International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 987-994 www.ijprajournal.com ISSN: 2456-4494

Pharmacovigilance Approaches to Herb–Drug Interaction Safety Assessment

Miss. Gauri BhudeoJathe*, Mr. Umesh Premdas Jadhao, Mr. Tushar A Rode, Dr Anil V Chandewar
[Student of pharmacognosy department]
[Student of pharmacognosy department]
[Assistant professor]
[Principal Yavatmal Zilla Vikas Samiti's Pataldhamal Wadhwani College of Pharmacy]

Date of Submission: 25-03-2025 Date of Acceptance: 05-04-2025

ABSTRACT
The increasing global interest in complementary and alternative medicine has led to a rise in the concurrent use of herbal supplements and pharmaceutical drugs, increasing the risk of herb-drug interactions (HDIs). HDIs occur when active herbal components alter the pharmacokinetics or pharmacodynamics of conventional medications, potentially causing therapeutic failures, increased toxicity, or adverse effects. This article explores the mechanisms of HDIs, pharmacovigilance approaches, regulatory perspectives, assessment methodologies, and real-world case studies. Major challenges in HDI monitoring include underreporting of adverse events, variability in herbal composition, and lack of standardization. Pharmacovigilance frameworks are critical in identifying and mitigating these risks through national reporting programs, specialized monitoring tools, and professional education. Additionally, regulatory bodies like the FDA, EMA, MHRA, WHO, and India's Ministry of AYUSH play a crucial role in developing guidelines for HDI risk assessment. Future research must focus on standardized methodologies, advanced technologies (AI, big data analytics), and regulatory harmonization to enhance HDI surveillance and safety. Healthcare professionals and consumers must be educated about the potential risks associated with herbal and pharmaceutical co-administration to promote safer medical practices.

Keywords: -Herb-drug interactions (HDIs), pharmacovigilance, adverse drug reactions (ADRs), regulatory frameworks, traditional herbal medicine, complementary and alternative medicine (CAM), safety assessment, public health, artificial intelligence (AI).

I. INTRODUCTION

A growing public interest in complementary and alternative medicine has led to an increase in the usage of herbal supplements alongside traditional medications. While many people believe herbal remedies are harmless because of their natural origins, these chemicals can interact with prescription pharmaceuticals, posing substantial health hazards. Understanding and monitoring these herb-drug interactions (HDIs) is critical to ensure patient safety.[01]

- **An overview of interactions between herbs and drugs.**

Herb-drug interactions occur when the active components in herbal supplements alter the pharmacokinetics or pharmacodynamics of prescription medications. These interactions can reduce therapeutic efficacy, increase toxicity, and cause unforeseen side effects. For example, St. John's Wort, which is commonly used to treat depression, may change the metabolism of a number of medications, including antidepressants, birth control pills, and anticoagulants, potentially leading to therapeutic failures or adverse effects.[02]

- **Pharmacovigilance in the Safety Assessment of Herb-Drug Interactions.**

Pharmacovigilance, which is the science and practice of identifying, assessing, understanding, and preventing side effects or other drug-related issues, is crucial in HDI monitoring. Implementing effective pharmacovigilance systems helps healthcare practitioners and regulatory bodies to recognize and control dangers connected with the concurrent use of herbal and pharmaceutical goods.[03]

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 987-994 www.ijprajournal.com ISSN: 2456-4494

- **Impact on Public Health and Prevalence**

Herbal supplements are frequently used in conjunction with prescription drugs. Over one-third of adults in the US report taking herbal supplements, and higher levels of education and advanced age are linked to higher consumption rates. Despite their widespread use, many people believe that because herbal products come from natural sources, they are always safe. However, there may be serious health concerns if prescription drugs and herbal supplements are taken at the same time. For example, using warfarin, an anticoagulant, along with herbs like garlic, ginkgo, etc., can make bleeding more likely. Effective pharmacovigilance techniques must be used to monitor and evaluate these interactions, guaranteeing patient safety and well-informed clinical practice, given the prevalence of herbal supplement usage and the possibility of negative interactions with prescription drugs.[04]

CHALLENGES IN MONITORING HERB–DRUG INTERACTIONS

Monitoring and evaluating herb–drug interactions (HDIs) has become extremely difficult due to the growing prevalence of using herbal supplements and prescription drugs at the same time. Important difficulties include:

