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Review Paper

Pharmacovigilance of Herbal Medicines: Current Challenges and Future Perspectives

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ABSTRACT

Herbal medicines have been widely used across the world for the prevention and treatment of various diseases due to their natural origin and perceived safety. However, increasing reports of adverse drug reactions, toxicity, and herb–drug interactions have raised concerns regarding their safety. Pharmacovigilance plays a crucial role in monitoring, assessing, and preventing adverse effects associated with herbal medicines. This review highlights the importance of pharmacovigilance in herbal medicine, focusing on challenges such as lack of standardization, underreporting of adverse effects, variability in herbal preparations, and inadequate regulatory frameworks. It also discusses global pharmacovigilance systems and regulatory guidelines followed in different countries, including India. Furthermore, the need for proper documentation, awareness among healthcare professionals, and integration of traditional medicine into modern pharmacovigilance systems is emphasized. Strengthening pharmacovigilance practices for herbal medicines is essential to ensure their safe and effective use. This review provides insights into current issues and future perspectives for improving safety monitoring of herbal products. (1)

INTRODUCTION

Pharmacovigilance of herbal medicines refers to the science and activities involved in detecting, assessing, understanding, and preventing adverse effects or any other problems related to the use of herbal products. With the growing global use of herbal medicines—often perceived as natural and safe—there is an increasing need to monitor their safety and efficacy. Herbal preparations can cause adverse reactions due to factors such as poor quality control, contamination, adulteration with synthetic drugs or heavy metals, misidentification of plants, and herb–drug interactions. Unlike conventional drugs, many herbal products lack standardization, clinical evidence, and proper labelling. leading to unpredictable therapeutic outcomes. The World Health Organization (WHO)

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has recognized the importance of integrating herbal pharmacovigilance into national drug monitoring systems to ensure patient safety. In India, the Ministry of AYUSH has established the Pharmacovigilance Programme for Ayurveda, Siddha, Unani, and Homeopathy (ASU&H) to monitor and document adverse drug reactions associated with traditional medicines. The main objectives of herbal pharmacovigilance include ensuring safe use, identifying risks, maintaining product quality, and promoting rational therapy. However, challenges such as underreporting, lack of awareness among healthcare professionals, and limited scientific data still exist. Therefore, strengthening herbal pharmacovigilance systems is essential to enhance the credibility, safety, and effectiveness of herbal medicines in global healthcare.

Pharmacovigilance (PV) is the science and activities related to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems. While traditionally focused on synthetic drugs, the principles of PV are increasingly being applied to herbal medicines, traditional remedies, and dietary supplements. This has become crucial due to the global increase in the use of herbal products, driven by factors such as a perception of them being "natural" and therefore safe, and a growing interest in alternative therapies. However, this perception is often flawed, as herbal medicines are not without risks and can cause significant adverse reactions (ADRs) and drug-herb interactions. (2)

Need for pharmacovigilance of herbal medicine-

The need for robust PV systems for herbal medicines stems from several key factors:

- **Safety Concerns**: Herbal products can cause serious adverse effects, including hepatotoxicity (liver damage), nephrotoxicity (kidney damage), and allergic reactions. Case studies have documented instances of liver injury from ingredients like Tinospora cordifolia and severe skin reactions from metal-based Siddha medicines. (3)
- **Herb-Drug Interactions**: Herbal medicines are frequently used alongside conventional drugs, leading to potential interactions. These interactions can alter the efficacy or increase the toxicity of either the herb or the drug. For example, St. John's Wort is known to interact with various conventional drugs, including antidepressants and oral contraceptives. (4)
- **Adulteration and Contamination**: The lack of standardized manufacturing and quality control can lead to herbal products being adulterated with undeclared potent substances (e.g., steroids, heavy metals) or contaminated with pesticides, microbial toxins, or other hazardous materials.
- **Misidentification of Plants**: Improper identification of plant species used in preparations can lead to unintended toxic effects.
- **Dosage and Formulation Issues**: Unlike conventional medicines, the active ingredients, dosage, and standardization of herbal products can vary significantly. Traditional herbal preparations often contain multiple ingredients, making it difficult to pinpoint the causative agent of an ADR.

