, X., Zhong, X., & Khoo, K. (2015b). Interaction Between Warfarin and Chinese Herbal Medicines. *Singapore Medical Journal*, *56*(1), 11–18. https://doi.org/10.11622/smedj.2015004

Costache, I.-I., Miron, A., Hăncianu, M., Aursulesei, V., Costache, A. D., & Aprotosoaie, A. C. (2019). Pharmacokinetic Interactions between Cardiovascular Medicines and Plant Products. *Cardiovascular Therapeutics*, *2019*, 1–19. https://doi.org/10.1155/2019/9402781

Coumau, C., & Csajka, C. (2025). A Systematic Review and Classification of the Effects of P-glycoprotein Inhibitors and Inducers in Humans, Using Digoxin, Fexofenadine, and Dabigatran as Probe Drugs. *Clinical Pharmacokinetics*, *64*(6), 849–863. https://doi.org/10.1007/s40262-025-01514-3

Czigle, S., Nagy, M., Mladěnka, P., & Tóth, J. (2023). Pharmacokinetic and Pharmacodynamic Herb-drug Interactions—part I. Herbal Medicines of The Central Nervous System. *PeerJ*, *11*(e16149), 1–51. https://doi.org/10.7717/peerj.16149

Del Re, M., Roncato, R., Argentiero, A., Berrino, L., Botticelli, A., Capuano, A., … Danesi, R. (2025). Clinical Relevance and Methodological Approach for The Assessment of Drug–drug Interactions in Cancer Patients: a Position Statement from the Italian Association of Medical Oncology (AIOM) and the Italian Society of Pharmacology (SIF). *ESMO Open*, *10*(6), 105119. https://doi.org/10.1016/j.esmoop.2025.105119

Di Minno, A., Frigerio, B., Spadarella, G., Ravani, A., Sansaro, D., Amato, M., … Baldassarre, D. (2017). Old and New Oral Anticoagulants: Food, Herbal Medicines and Drug Interactions. *Blood Reviews*, *31*(4), 193–203. https://doi.org/10.1016/j.blre.2017.02.001

Djuv, A., & Nilsen, O. G. (2012). Aloe Vera Juice: IC50 and Dual Mechanistic Inhibition of CYP3A4 and CYP2D6. *Phytotherapy Research*, *26*(3), 445–451. https://doi.org/10.1002/ptr.3564

Elfahmi, Woerdenbag, H. J., & Kayser, O. (2014). Jamu: Indonesian Traditional Herbal Medicine Towards Rational Phytopharmacological Use. *Journal of Herbal Medicine*, *4*(2), 51–73. https://doi.org/10.1016/j.hermed.2014.01.002

Gamil, N. M., Elsayed, H. A., Hamed, R. M., Salah, E. T., Ahmed, A. M., Mostafa, H. A., …

Abou-Hussein, D. (2025). Insights from Herb Interactions Studies: a Foundational Report for Integrative Medicine. *Future Journal of Pharmaceutical Sciences*, *11*(46), 1–27. https://doi.org/10.1186/s43094-025-00794-7

Grimstein, M., & Huang, S.-M. (2018). A Regulatory Science Viewpoint on Botanical–drug Interactions. *Journal of Food and Drug Analysis*, *26*(2), S12–S25. https://doi.org/10.1016/j.jfda.2018.01.013

Guengerich, F. P. (2022). Inhibition of Cytochrome P450 Enzymes by Drugs-Molecular Basis and Practical Applications. *Biomolecules & Therapeutics*, *30*(1), 1–18. https://doi.org/10.4062/biomolther.2021.102

Hemaiswarya, S., Prabhakar, P. K., & Doble, M. (2022). Synergistic Herb Interactions with Cardiovascular Drugs. In *Herb-Drug Combinations A New Complementary Therapeutic Strategy* (1st ed., pp. 131–144). Singapore: Springer Nature Singapore. https://doi.org/10.1007/978-981-19-5125-1_9

Kansara, M. B., & Jani, A. J. (2017). Possible Interactions between Garlic and Conventional Drugs: a Review. *Pharmaceutical and Biological Evaluations*, *4*(2), 73–81. https://doi.org/10.26510/2394-0859.pbe.2017.12

