Herbovigilance Unveiled: The Science Of Protecting Nature's Legacy

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ABSTRACT: Herbal medicines stand as a cornerstone of global healthcare, approximately 80% of the world's population in many regions relying on them as their primary source of care. This deep-rooted reliance is built on cultural tradition, accessibility, and a pervasive, yet dangerous, belief that "natural" is synonymous with "safe." This perception, however, stands in stark contrast to a rising tide of documented adverse events, from severe hepatotoxicity to life-threatening herb-drug interactions, which expose a critical gap in patient safety. This article argues that the traditional discipline of pharmacovigilance (PV) must evolve into a specialized field of herbovigilance to effectively meet the unique challenges of herbal remedies. Our work reveals that the key hurdles are not just biological but systemic, stemming from inconsistent product quality, rampant underreporting of side effects, and a fragmented global regulatory landscape. To overcome these, we propose a strategic roadmap powered by technological innovation. We envision a future where artificial intelligenc**e** sifts through vast data to detect safety signals in real-time, blockchain ensures transparent and trustworthy supply chains, and advanced tools like DNA barcoding guarantee product authenticity. This is more than a regulatory need; it is a moral imperative to protect public health and secure a credible, sustainable future for an industry poised to shape the future of medicine.

Keywords: Herbal medicines, Pharmacovigilance (PV), Herbovigilance , Adverse drug reactions (ADR), Regulatory frameworks , Future perspectives in herbovigilance.

INTRODUCTION

The World Health Organization (WHO) defines herbal medicines as a broad category encompassing finished labelled medical goods containing active substances originating from plants, parts of plants, or combinations thereof [77]. For hundreds of years, herbal remedies have played an important role in healing systems such as Ayurveda, Traditional Chinese Medicine, and Unani. In recent decades, their appeal has grown worldwide because people regard them as natural, inexpensive, and directly related to culture and tradition [1,9]. Consumer interest and industry investment have both contributed to the gradual rise in global demand for herbal items. [8].The worldwide herbal medicine market is now a multi-billion-dollar industry, a testament to the increasing consumer demand for natural alternatives. Herbal medicine is a key source of treatment for approximately 80% of the world's population living in developing countries. Herbs are considered an integral element of the culture of such societies [13]. Although many people believe that herbal medications are always safe, research and clinical studies demonstrate that this is not always the case. Side effects reported include liver damage, renal damage, allergic responses, and hazardous herb-drug combinations. A well-known example is the combination of *Hypericum perforatum* (*St. John's Wort*) with

antidepressants and anticoagulants [2,4,7]. Furthermore, difficulties like insufficient standards, contamination with heavy metals or pesticides, and unintentional or intentional adulteration make safety concerns much more serious [1,3,6]. Pharmacovigilance, which means the continuous monitoring and assessment of medicine safety, is essential to protect patients. It is defined as "the study of the safety of marketed drugs under the practical conditions of clinical usage in large communities" [11].

However, current PV systems were created specifically for modern pharmaceutical medications. Applying the same procedures to herbal remedies is problematic because of concerns such as ambiguous plant names, variability in plant components, variances in preparation methods, and underreporting of side effects by both patients and practitioners [1,5,8]. To overcome these issues, international organizations like the World Health Organization advocate distinct methods for monitoring herbal medications[3,7]. National activities are also expanding. For example, India's AYUSH ministry has encouraged people to report adverse responses to Ayurvedic, Siddha, and Unani products, while the Lareb database in the Netherlands keeps track of incidents involving herbal supplements. These activities demonstrate that, while awareness is growing, many reported occurrences are serious, emphasizing the critical need for increased monitoring [6,7]. Building a strong pharmacovigilance system for herbal medicines is critical not just for patient safety, but also for fostering public trust and promoting fair international trade. Recording and evaluating safety signals helps companies improve product quality, regulators set higher standards, and health professionals advise safe use [3,8,7].