Challenges in Herbal Medicine Pharmacovigilance-

Applying the conventional PV model to herbal medicines presents unique and significant challenges:

1. **Underreporting**: This is a major issue. Both healthcare professionals and the public often fail to report ADRs associated with herbal products, believing them to be safe. Patients

may not even disclose their use of herbal remedies to their doctors. (5)

2. **Lack of Standardization and Quality Control**: The quality of herbal products can be highly variable. Factors such as the plant's origin, the season of collection, processing methods, and the presence of adulterants can all influence the safety and efficacy of the final product. (6)
3. **Complex Chemical Composition**: Herbal products are typically a mixture of many chemical compounds, not a single active molecule. This makes it difficult to establish a clear dose-response relationship or identify the specific component responsible for an adverse effect. (7)
4. **Misinformation and Lack of Awareness**: The public's belief in the inherent safety of "natural" products, coupled with a lack of awareness among healthcare professionals about potential risks, contributes to the problem. Many practitioners are not formally trained in traditional medicine, making it difficult to assess and interpret causality reports.
5. **Difficulty in Causality Assessment**: Establishing a causal link between an herbal product and an ADR can be challenging. It requires a detailed understanding of the herb's pharmacology, potential interactions, and a thorough patient history, including the use of all concomitant medications. (8)
6. **Regulatory Hurdles**: In many countries, herbal products are classified as dietary supplements or foods, not medicines. This classification often means they are not subject to the same stringent regulations for safety and efficacy as conventional drugs.

Strategies to Improve Herbal Medicine Pharmacovigilance-

To address these challenges, several strategies are being implemented and recommended by global organizations like the World Health Organization (WHO):

- **Strengthening Regulatory Frameworks**: Countries need to establish clear and stringent regulations for the manufacturing, labeling, and marketing of herbal products. This includes implementing Good Manufacturing Practices (GMP) and requiring evidence of quality and safety before products can be sold. (9)
- **Enhancing Spontaneous Reporting Systems**: The existing spontaneous reporting systems should be expanded and promoted to specifically include herbal products. Healthcare professionals and patients need to be educated on the importance of reporting all suspected ADRs, regardless of whether they are from conventional or herbal medicines. (10)
- **Improving Data Collection and Analysis**: Reporting forms should be adapted to capture crucial information about herbal products, such as the specific plant species (using proper scientific binomial names), the parts of the plant used, the preparation method, and the batch number.
- **Education and Training**: Training programs for healthcare professionals should be updated to include comprehensive information on herbal medicines, their potential risks, and the importance of PV. Public awareness campaigns can also help dispel the myth that "natural" means "safe." (11)
- **International Collaboration**: Global cooperation and data sharing are essential for detecting safety signals for widely used herbal products. The WHO's International Drug Monitoring Program plays a key role in this effort.

- **Research and Clinical Studies**: More systematic research, including observational studies and clinical trials, is needed to build a robust evidence base for the safety and efficacy of herbal medicines.

Global Perspective and Regulatory Frameworks-

The approach to herbal medicine regulation and pharmacovigilance varies significantly across the globe**.**

- **The World Health Organization (WHO):** is a specialized agency of the United Nations (UN) that is responsible for international public health. It was established on 7 April 1948, a date now celebrated annually as World Health Day. The WHO's headquarters is located in Geneva, Switzerland, and it operates through six regional offices across the world — Africa (AFRO), the Americas (PAHO/AMRO), South-East Asia (SEARO), Europe (EURO), Eastern Mediterranean (EMRO), and Western Pacific (WPRO). The primary objective of WHO, as stated in its Constitution, is the "attainment by all peoples of the highest possible level of health." Health, according to WHO, is not merely the absence of disease or infirmity but a state of complete physical, mental, and social well-being. The organization plays a vital role in setting global health standards, coordinating international responses to health emergencies, and supporting countries in strengthening their healthcare systems. The WHO has been a leader in advocating for the safe use of traditional and herbal medicines. It has published several key documents, including "WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems." These guidelines are designed to help countries integrate herbal medicine monitoring into their existing national PV programs. The WHO also promotes the use of standardized nomenclature, such as the Herbal Anatomical Therapeutic Chemical (HATC) classification system, to ensure consistency in reporting and data analysis.
- **European Union**: The EU has established a "Traditional Herbal Medicinal Products" (THMP) directive. This provides a simplified registration process for herbal products, provided they have a long history of traditional use and are proven to be safe. While this framework facilitates market access, it also places a responsibility on manufacturers to conduct continuous safety monitoring and report any adverse events. (12)