- **Adverse Events Are Underreported**

The underreporting of negative events is a significant barrier to HDI monitoring. Patients frequently neglect to tell medical professionals that they take herbal supplements, which results in incomplete medical histories and lost intervention chances. A lack of safety information on herbal products is a result of this underreporting, which is partially caused by the false belief that natural goods are always safe.[05]

- **Variability in the Composition of Herbal Products**

The composition of herbal products can vary greatly depending on a number of factors, including plant species, growing techniques, and processing processes. This fluctuation may result in uneven active component concentrations, making safety evaluations more difficult and raising the possibility of unfavourable interactions with prescription medications.[06]

- **Insufficient Standardization**

Quality control is impacted by the lack of established procedures for the manufacturing of herbal medicines. It becomes difficult to guarantee the consistency and safety of herbal products without defined procedures, which may result in unfavourable interactions with prescription medications.[07]

PHARMACOVIGILANCE TECHNIQUES FOR THE SAFETY EVALUATION OF HERB-DRUG INTERACTIONS (HDI)

To improve the tracking and reporting of herb–drug interactions (HDIs), herbal medications must be incorporated into current pharmacovigilance frameworks. Important tactics consist of:

- **Enrolment in National Pharmacovigilance Programs**

The systematic collecting and analysis of adverse event data pertaining to HDIs is made possible by the integration of herbal medicines into national pharmacovigilance systems. The creation of safety profiles for herbal goods and the detection of possible hazards are made easier by this connection. In order to help nations include herbal medicines into their pharmacovigilance systems, the World Health Organization (WHO) has created guidelines that highlight the significance of keeping an eye on the safety of herbal medicines within these frameworks.[08]

- **Creation of Specific Reporting Instruments**

It is essential to develop specialized databases and methods for recording and analysing adverse events connected to HDI. By allowing consumers and medical experts to record negative responses linked to herbal products, these specialized reporting systems improve the amount and quality of safety data. The necessity for specialized reporting methods to enhance the safety monitoring of herbal and traditional medicines has been brought to light by the International Society of Pharmacovigilance.[09]

- **Professional Education in Public and Healthcare** [10]

It is essential to inform the public and medical professionals about the possible dangers of HDIs and the significance of disclosing adverse events. Increasing understanding can result in safer usage of herbal products and more accurate reporting. According to a study in the Journal of Complementary and Alternative Medical Research, pharmacists play a crucial role in public education and guaranteeing the safe use of herbal product.

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 987-994 www.ijprajournal.com ISSN: 2456-4494

METHODOLOGIES FOR ASSESSING HERB-DRUG INTERACTIONS

Assessing herb-drug interactions (HDIs) is crucial for ensuring drug safety and efficacy.

- **In Vitro Studies**
  - These studies help in identifying potential interactions at the molecular level before proceeding to animal or human trials.
  - Enzyme Inhibition/Induction Assays.[11]
  - Examines the effect of herbal compounds on cytochrome P450 (CYP) enzymes and drug transporters (e.g., P-glycoprotein).
  - Transporter Interaction Studies.[12]
  - Determines whether herbal compounds affect drug transporters like Pglycoprotein (P-gp) or organic anion transporters.

- **In Vivo Animal Studies**
  - Animal models (e.g., rats, mice) are used to assess pharmacokinetic (PK) changes due to herb-drug interactions.
  - Pharmacokinetic (PK) Studies.[13]
  - Evaluates changes in absorption, distribution, metabolism, and excretion (ADME) of drugs when co-administered with herbal extracts.
  - Toxicity and Pharmacodynamic (PD) Assessments
  - Assesses potential adverse effects, efficacy changes, or toxicological outcomes.[14]

- **Clinical Studies**
  - Clinical trials or observational studies help confirm herb-drug interactions in humans.
  - Case Reports and Observational Studies
  - Reports of adverse interactions between herbs and drugs in real-world settings.[15]
  - Controlled Clinical Trials
  - Evaluates HDIs in a controlled setting using placebo or active comparator groups.[16]

- **Computational Approaches**
  - In Silico Prediction Models
  - Uses machine learning or molecular docking to predict potential HDIs.[17]
  - Network Pharmacology & Systems Biology Approaches
  - Integrates multi-omics data to study complex HDI mechanisms.[18]

CASE STUDY AND EXAMPLE

❖ **Case Study: - St. John's Wort and Warfarin [19]**

➢ Background

St. John's Wort (Hypericum perforatum) is a widely used herbal remedy for depression, anxiety, and sleep disorders. However, it has been documented to interact with various prescription medications, particularly warfarin, a commonly used anticoagulant.