In addition, pharmacovigilance plays a central role in building global trade credibility, as herbal medicines are widely exported across borders with varying quality standards. Strengthening pharmacovigilance ensures compliance with international regulations, boosts consumer trust, and protects industries from legal and reputational risks [23]. Moreover, herbal pharmacovigilance supports innovation by generating safety data that can be used to refine formulations, develop standardized extracts, and create evidence-based labeling [12]. The integration of digital health technologies such as mobile ADR reporting apps, big data analytics, and blockchain for supply chain transparency further enhances the ability to detect safety signals and ensure traceability [83]. Thus, pharmacovigilance in herbal industries not only safeguards patient safety but also promotes sustainable industry growth, fair international trade, and evidence-based integration of traditional remedies into modern healthcare systems. This review article aims to explore the multifaceted role of pharmacovigilance in the herbal industry, moving beyond a simple overview to a comprehensive analysis of the existing challenges and a forward-looking discussion of potential solutions. By drawing on recent research, technological innovations, and changing regulatory frameworks, we will demonstrate that an effective herbovigilance system is not only a scientific imperative but a strategic advantage for a market seeking credibility and consumer trust. The herbal industry's future relies on a clear commitment to safety, grounded in rigorous science and global collaboration, that will ensure the enduring legacy of nature's remedies is protected for generations to come.

Role of Pharmacovigilance in Herbal Industries:

PV helps to identify harmful effects caused by incorrect use, contamination, or interactions with other medicines. By strengthening regulations, quality control, reporting systems, and educating both users and healthcare providers, pharmacovigilance reduces risks and promotes herbal products safety [3]. Herbal therapies are regularly used together with other drugs, and it is vital to recognize the outcomes of this combined application and to check for any adverse effects that may emerge [12]. To effectively manage herbal medicines and particularly to assess the reasons behind adverse events, national pharmacovigilance centers (or their equivalent institutions) will need to develop specific technical skills. This includes having

trained personnel in the relevant technical domains and the appropriate facilities to analyze the products involved, for which there is often a lack of sufficient and reliable information support [10,11,12].

The distinct aims of Pharmacovigilance are to [12]:

i. Enhance the quality of healthcare and security concerning administration of medications and all medical and paramedical procedures.
ii. Engage in the evaluation of the benefits, drawbacks, effectiveness, and risks of pharmaceuticals, fostering their safe, rational, and more effective (including cost-effective) application.
iii. Foster understanding, education, and clinical training in pharmacovigilance, along with its proficient communication to the public.

1. **Detection of Adverse Drug Reactions (ADRs)**:
   Contrary to the common perception, herbal medicines are not always harmless. Many cases of liver toxicity, renal failure, and allergic reactions have been reported due to herbal formulations. PV systems help in detecting, identifying, and documenting these adverse drug reactions systematically. By collecting real-world safety data, PV ensures that unexpected side effects are identified at an early stage. It also plays an important role in detecting herb–drug interactions, which may worsen the therapeutic effect of conventional medicines. For example, *St. John's Wort* (a herbal antidepressant) interacts with drugs like warfarin and oral contraceptives, reducing their efficacy. Thus, PV ensures continuous safety monitoring of herbal medicines in real-life use [73].
2. **Quality Control and Standardization:**
   One of the biggest challenges in herbal medicines is variability in raw materials. Differences in soil quality, cultivation practices, harvesting time, and processing methods may affect the active constituents. Furthermore, cases of adulteration and contamination with heavy metals, pesticides, or synthetic drugs are common. PV plays an important role by linking adverse reaction data with product quality, thereby identifying issues in manufacturing and processing. Establishing consistent standards for herbal medicines, along with strict PV monitoring, helps reduce risks to consumers. For example, improper processing of *Aristolochia* led to severe kidney damage cases in Belgium, highlighting the urgent need for PV-backed quality checks [12].
3. **Awareness and Education:**
   Many consumers believe that "herbal means safe." This misconception contributes to the underreporting of adverse effects. PV plays a vital role in spreading awareness among healthcare professionals, traditional practitioners, and patients about possible risks associated with herbal medicines. Through workshops, training sessions, and public awareness campaigns, PV encourages rational use of herbal drugs. Additionally, PV programs train healthcare workers to document negative effects related to herbal products, bridging the difference between conventional medicine and modern safety monitoring. This awareness ultimately reduces irrational use and self-medication practices [73].
4. **Systematic ADR Reporting in Traditional Systems:**
   India has a long history of Ayurveda, Siddha, and Unani (ASU) systems of medicine. While these systems are effective, adverse events often go unreported. PV programs in herbal industries aim to establish a structured reporting system where practitioners of ASU medicine can record and report ADRs. Training of traditional practitioners, community involvement, and collaboration with modern healthcare providers ensure that safety signals are not missed. Importantly, PV data is also used to support regulatory decisions such as product approvals, labelling modifications, product recalls, or even bans, thereby protecting consumers and ensuring credibility of herbal goods in the global market [74].