Khan, S., & Khan, S. U. (2020). Adverse Drug Event of Hypokalaemia-induced Cardiotoxicity Secondary to The Use of Laxatives: A Systematic Review of Case Reports. *Journal of Clinical Pharmacy and Therapeutics*, *45*(5), 927–936. https://doi.org/10.1111/jcpt.13204

Leite, P. M., Martins, M. A. P., & Castilho, R. O. (2016). Review on Mechanisms and Interactions in Concomitant Use of Herbs and Warfarin Therapy. *Biomedicine & Pharmacotherapy*, *83*, 14–21. https://doi.org/10.1016/j.biopha.2016.06.012

Li, J., Liang, Q., & Sun, G. (2019). Interaction between Traditional Chinese Medicine and Anticoagulant/Antiplatelet Drugs. *Current Drug Metabolism*, *20*(9), 701–713. https://doi.org/10.2174/1389200220666190827160212

Li, X., Hu, J., Wang, B., Sheng, L., Liu, Z., Yang, S., & Li, Y. (2014). Inhibitory Effects of Herbal Constituents on P-glycoprotein in Vitro and in Vivo: Herb–drug Interactions Mediated via P-gp. *Toxicology and Applied Pharmacology*, *275*(2), 163–175. https://doi.org/10.1016/j.taap.2013.12.015

Liang, R.-J., Hsu, S.-H., Chang, T.-Y., Chiang, T.-Y., Wang, H.-J., & Ueng, Y.-F. (2022). Metabolism-involved Drug Interactions with Traditional Chinese Medicines in Cardiovascular Diseases. *Journal of Food and Drug Analysis*, *30*(3), 331–356. https://doi.org/10.38212/2224-6614.3421

Likhodii, S., Chin, A. C., & Baskin, L. B. (2024). Role of Therapeutic Drug Monitoring to Identify Clinically Significant Drug–herbal Supplement Interaction. In A. Dasgupta (Ed.), *Therapeutic Drug Monitoring* (2nd ed., pp. 515–544). Elsevier. https://doi.org/10.1016/B978-0-443-18649-3.00015-X

Madaudo, C., Coppola, G., Parlati, A. L. M., & Corrado, E. (2024). Discovering Inflammation in Atherosclerosis: Insights from Pathogenic Pathways to Clinical Practice. *International Journal of Molecular Sciences*, *25*(11), 6016. https://doi.org/10.3390/ijms25116016

Marx, W., McKavanagh, D., McCarthy, A. L., Bird, R., Ried, K., Chan, A., & Isenring, L. (2015). Correction: The Effect of Ginger (Zingiber officinale) on Platelet Aggregation: A Systematic Literature Review. *PLOS ONE*, *10*(11), e0143675. https://doi.org/10.1371/journal.pone.0143675

Moeinipour, Z., Akaberi, M., & Sobhani, Z. (2024). Ginkgo biloba L.: An Updated Review on the Pharmacological Activities, Pharmacokinetics and Drug Interactions. *Traditional and Integrative Medicine*, *9*(4), 442–463. https://doi.org/10.18502/tim.v9i4.17478

Moreira, D. de L., Teixeira, S. S., Monteiro, M. H. D., De-Oliveira, A. C. A. X., & Paumgartten, F. J. R. (2014). Traditional Use and Safety of Herbal Medicines. *Revista Brasileira de Farmacognosia*, *24*(2), 248–257. https://doi.org/10.1016/j.bjp.2014.03.006

Morris, M. E., & Ren, T. (2022). Diet/Nutrient Interactions with Drug Transporters. In G. You & M. E. Morris (Eds.), *Drug Transporters: Molecular Characterization and Role in Drug Disposition* (3rd ed., pp. 515–541). Wiley. https://doi.org/10.1002/9781119739883.ch25

Netala, V. R., Teertam, S. K., Li, H., & Zhang, Z. (2024). A Comprehensive Review of Cardiovascular Disease Management: Cardiac Biomarkers, Imaging Modalities, Pharmacotherapy, Surgical Interventions, and Herbal Remedies. *Cells*, *13*(17), 1471. https://doi.org/10.3390/cells13171471

Nicolussi, S., Drewe, J., Butterweck, V., & Meyer zu Schwabedissen, H. E. (2020). Clinical Relevance of St. John's Wort Drug Interactions Revisited. *British Journal of Pharmacology*, *177*(6), 1212–1226. https://doi.org/10.1111/bph.14936