The European Union (EU) is a political and economic union of 27 European countries that work together to promote peace, stability, and prosperity across Europe. Established by the Maastricht Treaty in 1993, the EU evolved from earlier European cooperation efforts, such as the European Economic Community (EEC). Its headquarters are located in Brussels, Belgium, with key institutions also based in Strasbourg (France) and Luxembourg. The EU operates through a unique system of supranational institutions and intergovernmental decision-making, where member states share sovereignty in certain areas while maintaining national independence in others. The major institutions of the EU include the European Commission (executive body), European Parliament (legislative body representing EU citizens), Council of the European Union (representing member states), European Council (setting overall policy direction), and the Court of Justice of the European Union (CJEU) (ensuring uniform interpretation of EU law). Economically, the EU functions as a single

market, allowing the free movement of goods, services, capital, and people among member states. It has its own currency, the Euro (€), used by 20 of the 27 members, known collectively as the Eurozone. The EU also plays a major role in global trade, being one of the world's largest trading blocs. In public health and pharmaceutical regulation, the EU maintains high standards through agencies such as the European Medicines Agency (EMA), which oversees the scientific evaluation, supervision, and safety monitoring of medicines, including herbal and traditional products. The EU also supports pharmacovigilance systems through the EudraVigilance database, which collects and evaluates reports of adverse drug reactions from across member states to ensure medicine safety and effectiveness.Beyond health, the EU is active in areas like environmental protection, digital innovation, research, education (e.g., Erasmus+), and human rights. It has established policies promoting climate action through the European Green Deal and aims for sustainable development in line with global standards. Overall, the European Union stands as a powerful example of regional integration, promoting unity, economic cooperation, and shared governance while ensuring high standards in healthcare, safety, and social welfare for its citizens.

- **United States**: In the U.S., most herbal products are classified as "dietary supplements" under the Dietary Supplement Health and Education Act (DSHEA) of 1994. This means they are not regulated as drugs, and manufacturers are not required to prove their safety and efficacy before marketing. The responsibility for safety lies with the manufacturer, who must report serious adverse events to the FDA. This regulatory gap is a major challenge for pharmacovigilance. The United States (U.S.) is a federal republic comprising 50 states, a federal district (Washington, D.C.), and several territories. It is one of the world's most developed and influential nations, playing a leading role in global politics, economics, science, and healthcare. The country operates under a federal system of government, meaning powers are divided between the federal (national) government and state governments. The U.S. Constitution, adopted in 1787, is the supreme law of the land and establishes three branches of government — the Executive (President), Legislative (Congress), and Judicial (Supreme Court) — ensuring a system of checks and balances.Economically, the U.S. has one of the largest and most advanced economies in the world, driven by technology, finance, pharmaceuticals, healthcare, and innovation. In terms of healthcare and medicine regulation, the United States Food and Drug Administration (FDA) plays a central role. The FDA, an agency of the Department of Health and Human Services (HHS), is responsible for ensuring the safety, efficacy, and quality of drugs, medical devices, vaccines, cosmetics, and food products. It also oversees pharmacovigilance activities, including the monitoring of adverse drug reactions through systems such as the FDA Adverse Event Reporting System (FAERS) and MedWatch (a public reporting program).In the U.S., most herbal products are classified as "dietary supplements" under the Dietary Supplement Health and Education Act (DSHEA) of 1994, rather than as drugs. This means they are not subject to the same strict premarket approval requirements as pharmaceutical medicines. Manufacturers are responsible for ensuring product safety and proper labeling, while the FDA takes

regulatory action if a product is found to be unsafe or falsely marketed. Additionally, the National Center for Complementary and Integrative Health (NCCIH), part of the National Institutes of Health (NIH), conducts research on the safety and efficacy of herbal and traditional remedies. The Centers for Disease Control and Prevention (CDC) also plays a crucial role in public health, disease prevention, and emergency response, while agencies like the Environmental Protection Agency (EPA) and U.S. Department of Agriculture (USDA) regulate environmental and food-related safety. The U.S. healthcare system combines public and private sectors, with programs like Medicare and Medicaid providing coverage for specific populations. Overall, the United States maintains a highly structured regulatory framework for health and medicine, emphasizing innovation, patient safety, and scientific evidence while facing ongoing challenges such as healthcare accessibility, drug pricing, and herbal product regulation.