5. **Global Harmonization of Herbal Safety Standards:**

Herbal medicines are traded internationally, and variations in safety regulations between countries can cause confusion. PV plays an important function in harmonizing safety standards globally. International reporting databases such as the WHO-Uppsala Monitoring Centre (UMC) collect ADR reports from herbal medicines worldwide. This helps in identifying herb–drug interactions and formulation-related risks on a global scale. For example, herbal remedies used in Asia may have different safety profiles when marketed in Europe or America. Harmonization ensures that risks are addressed consistently, boosting consumer confidence and trade credibility [51].

6. **Specialized Herbal PV Systems:**

Unlike synthetic drugs, herbal formulations are often mixtures of multiple active and inactive components. This complexity makes ADR detection and causality assessment more difficult. Therefore, herbal medicines require specialized PV systems tailored to their unique challenges. These systems take into account raw material variability, risks of adulteration, and differences in preparation methods. PV also oversees herbal products throughout their journey from processing, manufacturing, distribution, to commercialization. By integrating toxicology data with real-world safety reports, PV provides a holistic picture of herbal medicine safety [75].

7. **Lifecycle Safety Monitoring:**

Pharmacovigilance does not stop at ADR detection , it ensures safety throughout the product lifecycle. From pre-clinical research and clinical evaluation to post-marketing surveillance, PV continuously evaluates safety signals. This helps identify long-term toxicities, cumulative effects, or delayed adverse reactions in consumers. Lifecycle monitoring is particularly important in herbal industries since many formulations are marketed with little or no clinical trial data. Post-marketing PV fills this gap by providing scientific evidence on safety and efficacy [76].

8. **International Guidelines and Cooperation:**

The World Health Organization (WHO) has emphasized the significance of including herbal medicines into national PV systems. The WHO guidelines (2004) provide a framework for countries to systematically monitor, evaluate, and respond to ADRs from herbal medicines. PV facilitates international cooperation by enabling countries to share safety data and experiences through global databases. This ensures better consumer protection and helps developing countries strengthen their PV capacity for herbal industries [3].

9. **Regulatory Support and Policy Development:**

Finally, PV provides evidence-based data that supports regulatory bodies in decision-making. This includes approval of new herbal products, updates in safety labeling, product recalls, or bans of harmful products. For instance, Kava-based supplements were banned in some countries after PV data linked them to severe liver toxicity. By guiding policy decisions, PV ensures that herbal medicines meet both safety and efficacy standards before reaching consumers. Regulatory action based on PV strengthens public trust in herbal industries and enhances their credibility in global markets [12].