➢ Case Report

A 65-year-old male patient on long-term warfarin therapy for atrial fibrillation started taking St. John's Wort for mild depression. After four weeks, he was admitted to the emergency department with a stroke due to a significantly reduced INR (International Normalized Ratio), indicating reduced anticoagulation efficacy.

➢ Mechanism of Interaction

St. John's Wort is known to induce cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp), which leads to increased metabolism and clearance of warfarin, thereby reducing its anticoagulant effect.

➢ Outcome and Management [20]

- The patient's St. John's Wort intake was discontinued immediately.
- Warfarin dosage was adjusted and monitored closely.
- Within two weeks, INR levels returned to the therapeutic range.
- The patient was educated about potential herb-drug interactions before taking any new supplement.

❖ **Example: – Ginkgo Biloba and Aspirin [21][22]**

➢ Background

Ginkgo biloba is commonly used for memory enhancement and cognitive function. It contains flavonoids and terpenoids, which have mild antiplatelet properties. When combined with aspirin, a blood thinner, it can increase the risk of bleeding complications.

➢ Clinical Evidence

A 70-year-old female with a history of stroke was taking aspirin (75 mg daily) for secondary stroke prevention. She started using Ginkgo biloba extract (120 mg daily) for memory enhancement. After two months, she developed spontaneous intracranial haemorrhage, confirmed via CT scan.

➢ Mechanism of Interaction

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 987-994 www.ijprajournal.com ISSN: 2456-4494

Ginkgo biloba inhibits platelet-activating factor (PAF), leading to enhanced antiplatelet activity when combined with aspirin.

The combination resulted in excessive bleeding risk.

- ➢ Outcome and Management
- o Ginkgo biloba was discontinued immediately.
- o The patient was monitored in the hospital and recovered with supportive care.
- o The patient was advised against using herbal supplements without medical consultation.

REGULATORY PERSPECTIVES ON HERB-DRUG INTERACTIONS

Herb-drug interactions (HDIs) pose a challenge for regulatory agencies worldwide due tovariability in herbal composition, lack of standardized testing, and limited clinical trial. Several regulatory bodies, including the FDA (USA), EMA (Europe), MHRA (UK), and WHO, have established guidelines for assessing and managing HDIs.

- **U.S. Food and Drug Administration (FDA) Perspective [24]**

✓ **Guidelines & Regulations**

- o TheFDA categorizes herbal products as dietary supplements under the Dietary Supplement Health and Education Act (DSHEA) of 1994.
- o Unlike pharmaceuticals, herbal products are not required to undergo rigorous pre-market approval. However, manufacturers must ensure safety, labelling accuracy, and good manufacturing practices (GMP).
- o The FDA's Guidance for Industry on Drug Interaction Studies (2020) recommends in vitro and in vivo testing of CYP enzymes and drug transporters for potential HDIs.

✓ **Challenges**

- o Lack of mandatory clinical trialsfor herbs.
- o Variability in herbal composition makes standardization difficult.
- o Post-market surveillance is limited.

- **European Medicines Agency (EMA) Perspective [25]**

✓ **Guidelines & Regulations**

- o The EMA classifies herbal products as traditional herbal medicinal products (THMPs) under the Traditional Herbal Medicinal Products Directive 2004/24/EC.
- o The Committee on Herbal Medicinal Products (HMPC) evaluates evidence for HDIs, pharmacokinetics, and pharmacodynamics.
- o The EMA requires in vitro and in vivo testing for enzyme induction, inhibition, and transporter-mediated interactions.
- o Herbal monographs are created for safety evaluations, listing known HDIs and contraindications.

✓ **Challenges**

- o Many herbal products lack clinical HDI data, making risk assessment difficult. Differences in herbal formulations (e.g., extracts vs. raw plants) affect interaction outcomes.

- **UK's Medicines and Healthcare Products Regulatory Agency (MHRA) Perspective [26]**

✓ **Guidelines & Regulations**

- o The MHRA follows EMA directives and assesses HDIs under the THMPs framework.
- o Herbal products must be registered under the Traditional Herbal Registration (THR) scheme and comply with quality and safety standards.
- o Post-market monitoring is done through the Yellow Card Scheme, where healthcare professionals and consumers can report herb-drug interactions and adverse reactions.

✓ **Challenges**

- o Many herbal products are sold as food supplements, bypassing MHRA regulations.
- o Limited enforcement of HDI reporting compared to pharmaceuticals.