- **India**: India has a rich tradition of Ayurvedic, Siddha, and Unani (ASU) medicine. The Indian government has established a national pharmacovigilance program for ASU drugs to systematically monitor adverse reactions. This is a positive step toward integrating traditional medicine into the national PV framework. (13) India has a rich and ancient tradition of using herbal and traditional systems of medicine, primarily Ayurveda, Siddha, and Unani (ASU), which have been practiced for thousands of years as part of the country's cultural and healthcare heritage. These systems emphasize a holistic approach to health, focusing on the balance of body, mind, and spirit, and use natural substances derived from plants, minerals, and animal sources for prevention and treatment of diseases. With the increasing global recognition and commercialization of traditional medicines, the Government of India has taken significant steps to ensure their safety, efficacy, and quality through proper pharmacovigilance mechanism. To systematically monitor and evaluate the safety of traditional medicines, the Ministry of AYUSH (Ayurveda, Yoga & Naturopathy, Unani, Siddha, and Homeopathy) launched the National Pharmacovigilance Program for ASU&H Drugs in 2008, which was later revamped and strengthened in 2017. The program's main objective is to create a structured system for collecting, analyzing, and reporting Adverse Drug Reactions (ADRs) and Adverse Events (AEs) associated with Ayurveda, Siddha, Unani, and Homeopathic drugs. The initiative aims to ensure the safe and rational use of traditional medicines, build public trust, and integrate traditional systems into the national pharmacovigilance framework.

Key Technical and Methodological Aspects-

1. **Causality Assessment**: Determining if an ADR is caused by an herbal product is a complex task. Standard causality assessment tools, such as the Naranjo scale, were developed for single-molecule drugs and may not be entirely suitable for multi-ingredient herbal formulations. New and adapted methods are being developed, often incorporating specific criteria for herbal products, such as:

- Confirmation of the plant species used (e.g., via DNA barcoding or phytochemical analysis).
- Information on the specific part of the plant used (e.g., leaf, root, bark).

- Details of the preparation method (e.g., decoction, tincture, extract).
- The presence of other concomitant medications or pre-existing conditions.
- Roussel Uclaf Causality Assessment Method (RUCAM): This tool is often used for assessing drug-induced liver injury, and its principles can be adapted for herb-induced liver injury. (14)

2. **Standardized Nomenclature**: The lack of a uniform naming system is a significant hurdle. A single plant species may have multiple common names, and different plant species may share the same common name. The use of Latin binomial names (e.g., Ginkgo biloba) is crucial for accurate reporting and data aggregation. The WHO's HATC system is a key initiative to standardize this.
3. **The Role of Post-Marketing Surveillance**: Since many herbal products lack extensive pre-clinical and clinical trial data, post-marketing surveillance becomes the primary source of safety information. This includes:

- **Spontaneous Reporting**: This remains the backbone of PV, but its effectiveness for herbal medicines is limited by underreporting. Efforts are underway to make reporting systems more user-friendly and to raise awareness among healthcare professionals and consumers
- **Active Surveillance**: This involves actively seeking out adverse events, for example, through follow-up studies in specific patient populations or targeted monitoring of products with known safety concerns.
- **Signal Detection**: This is the process of identifying new, previously unknown adverse effects from analyzing large databases of reported cases. Sophisticated statistical tools are being adapted to detect signals for herbal products.

Emerging Trends and Future Directions-

- **Integration with Modern Technology**: Mobile apps and web-based platforms are being developed to make it easier for patients and healthcare providers to report adverse events. These tools can also provide a structured way to collect the detailed information needed for causality assessment. (15
- **Herbal Drug Interactions (HDIs)**: Research on HDIs is an area of growing importance. Studies are using "omics" technologies (e.g., genomics, proteomics, metabolomics) to understand the mechanisms by which herbal components interact with drug-metabolizing enzymes (e.g., cytochrome P450 enzymes). This can help predict and prevent dangerous interactions. (16)
- **Real-World Evidence (RWE)**: The use of large-scale electronic health records (EHRs) and insurance claims data is becoming a new source of information for PV. By analyzing RWE, researchers can identify potential safety issues with herbal products in real-world clinical practice. (17)
- **Ethnobotanical Documentation**: There is a renewed effort to systematically document the traditional uses and safety profiles of medicinal plants from different cultures. This information is vital for a risk-benefit assessment of traditional remedies.

Specific Examples of Reported Adverse Effects

- **Hepatotoxicity**: Cases of liver damage have been linked to a variety of herbs, including Tinospora cordifolia, germander (Teucrium chamaedrys), and some Chinese herbal formulations.
- **Nephrotoxicity**: Renal failure has been associated with the use of aristolochic acid-

containing herbs, leading to a global ban on these products.