Challenges in Herbal Pharmacovigilance:

Pharmacovigilance is complicated by the diversity of herbal products, which raises fundamental problems about optimal herb naming systems and botanical identity confirmation. Such issues are uncommon in the supervision of synthesized drugs. Furthermore, present pharmacovigilance frameworks and pharmaceutical-specific electronic data systems do not sufficiently handle concerns like as nomenclature irregularities and adulteration [10]. Using the current approach and its instruments to oversee the safety of herbal medications presents significant issues beyond those discussed for traditional medicines [11]. Lately, its areas of concern have expanded to encompass the herbal remedies, conventional and complementary therapies, blood derivatives, biological products, medical instruments, vaccines, etc [12].The following are the major obstacles to efficient monitoring and regulation of herbal goods.

1. **Quality and standardization issue**:

Quality concerns in herbal medicines often arise from contamination with pesticides, heavy metals, microbes, mycotoxins, and pyrrolizidine alkaloids. Regulatory guidelines such as the European Pharmacopoeia and ICH Q3D set specific limits and testing standards for these impurities. While ongoing surveillance and improved industry practices have reduced some risks (e.g., lower pyrrolizidine alkaloid levels in recent years), complete elimination of such contaminants remains difficult. Regular monitoring and data evaluation are therefore essential to maintain the safety and consistency of herbal medicinal products [14]. Quality assurance and control measures are critical to ensuring the safety and effectiveness of natural medicines. Inadequate regulation and poor quality control might result in a high frequency of adverse responses caused by low quality herbal medicines, particularly when adulterated with unreported powerful chemicals or contaminated with potentially harmful substances and residues [12]. The standards and techniques for quality control of finished herbal products, particularly mixed herbal medicines, are significantly more complex than those for other pharmaceuticals [12]. In general, the quality of source materials is determined not only by intrinsic (genetic) variables, but also by extrinsic ones such as environmental circumstances, good agriculture and collection practices (GACP) for medicinal plants, which include plant selection and cultivation [14,3]. One of the biggest issues frequently encountered in the quality control of completed herbal medicinal goods, especially combination herbal medicines, is the difficulty of determining the presence of all the plants or beginning ingredients [14,15]. To ensure the safety and effectiveness of herbal medicines, WHO continues to recommend the establishment of quality assurance and control measures such as national quality specifications and standards for herbal materials, GMP for herbal medicines, labelling, and licensing schemes for manufacturing, import, and marketing, in nations where herbal medicines are regulated [15].

2. **Pharmacogenomics & Individual Variability :**

a. **Herb-drug interaction:**

Herb–drug interactions present a major barrier to pharmacovigilance because they can unpredictably alter the safety and efficacy of conventional medicines. Commonly used herbs such as *St. John's wort, Ginkgo biloba, garlic, ginseng, and Echinacea* affect metabolic enzymes and transporters including CYP450 isoforms, UDP-glucuronosyltransferases, and P-glycoprotein, leading to reduced therapeutic drug levels or enhanced toxicity. For instance, *St. John's wort* lowers plasma concentrations of cyclosporine and antidepressants, while *ginkgo* has been associated with increased bleeding when combined with anticoagulants. These effects are further complicated by pharmacogenomic variability, since polymorphisms in CYP2C19, CYP2D6, and CYP2B6 or transporter genes determine the extent of interaction, making some individuals highly vulnerable while others are unaffected. Because herbal formulations are often polyherbal, patients frequently self-medicate, and genotype-specific responses vary across populations, adverse events are difficult to attribute to herbal use. This complexity hampers signal

detection, weakens the accuracy of safety databases, and limits the ability of pharmacovigilance systems to develop reliable guidelines, underscoring herb–drug interactions as one of the most challenging areas in monitoring herbal medicines [17,19].

b. Herb-Herb interaction :