- **World Health Organization (WHO) Perspective [27]**

✓ **Guidelines & Regulations**

- o WHO has established Guidelines on Safety Monitoring of Herbal Medicines in Pharmacovigilance Systems (2004).
- o WHO emphasizes pharmacovigilance systems to report HDIs and adverse events in developing countries.
- o Promotes the integration of traditional medicine into national healthcare policies.

✓ **Challenges**

- o Lack of global standardization in assessing HDIs.
- o Limited funding and resources for herbal pharmacovigilance in many countries.

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 987-994 www.ijprajournal.com ISSN: 2456-4494

- **INDIAN REGULATORY PERSPECTIVES** [28]

In India, the regulation of herbal medicines and the assessment of herb-drug interactions (HDIs) are primarily governed by the Drugs and Cosmetics Act of 1940 and its subsequent amendments. The Ministry of AYUSH (Ayurveda, Yoga & Naturopathy, Unani, Siddha, and Homoeopathy) and the Central Drugs Standard Control Organisation (CDSCO) are the key regulatory bodies overseeing these aspects.

✓ **Regulatory Framework**

- **Drugs and Cosmetics Act of 1940**: This act provides the legal framework for the regulation of drugs and cosmetics in India, including herbal medicines. It classifies herbal products under Ayurvedic, Siddha, and Unani drugs and mandates adherence to specified standards. However, the act has been critiqued for its limited focus on HDIs.

- **Schedule T:** Part of the Drugs and Cosmetics Act, Schedule T outlines Good Manufacturing Practices (GMP) for Ayurvedic, Siddha, and Unani medicines. It emphasizes quality control but does not explicitly address HDIs.

FUTURE DIRECTIONS AND RESEARCH NEEDS IN PHARMACOVIGILANCE FOR HERB-DRUG INTERACTION (HDI) SAFETY ASSESSMENT

The increasing global use of herbal medicines alongside conventional pharmaceuticals necessitates a robust pharmacovigilance system to monitor and assess herb-drug interactions (HDIs). Future research must focus on integrating herbal pharmacovigilance into mainstream drug safety surveillance by developing standardized reporting systems, improving healthcare professional awareness, and leveraging advanced technologies like artificial intelligence (AI) and big data analytics. Establishing dedicated herbal pharmacovigilance centres within existing drug monitoring frameworks will ensure systematic data collection on HDI-related adverse events.

A key research priority is the development of validated methodologies for detecting and assessing HDIs. This includes clinical trial designs that evaluate HDI risks, in vitro and in vivo mechanistic studies, and population-based observational studies. Given the variability in herbal formulations, metabolomic and pharmacokinetic studies should be expanded to identify how different herbal constituents interact with drug metabolism pathways, particularly cytochrome P450 enzymes and drug transporters. Additionally, multi-omics approaches integrating genomics, proteomics, and metabolomics can help predict individual variability in HDIs, aiding in personalized medicine.

Regulatory frameworks also need to evolve to accommodate herb-drug interactions. While agencies like the FDA, EMA, and WHO have emphasized the importance of pharmacovigilance for herbal products, there is still a lack of specific guidelines on HDI risk assessment. Future efforts should focus on harmonizing global regulations to ensure that herbal products undergo rigorous preclinical and clinical safety evaluations similar to pharmaceuticals. Strengthening post-market surveillance and promoting active reporting systems (e.g., electronic health records-based reporting and mobile apps for adverse event reporting) will help bridge the gap between traditional knowledge and modern drug safety practices.

Lastly, improving healthcare professional and consumer education is critical for effective HDI risk management. Future initiatives should include integrating herbal pharmacovigilance training into medical and pharmacy curricula, promoting evidence-based practice, and conducting large-scale public awareness campaigns about the potential risks of self-medication with herbal supplements. Encouraging interdisciplinary collaboration between pharmacologists, toxicologists, herbalists, and clinicians will further enhance the safety and efficacy of herbal medicine use in conjunction with conventional drugs.

II. CONCLUSION

Herb-drug interactions (HDIs) present a growing public health concern, particularly as herbal supplement use rises alongside pharmaceutical medications. Understanding the pharmacokinetic and pharmacodynamic mechanisms behind HDIs is essential for preventing adverse outcomes. The role of pharmacovigilance in HDI monitoring is crucial, but underreporting, product variability, and insufficient standardization remain major obstacles.