- **Cardiovascular Effects**: Ephedra, a stimulant often used in weight-loss supplements, has been linked to heart attacks and strokes, leading to its ban in several countries.
- **Bleeding**: Ginkgo biloba and garlic supplements can have antiplatelet effects and may increase the risk of bleeding, especially when taken with blood-thinning medications like warfarin. (18)

The Role of Key Stakeholders-

Effective pharmacovigilance of herbal medicine requires the active participation of various stakeholders:

1. **Regulatory Authorities**:

- Function: They are responsible for establishing and enforcing a legal framework for the safety and quality of herbal products.
- Activities: This includes product registration, licensing of manufacturers, and taking regulatory actions such as issuing safety alerts, adding warnings to product labels, or withdrawing products from the market based on safety signals.
- Challenges: A key challenge is the wide range of herbal products available, from well-known traditional remedies to complex multi-herb formulations and dietary supplements. The regulatory classification often dictates the level of oversight, with supplements having less stringent requirements than licensed medicines.

2. **Healthcare Professionals (HCPs)**:

- Function: As the first point of contact for patients, HCPs are crucial for identifying and reporting suspected adverse events.
- Activities: They should take a detailed medication history, including the use of all herbal products and supplements. They must be aware of potential herb-drug interactions and be able to assess the causality of a reported event.
- Challenges: Many HCPs lack formal training in herbal medicine and may not be aware of the potential risks. There is a need for continuous medical education and awareness campaigns to bridge this knowledge gap.

3. **Patients and Consumers**:

- Function: Patients are an invaluable source of real-world safety data. Their reports can be the first indication of a safety issue.
- Activities: Patients should be encouraged to report any unexpected or unwanted effects from herbal products to their doctor, pharmacist, or directly to the national PV center.
- Challenges: Underreporting is a significant problem, as many consumers believe herbal products are safe and do not think to report adverse effects. A culture of safety reporting needs to be cultivated among the general public.

4. **Manufacturers and Industry**:

- Function: Manufacturers are legally and ethically responsible for the safety of their products.
- Activities: They must adhere to Good Manufacturing Practices (GMP) to ensure quality and prevent contamination and adulteration. They are also required to establish a robust PV system to collect, analyze, and report all adverse events

associated with their products to the regulatory authorities.

- Challenges: The diverse and often unregulated nature of the herbal medicine industry, with many small-scale producers, makes it difficult to enforce these standards consistently.

Specific Case Studies and Lessons Learned-

Examining specific examples of safety issues with herbal products highlights the importance of pharmacovigilance:

- **Aristolochic Acid**: This group of compounds, found in various plants (Aristolochia species), was used in traditional medicine for various ailments. However, PV data revealed its association with a unique form of kidney failure (Chinese herbal nephropathy) and urothelial cancers. The global ban on aristolochic acid-containing herbs is a landmark success story of PV in action. (19)
- **Kava (Piper methysticum)**: Used traditionally for its anxiolytic properties, kava was linked to cases of severe hepatotoxicity, leading to its withdrawal or restricted use in many countries. Subsequent research suggested that the type of extract, part of the plant used (e.g., aerial parts vs. root), and solvent extraction methods were contributing factors. This case underscores the complexity of causality assessment and the importance of quality control. (20)
- **Contamination with Heavy Metals**: Reports from various parts of the world have documented herbal products, especially traditional Chinese or Ayurvedic preparations, contaminated with heavy metals like lead, mercury, and arsenic. These contaminants can be present naturally in the soil or introduced during the manufacturing process. PV systems that actively monitor for such contamination are vital for public safety. (21)

Moving Beyond Spontaneous Reporting

While spontaneous reporting is the foundation of PV, it is insufficient on its own for herbal medicines due to the high rate of underreporting. Therefore, a multi-pronged approach is necessary:

- **Intensive Monitoring**: This involves focused, active surveillance of specific herbal products for a limited time, for example, after they are newly introduced to the market. This can provide a more accurate and complete picture of a product's safety profile.
- **Electronic Health Record (EHR) Data Mining**: As mentioned previously, analyzing large-scale EHR databases can reveal patterns of adverse events that may not have been formally reported. This method is particularly promising for identifying subtle, long-term effects or interactions.
- **Pharmacogenomics**: Future research will likely focus on how a person's genetic makeup influences their response to herbal medicines. This personalized approach could help predict who is at a higher risk of experiencing an adverse reaction. (22)

Advantages Of A Robust Pharmacovigilance System for Herbal Medicine

A well-functioning pharmacovigilance (PV) system for herbal medicine offers numerous benefits, not just for patient safety but also for the broader healthcare landscape.