One of the most overlooked challenges in pharmacovigilance is the risk of interactions between multiple herbal products consumed simultaneously. Many patients use complex polyherbal formulations or combine different herbal remedies without medical guidance, which increases the potential for unexpected effects. Several herbs such as *St. John's wort, Schisandra, Astragalus, Ginkgo biloba, and Turmeric* are known to alter the activity of cytochrome P450 enzymes, UDP-glucuronosyltransferases, or transporters like P-glycoprotein. These biochemical changes can enhance or reduce the systemic exposure of other herbal constituents taken together. For instance, *St. John's wort* strongly induces CYP3A4, potentially lowering the effectiveness of co-administered herbs metabolized by this pathway, while others such as *Turmeric or Schisandra* may act as enzyme inhibitors and increase toxicity risk. Since most herbal medicines are polyherbal by nature, pinpointing the culprit component in an adverse reaction is extremely difficult. This lack of clarity creates major obstacles for pharmacovigilance, as it complicates signal detection, causality assessment, and patient safety monitoring [18].

c. Herb- Food interaction :

In addition to herb–herb combinations, interactions between herbal products and common foods present another important safety concern. Many fruits and beverages contain bioactive compounds that significantly influence the metabolism of herbal constituents. *Grapefruit juice* is a well-documented inhibitor of CYP3A4, which can increase the concentration and toxicity of co-administered herbs or drugs. *Cranberry juice* has been linked with enhanced bleeding when combined with warfarin, while *pomegranate juice* has been reported to cause serious reactions such as priapism when used alongside sildenafil. Similarly, *turmeric and grapefruit* may worsen tacrolimus-related nephrotoxicity. These interactions are often unpredictable, vary with the individual's genetic background and dietary habits, and may occur even at low consumption levels. A further challenge lies in the fact that patients rarely report dietary details when adverse events occur, leaving pharmacovigilance systems with incomplete data. As a result, herb–food interactions remain a poorly recognized but clinically relevant barrier to ensuring the safe integration of herbal medicines into routine healthcare [18]. As a whole ,herb–drug, herb–herb, and herb–food interactions demonstrate how genetic diversity complicates the safe use and monitoring of herbal medicines. Variations in drug-metabolizing enzymes and transporters can cause the same herbal combination to be well tolerated in one patient yet harmful in another, making outcomes highly unpredictable. The presence of polyherbal preparations, dietary influences, and inconsistent product quality further obscures causal links, while limited pharmacogenomic data and underreporting weaken the reliability of pharmacovigilance signals. These

challenges indicate that pharmacogenomics is not a peripheral issue but a core obstacle in assessing herbal medicine safety, highlighting the need for standardized clinical research, population-specific surveillance, and the incorporation of genetic profiles into pharmacovigilance frameworks [17-19].

d. Adverse Drug Reaction Reporting :

Adverse drug reaction (ADR) reporting for herbal medicines remains highly inconsistent and fragmented, posing a significant barrier to effective pharmacovigilance. A thorough study and meta-analysis found that the reporting rates of adverse events from herbal medicines varied widely, ranging from 0.03% to nearly 30%, with a pooled median of just 1.42%.The variability depended strongly on who reported the event, with consumers often contributing higher reporting rates compared to health professionals. However, most reports lacked critical details such as batch numbers, brand names, dosage forms, or potential contaminants, making it difficult to establish causality or identify specific risks. This underreporting and poor-quality data hinder the detection of safety signals and weaken the reliability of pharmacovigilance databases. Moreover, the absence of standardised reporting forms, limited patient awareness, and inadequate follow-up systems further compound the challenge. To strengthen herbal pharmacovigilance, there is a pressing need for standardised global reporting mechanisms, patient-friendly reporting tools, and greater collaboration between consumers, medical professional, manufacturers, and regulators [20]. As outlined in WHO guidelines, post-marketing pharmacovigilance systems primarily depend on voluntary ADR reporting from healthcare professionals, especially those directly involved in patient care. Their medical expertise and familiarity with patients' clinical histories enable accurate identification and assessment of adverse effects. This is particularly crucial for non-prescription medicines, including herbal products, where pharmacy professional and nurses can significantly contribute to safety monitoring. WHO also emphasizes the importance of consumer involvement in ADR reporting, recognizing that patients and caregivers can provide valuable insights into previously unrecognized adverse effects. However, only a few national regulatory authorities currently mandate the collection of direct consumer reports. The CIOMS Working Group has proposed several policy approaches to guarantee that customer reports are processed with appropriate respect and handled rationally, thereby enhancing the overall pharmacovigilance framework [3].