Regulatory agencies worldwide, including the FDA, EMA, WHO, and India's Ministry of AYUSH, are working toward enhancing HDI safety monitoring, but standardized guidelines for preclinical and clinical HDI assessments are still

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 987-994 www.ijprajournal.com ISSN: 2456-4494

lacking. Future efforts should focus on improving regulatory harmonization, integrating AI-driven data analysis, expanding clinical trials, and strengthening healthcare education.

To minimize HDI-related risks, patients should be encouraged to disclose their use of herbal supplements to healthcare providers, while clinicians must be trained to recognize and manage potential HDIs. By fostering collaboration between researchers, regulators, and healthcare professionals, a safer and more effective integration of herbal and conventional medicines can be achieved.

III. SUMMARY

The widespread use of herbal supplements alongside prescription drugs has led to growing concerns about herb-drug interactions (HDIs). These interactions may significantly impact drug efficacy and safety, causing reduced therapeutic effects or increased risks of toxicity. This article provides an in-depth analysis of HDI mechanisms, focusing on how herbal components influence drug metabolism.The role of pharmacovigilance in monitoring HDIs is discussed, highlighting key challenges such as underreporting, variability in herbal composition, and lack of product standardization. National pharmacovigilance programs, specialized adverse event reporting tools, and healthcare professional education are emphasized as crucial measures to enhance HDI safety surveillance.The regulatory landscape is explored across different regions, including the FDA (USA), EMA (Europe), MHRA (UK), WHO, and India's Ministry of AYUSH. While some progress has been made, a lack of standardized HDI testing and harmonized global regulations remains a significant challenge.

Finally, future directions in HDI research call for validated methodologies, advanced technologies (AI, big data analytics, multi-omics approaches), and regulatory enhancements. Improving public awareness, healthcare training, and interdisciplinary collaboration is necessary to ensure safe and effective herbal medicine use.

KEY POINTS

✔ Herbal supplements interact with prescription drugs, affecting metabolism and efficacy.

✔ Pharmacovigilance systems are crucial but face underreporting and standardization challenges.

✔ Regulatory agencies worldwide have varying approaches to HDI assessment, but harmonization is needed.

✔ Advanced methodologies, including in vitro, in vivo, and AI-driven computational models, improve HDI detection.

✔ Case studies (St. John's Wort-Warfarin, Ginkgo Biloba-Aspirin) demonstrate the real-world risks of HDIs.

✔ Future research should focus on AI integration, personalized medicine, and better public awareness.

REFERENCES

[1]. Parray, S. (2017). Herb-drug interaction and role of pharmacovigilance. International Journal of Advanced Pharmacy and Medical Bio allied Sciences, 3(1), 75-78. Retrieved from https://www.researchgate.net/publication/319260848_Herb-drug_interaction_and_role_of_pharmacovigilance

[2]. Melillo, E. (2024, August 23). I'm a pharmacist - beware the potentially dangerous effects of this common herbal supplement. New York Post. Retrieved from (https://nypost.com/2024/08/23/lifestyle/st-johns-wort-can/)

[3]. Ekor, M. (2014). The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. 'Frontiers in Neurology', 4, 177. ([PMC](https://pmc.ncbi.nlm.nih.gov/articles/PMC2000738/?)

[4]. Kunle, O. F., Egharevba, H. O., & Ahmadu, A. A. (2012). Standardization of herbal medicines—A review. 'International Journal of Biodiversity and Conservation', 4(3), 101-112. [Academic Journals] (https://academicjournals.org/article/article1380017716_Kunle%20et%20al.pdf/1000?utm)

[5]. Shetti, S., Kumar, C. D., Srivastava, N. K., & Sharma, I. P. (2011). 'Pharmacovigilance of herbal medicines: Current state and future directions. Pharmacognosy Magazine', 7(25), 69-73. ([link.springer.com] (https://link.springer.com/referenceworkentry/10.1007/978-3-031-21973-3_40))

[6]. Fokunang, E. T., Fonmboh, D. J., Mballa, R. N., Nyuyki, A. B., Fukunaga, L. B., Kaba, N., Abong, T. B., Duerr, R.,

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 987-994 www.ijprajournal.com ISSN: 2456-4494

Richard, E., Ondoua, M. T. A., & Fokunang, C. N. (2020). Pharmacovigilance of natural herbal medicines research for efficacy, safety, and quality assurance of phytomedicine products. 'Journal of Complementary and Alternative Medical Research', 12(1), 21-37. ([link.springer.com] (https://link.springer.com/referenceworkentry/10.1007/978-3-031-21973-3_40-1?utm))