Nyulas, K.-I., Simon-Szabó, Z., Pál, S., Fodor, M.-A., Dénes, L., Cseh, M. J., … Nemes-Nagy, E. (2024). Cardiovascular Effects of Herbal Products and Their Interaction with Antihypertensive Drugs—Comprehensive Review. *International Journal of Molecular Sciences*, *25*(12), 6388. https://doi.org/10.3390/ijms25126388

Parveen, A., Parveen, B., Parveen, R., & Ahmad, S. (2015). Challenges and Guidelines for Clinical Trial of Herbal Drugs. *Journal of Pharmacy And Bioallied Sciences*, *7*(4), 329.

https://doi.org/10.4103/0975-7406.168035

Purwono, S., Nisa, U., Astana, P. R. W., Wijayaningsih, R. A., Wicaksono, A. J., Wahyuningsih, M. S. H., … Fakhrudin, N. (2023). Factors Affecting the Perception of Indonesian Medical Doctors on Herbal Medicine Prescription in Healthcare Facilities: Qualitative and Quantitative Studies. *Journal of Herbal Medicine*, *42*(100747), 1–8. https://doi.org/10.1016/j.hermed.2023.100747

Qiang, T., Li, Y., Xu, X., Lin, W., & Wang, X. (2020). Effect of Herbs for Treating Coronary Heart Disease on The CYP450 Enzyme System and Transporters. *American Journal of Translational Research*, *12*(7), 3182–3197.

Reis, A. H. (2016). On the Etiology of Cardiovascular Diseases: A New Framework for Understanding Literature Results. *Medical Hypotheses*, *92*, 94–99. https://doi.org/10.1016/j.mehy.2016.04.046

Rombolà, L., Scuteri, D., Marilisa, S., Watanabe, C., Morrone, L. A., Bagetta, G., & Corasaniti, M. T. (2020). Pharmacokinetic Interactions between Herbal Medicines and Drugs: Their Mechanisms and Clinical Relevance. *Life*, *10*(7), 106. https://doi.org/10.3390/life10070106

Saha, N. (2018). Clinical Pharmacokinetics and Drug Interactions. In D. Vohora & G. Singh (Eds.), *Pharmaceutical Medicine and Translational Clinical Research* (pp. 81–106). Elsevier. https://doi.org/10.1016/B978-0-12-802103-3.00006-7

Sakti, A. S., Nityasa, A. R., & Saputri, F. C. (2020). Effect of Uncaria gambir and Uncaria sclerophylla on Pulmonary- Thromboembolism Mice. *Pharmacognosy Journal*, *12*(1), 192–196. https://doi.org/10.5530/pj.2020.12.29

Shadrack, K., Faraj, A., Alex, M. K., & Kenneth, N. (2019). Anti-thrombotic Effect of Zingiber officinale (Ginger) in Sprague Dawley Rats. *International Journal of Research in Medical Sciences*, *7*(9), 3239–3245. https://doi.org/10.18203/2320-6012.ijrms20193905

Shaikh, A. S., Thomas, A. B., & Chitlange, S. S. (2020). Herb–Drug Interaction Studies of Herbs used in Treatment of Cardiovascular Disorders—A Narrative Review of Preclinical and cCinical Studies. *Phytotherapy Research*, *34*(5), 1008–1026. https://doi.org/10.1002/ptr.6585

Shaito, A., Thuan, D. T. B., Phu, H. T., Nguyen, T. H. D., Hasan, H., Halabi, S., … Pintus, G. (2020). Herbal Medicine for Cardiovascular Diseases: Efficacy, Mechanisms, and Safety. *Frontiers in Pharmacology*, *11*(422), 1–32. https://doi.org/10.3389/fphar.2020.00422

Shang, H., Wang, Z., Ma, H., Sun, Y., Ci, X., Gu, Y., … Si, D. (2021). Influence of Verapamil

on The Pharmacokinetics of Rotundic Acid in Rats and Its Potential Mechanism. *Pharmaceutical Biology*, *59*(1), 198–206. https://doi.org/10.1080/13880209.2021.1871634