e. Self-Medication with Over-the-Counter Medicines:

Self-medication and the unsupervised use of over-the-counter (OTC) medicines, including herbal products, pose significant public health concerns. A research in Thailand revealed that 88.2% of the working-age population practiced self-medication, primarily with nonsteroidal anti-inflammatory drugs and antibiotics, yet over 40% of conditions remained unresolved, requiring further medical attention [11]. Similarly, a Latvian survey showed that while 38.3% of respondents considered herbal remedies safe, 57.3% regarded combining them with conventional medicines as unsafe, with commonly used herbs such as *grapefruit, St. John's wort, and valerian* recognized to interact with prescription drugs [22]. Reviews further highlight that

self-medication with herbal supplements and OTC products carries risks of improper self-diagnosis, significant adverse responses, and herb–drug interactions, particularly when undertaken without physician oversight [22].

3. Regulatory Gaps & PV Modelling :

a. Regulatory frameworks & policy gaps

Herbal medicines often face fragmented regulatory frameworks, as they are classified differently across countries sometimes as dietary supplements, sometimes as traditional remedies, and in fewer cases as medicinal products. This inconsistent categorization results in weaker safety and efficacy requirements, creating significant policy gaps that hinder effective pharmacovigilance and monitoring of herbal products [21].

b. Quality control & standardization

The lack of uniform quality control and standardization in herbal medicines remains a critical challenge. Fluctuation in sources of raw material, plant species, harvesting, and processing methods can alter product consistency, potency, and safety. Without strict regulatory oversight and harmonized quality assurance mechanisms, ensuring the reliability and safety of herbal medicines is difficult [22].

c. Global regulatory challenges & harmonization

The global expansion of the herbal medicine market has highlighted the urgent need for harmonized international regulatory standards. Currently, countries differ widely in their requirements for safety, labelling, and approval of herbal medicines, leading to inconsistent pharmacovigilance practices. Greater international cooperation and standardization are required to ensure uniform safety monitoring and consumer protection worldwide [23].

d. Signal detection & data sources :

Signal detection in herbal pharmacovigilance draws upon multiple data sources, with case reports, regulatory documents, and labelling changes serving as primary contributors for identifying early safety signals in both the EU and USA [24]. Meta-analysis of adverse event data from clinical trials, observational studies, and spontaneous reporting systems shows that adverse event frequencies vary widely depending on product type and reporting method, highlighting the importance of integrating different data sources for accurate safety profiling [25]. However, spontaneous reporting systems for herbal and conventional medicines remain underdeveloped in many countries, with issues such as low awareness among healthcare professionals, poor infrastructure, and inconsistent integration into national pharmacovigilance programs [26]. In addition, signal detection of herb–drug interactions is particularly challenging due to limited pharmacokinetic evidence, variability in product formulations, and underreporting, requiring a combination of clinical, experimental, and database evidence to strengthen signal validation [27].

e. Awareness and Education Deficits:

A major challenge in the pharmacovigilance of herbal medicines is the lack of awareness and education among healthcare professionals regarding safe use and ADR reporting. Many community pharmacists are unfamiliar with the concept of Phyto vigilance, have not received adequate training, and remain unaware of formal systems for reporting adverse reactions related to herbal products. This gap restricts their ability to identify risks, provide proper guidance to patients, and contribute effectively to pharmacovigilance systems [28]. Similarly, a study conducted among health professionals in Ethiopia revealed low levels of awareness about herbal medicine safety and poor knowledge of herb-drug interactions. Many practitioners were not

adequately informed about ADR monitoring processes, underlining the urgent need to integrate herbal pharmacovigilance into medical and pharmacy curricula [29].