1. **Enhanced Patient Safety**: This is the primary advantage. A PV system enables the early detection of safety signals and previously unknown adverse reactions (ADRs). This leads to timely warnings, regulatory actions (e.g., product recalls, labeling changes), and ultimately, a reduction in harm to patients

from contaminated, adulterated, or inherently toxic herbal products. For instance, the system can quickly identify and address issues like liver damage caused by a specific herbal supplement.

2. **Increased Public and Healthcare Professional Confidence**: By demonstrating a commitment to safety, a robust PV system builds trust in both herbal medicine products and the regulatory bodies that oversee them. This encourages more open conversations between patients and healthcare professionals (HCPs) about herbal medicine use, which is crucial for preventing drug-herb interactions and managing potential side effects. When patients feel confident that safety is a priority, they are more likely to disclose their use of herbal remedies.
3. **Improved Quality and Manufacturing Standards**: The requirement for manufacturers to report adverse events and adhere to Good Manufacturing Practices (GMP) incentivizes them to improve quality control. This includes ensuring proper plant identification, preventing contamination with heavy metals or pesticides, and using standardized extraction processes. PV data can also highlight problems in the supply chain or manufacturing process that need to be addressed.
4. **Informed Decision-Making for Clinicians and Regulators**: The data collected through PV provides an evidence base for risk-benefit assessments. This allows regulators to make informed decisions about product marketing and labeling. For HCPs, this information is invaluable for providing accurate advice to patients about which herbal products are safe to use and which should be avoided, especially in specific patient populations (e.g., pregnant women, patients with liver or kidney disease).
5. **Scientific Validation and Documentation**: PV activities contribute to the scientific documentation of the safety profile of herbal medicines. The collection of real-world data can complement traditional clinical trials and help to validate or refute claims of safety. This can also lead to new research questions about the pharmacology and toxicology of specific herbal compounds. (23)

Disadvantages and Challenges of Pharmacovigilance for Herbal Medicine

Despite the clear advantages, implementing and maintaining a robust PV system for herbal medicine is fraught with significant challenges and disadvantages.

1. **Underreporting**: This is arguably the most significant drawback. The perception that "natural" means "safe" leads to a low reporting rate of ADRs by both patients and HCPs. Patients may not even associate a symptom with an herbal product, and HCPs may not consider herbal use in their differential diagnosis. This makes it very difficult to get a true picture of the safety issues.
2. **Lack of Standardization and Quality Control**: Unlike conventional pharmaceuticals, which have a single, well-defined active ingredient, herbal products can be highly variable. The chemical composition can differ based on the plant species, growing conditions, harvest time, and processing methods. This makes it extremely challenging to link an adverse event to a specific product or batch, as the same product from two different manufacturers may have a completely different chemical profile.
3. **Complex Causality Assessment**: Establishing a causal link between an herbal product and an ADR is difficult.

- Multi-component products: Most herbal products contain a mixture of compounds, making it hard to identify the single culprit.
- Confounding factors: Patients using herbal medicine often use conventional drugs as well, making it difficult to differentiate between a drug-herb interaction and a side effect of the herb itself.
- Delayed effects: Some adverse effects (e.g., liver damage) may not appear for weeks or months after use, making it hard for patients or doctors to connect the symptom to the herbal product.

4. **Regulatory Gaps and Misclassification**: In many countries, herbal products are not classified as medicines but as dietary supplements, food, or traditional remedies. This means they are often not subject to the same stringent regulations for pre-market approval or post-market surveillance. This regulatory gray area hinders the ability of PV systems to effectively monitor these products.
5. **Lack of Scientific Data**: Many herbal products have not been subjected to rigorous clinical trials. This means there is often a lack of pre-existing data on their pharmacology, toxicology, and potential side effects, making it difficult for PV systems to predict and interpret emerging safety signals. The absence of a clear dose-response relationship also complicates risk assessment.
6. **Economic and Resource Constraints**: For many countries, especially developing nations with a high prevalence of traditional medicine use, establishing and funding a comprehensive PV system for herbal medicine is a major challenge. The cost of training personnel, setting up reporting infrastructure, and conducting detailed analysis can be prohibitive.

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