Soleymani, S., Bahramsoltani, R., Rahimi, R., & Abdollahi, M. (2017). Clinical Risks of St John's Wort (Hypericum perforatum) Co-administration. *Expert Opinion on Drug Metabolism & Toxicology*, *13*(10), 1047–1062. https://doi.org/10.1080/17425255.2017.1378342

Soyata, A., Nur Hasanah, A., & Rusdiana, T. (2020). Interaction of Warfarin with Herbs Based on Pharmacokinetic and Pharmacodynamic Parameters. *Indonesian Journal of Pharmaceutics*, *2*(2), 69–76. https://doi.org/10.24198/idjp.v2i2.27289

Sultan, S., Jahangir, A., Gussak, I. B., Kostis, J. B., Tajik, A. J., & Jahangir, A. (2017). Interactions between Supplements and Medications. In I. B. Gusak & J. B. Kostis (Eds.), *Iatrogenicity Cause and Consequences of Iatrogenesis in Cardiovascular Medicine*. Rutgers University Press.

Sumarya, I. M., Suarda, I. W., Sudaryati, N. L. G., & Sitepu, I. (2020). Benefits of Biopharmaca Products Towards Healthy Indonesia. *Journal of Physics: Conference Series*, *1469*(012133), 1–8. https://doi.org/10.1088/1742-6596/1469/1/012133

Sun, D., Gao, W., Hu, H., & Zhou, S. (2022). Why 90% of clinical drug development fails and how to improve it? *Acta Pharmaceutica Sinica B*, *12*(7), 3049–3062. https://doi.org/10.1016/j.apsb.2022.02.002

Surana, A. R., Agrawal, S. P., Kumbhare, M. R., & Gaikwad, S. B. (2021). Current Perspectives in Herbal and Conventional Drug Interactions based on Clinical Manifestations. *Future Journal of Pharmaceutical Sciences*, *7*(103), 1–12. https://doi.org/10.1186/s43094-021-00256-w

Szallasi, A. (2023). The Vanilloid (Capsaicin) Receptor TRPV1 in Blood Pressure Regulation: A Novel Therapeutic Target in Hypertension? *International Journal of Molecular Sciences*, *24*(10), 8769. https://doi.org/10.3390/ijms24108769

Talasaz, A. H., McGonagle, B., HajiQasemi, M., Ghelichkhan, Z. A., Sadeghipour, P., Rashedi, S., … Bikdeli, B. (2024). Pharmacokinetic and Pharmacodynamic Interactions between Food or Herbal Products and Oral Anticoagulants: Evidence Review, Practical Recommendations, and Knowledge Gaps. *Seminars in Thrombosis and Hemostasis*, *51*(5), 560–571. https://doi.org/10.1055/s-0044-1790258

Tan, C. S. S., & Lee, S. W. H. (2021). Warfarin and Food, Herbal or Dietary Supplement Interactions: A Systematic Review. *British Journal of Clinical Pharmacology*, *87*(2),

352–374. https://doi.org/10.1111/bcp.14404

Thikekar, A. K., Thomas, A. B., & Chitlange, S. S. (2021). Herb-drug Interactions in Diabetes Mellitus: A Review based on Pre-clinical and Clinical Data. *Phytotherapy Research*, *35*(9), 4763–4781. https://doi.org/10.1002/ptr.7108

Vaou, N., Stavropoulou, E., Voidarou, C. (Chrysa), Tsakris, Z., Rozos, G., Tsigalou, C., & Bezirtzoglou, E. (2022). Interactions between Medical Plant-Derived Bioactive Compounds: Focus on Antimicrobial Combination Effects. *Antibiotics*, *11*(8), 1014. https://doi.org/10.3390/antibiotics11081014

Wang, H., Chen, Y., Wang, L., Liu, Q., Yang, S., & Wang, C. (2023). Advancing Herbal Medicine: Enhancing Product Quality and Safety Through Robust Quality Control Practices. *Frontiers in Pharmacology*, *14*, 1265178. https://doi.org/10.3389/fphar.2023.1265178

Zhuang, W., Liu, S., Zhao, X., Sun, N., He, T., Wang, Y., … Xi, S. (2021). Interaction Between Chinese Medicine and Warfarin: Clinical and Research Update. *Frontiers in Pharmacology*, *12*(751107), 1–13. https://doi.org/10.3389/fphar.2021.751107