Furthermore, consumer-related gaps add another dimension to this issue. Research from Saudi Arabia indicated that pharmacists often depend on informal or non-scientific sources of information when counselling patients about herbal products, while consumers themselves displayed substantial knowledge deficits about safety concerns and potential interactions. This mismatch in knowledge and communication not only reduces confidence in pharmacovigilance systems but also increases the risk of unreported ADRs. Addressing these challenges requires structured education programmes, professional training workshops, and public awareness initiatives to improve the understanding of herbal medicine safety and strengthen the overall pharmacovigilance framework [30].

f. Public health and Economic Impact :

Adverse drug reactions (ADRs), including those associated with herbal medicines, impose a significant burden on public health. They contribute to hospital admissions, prolonged hospital stays, and increased morbidity and mortality. For example, a study in France (IATROSTAT-ECO) showed that ADR-related hospital admissions had a mean cost per patient of €5,974 ± €4,232, with costs lower for preventable ADRs compared to non-preventable ones, demonstrating the importance of proactive monitoring and prevention strategies. [31] Similarly, in India, a six-month hospital-based study identified 458 ADRs, with around 27% requiring hospitalization or prolonged stay, leading to a combined direct and indirect costs of approximately INR 989,164.5, of which 79% represented direct patient care costs [32]. These findings highlight the heavy resource use and patient risk associated with ADRs, which are likely underestimated in the context of herbal medicine due to underreporting.The economic implications of ADRs extend beyond immediate medical costs, encompassing broader systemic burdens. In the United States, ADRs have been described as a leading cause of hospital admissions and a major contributor to healthcare expenditure, costing the system billions of dollars annually when accounting for hospitalizations, prolonged stays, additional diagnostics, and productivity loss [33]. In the case of herbal medicines, where monitoring systems are weaker and consumer use is often unsupervised, the potential public health and economic burden is considerable. Strengthening pharmacovigilance for herbal products not only reduces avoidable hospitalizations and treatment costs but also protects consumer trust and supports the long term development of the herbal medicine market [31,32,33].Figure 1 depicts the key obstacles associated with pharmacovigilance of herbal medicines.