[7]. Jain, S. D., Shrivastava, S. K., Agrawal, A., & Gupta, A. K. (2023). WHO guidelines for quality control of herbal medicines: From cultivation to consumption. 'International Journal of Pharmaceutical Chemistry and Analysis', 10(1), 1-10. ([IJPCA](https://www.ijpca.org/html-article)

[8]. World Health Organization. (2004). WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems. Retrieved from https://tdr.who.int/home/our-work/global-engagement/9241592214

[9]. International Society of Pharmacovigilance. (2024). A Framework for Promoting Safety Monitoring of Herbal Medicines: The International Society of Pharmacovigilance Special Interest Group on Herbal and Traditional Medicines. Drug Safety. Retrieved from https://link.springer.com/article/10.1007/s40264-024-01440-6

[10]. Yılmaz, S., & Yılmaz, S. (2021). The Safety of Herbal Medicines (Phyto vigilance) from Community Pharmacists' Perspective: A Cross-Sectional Study. Journal of Complementary and Alternative Medical Research, 12(1), 21-37. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9254090/

[11]. Pal, D., & Mitra, A. K. (2006). MDR- and CYP3A4-mediated drug-herbal interactions. Life Sciences, 78(18), 2131–2145.

[12]. Wang, E. J., et al. (2001). Inhibition of P-glycoprotein transport function by herbal medicines. Journal of Pharmacology and Experimental Therapeutics, 299(2), 575-582.

[13]. Zhou, S., et al. (2004). Interactions of herbs with cytochrome P450. 'Drug Metabolism Reviews, 36(1)', 57-97.

[14]. Awortwe, C., et al. (2019). Pharmacokinetics and pharmacodynamics of HDIs. 'Frontiers in Pharmacology, 10', 606.

[15]. Gurley, B. J., et al. (2008). Assessing the clinical significance of HDIs. 'Clinical Pharmacology & Therapeutics 84(4)', 467-477.

[16]. Unger, M., et al. (2013). Clinical relevance of HDIs. 'British Journal of Clinical Pharmacology, 75(3)', 587-595.

[17]. Yeung, E. Y. H., et al. (2021). In silico prediction of HDIs. 'Computational Toxicology, 20', 100190.

[18]. Zhang, A., et al. (2019). Systems pharmacology approach for studying HDIs. 'Drug Discovery Today, 24(5)', 1030-1040.

[19]. Yue, Q. Y., Bergquist, C., & Gerden, B. (2000). Safety of St. John's Wort in long-term use: A case study on warfarin interactions. The Lancet, 355(9203), 576-577.

[20]. Henderson, L., Yue, Q. Y., Bergquist, C., & Gerden, B. (2002). St. John's Wort (Hypericum perforatum): Drug interactions and clinical outcomes. British Journal of Clinical Pharmacology, 54(4), 349-356.

[21]. Izzo, A. A., & Ernst, E. (2001). Interactions between herbal medicines and prescribed drugs: A systematic review. Drugs, 61(15), 2163-2175.

[22]. National Centre for Complementary and Integrative Health. (n.d.). Herb-Drug Interactions. Retrieved from (https://www.nccih.nih.gov/health/providers/digest/herb-drug-interactions)

[23]. Bent, S., & Ko, R. (2004). Commonly used herbal medicines in the United States: A review. American Journal of Medicine, 116(7), 478-485.

[24]. U.S. Food and Drug Administration (FDA) (2020). Drug Interaction Studies—Study Design, Data Analysis, and Clinical Implications. Guidance for Industry. [Available at: FDA.gov] (https://www.fda.gov/)

[25]. European Medicines Agency (EMA) (2018). Guideline on the investigation of drug interactions. Committee on Herbal Medicinal Products (HMPC). [Available

at: ema.europa.eu] (https://www.ema.europa.eu/)

[26]. Medicines and Healthcare Products Regulatory Agency (MHRA) (2021). Herbal Medicines: Safety and Regulations. [Available at: gov.uk/mhra] (https://www.gov.uk/mhra)

[27]. World Health Organization (WHO) (2004). Guidelines on Safety Monitoring of Herbal Medicines in Pharmacovigilance Systems. [Available at: who.int] (https://www.who.int/)

[28]. Guidelines on good field collection practices for Indian medicinal plants, National Medicinal plant Board, India,Accessed March20, 2012http://nmpb.nic.in/WriteReadData/links/7687590193Good%20Field%20Collection%20Practicies%20(GFCPs)%20Booklet%20-%20Part%20-%20I.pdf