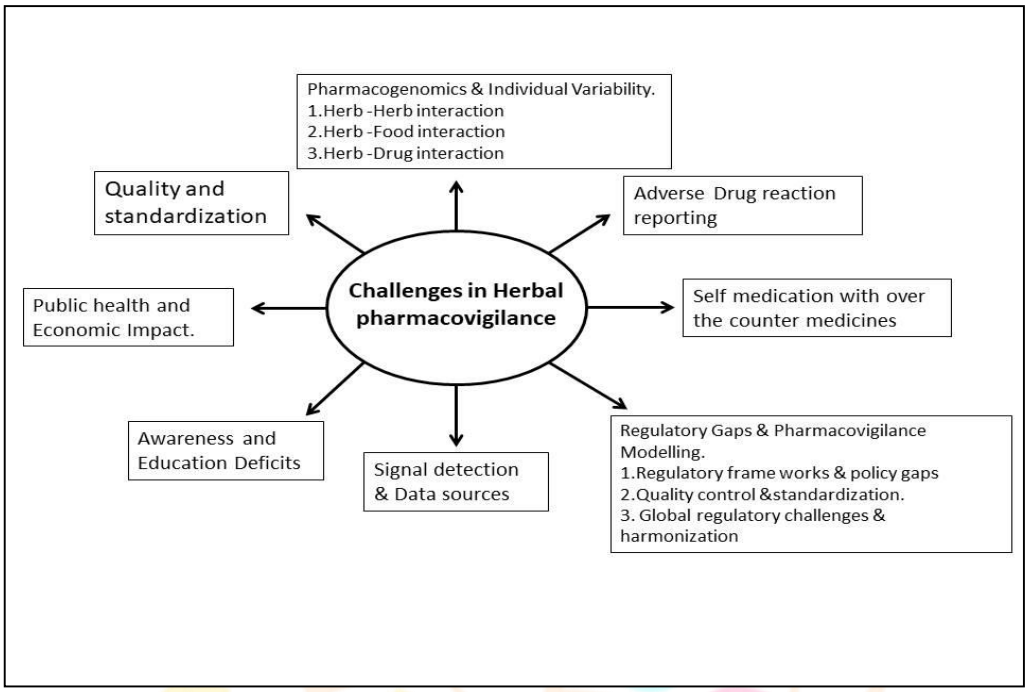

fig. 1 challenges in herbal pharmacovigilance

PHARMACOVIGILANCE SYSTEMS FOR HERBAL PRODUCTS: INTERNATIONAL PERSPECTIVES:

Pharmacovigilance for herbal medicines is handled differently across countries, with Canada serving as a notable example through its Natural Health Products (NHPs) framework. Under the Natural Health Products Regulations, herbal medicines undergo pre-market licensing for safety, efficacy, and quality, followed by post-market surveillance through Health Canada's vigilance systems. Adverse reaction reporting is mandated for manufacturers and encouraged for consumers and healthcare professionals, although under-reporting remains a significant challenge [34]. Globally, spontaneous reporting databases have shown that herbal-related adverse events account for a measurable proportion of all reports for instance, 6.8% of Canada's vigilance reports and 2.5% of US FDA reports involved herbal products between 2004-2016 highlighting both the importance of herbal pharmacovigilance and the ongoing need to strengthen awareness, reporting, and regulatory oversight [35].

In the United States, herbal medicines and dietary supplements are regulated under the Dietary Supplement Health and Education Act (DSHEA) and monitored by the Food and Drug Administration (FDA). Safety surveillance relies primarily on spontaneous adverse event reporting through the FDA Adverse Event Reporting System (FAERS), supported by case reports and observational studies. Studies indicate that reporting rates for herbal-related adverse events vary across data sources, with consumer reports playing a particularly important role in signal detection, underscoring the need for stronger awareness and standardized practices [25].

In Africa, pharmacovigilance frameworks for herbal medicines remain fragmented and underdeveloped. A WHO survey of 39 African countries revealed that although herbal medicines are included in many pharmacovigilance agendas, reporting rates are very low and hindered by inadequate regulatory structures, limited resources, and insufficient training of health professionals [36]. More recent assessments, such as in

Tanzania, show that while legal frameworks exist, many manufacturers and marketing authorization holders still lack effective systems to collect and evaluate herbal safety data, highlighting the urgent need for regulatory strengthening and capacity building [37].

In China, the National Medical Products Administration (NMPA) oversees the regulation of traditional Chinese medicines (TCMs), including herbal products. The NMPA has developed Good Pharmacovigilance Practices (GVP) to ensure the safety of these products. Despite these efforts, challenges persist, such as underreporting of adverse reactions and the need for improved data collection systems. Recent studies indicate that while regulatory frameworks are in place, their implementation and effectiveness require further enhancement to safeguard public health [38].

In Australia, Australia's Therapeutic Goods Administration (TGA) regulates herbal medicines through a risk-based approach, classifying them as either registered or listed medicines. Registered medicines undergo rigorous evaluation for quality, safety, and efficacy, while listed medicines are subject to less stringent requirements. The TGA mandates sponsors to report adverse reactions and maintain pharmacovigilance systems, ensuring ongoing monitoring of herbal medicine safety [39].

CASE STUDIES: EPHEDRA

Over the past few decades, numerous hazardous incidents have been caused by the overuse and abuse of products containing ephedra and its extracts. The U.S. Food and Drug Administration prohibited the distribution of dietary supplements that included *Ephedra* in 2004 after receiving over 18,000 reports of hazardous reactions linked to the substance [40,41]. In addition to more serious situations like arrhythmia, nephritis, gallstones, and perhaps death from heart or respiratory failure, toxic effects to Ephedra use include agitation, sweating, dysuria, and elevated blood pressure [42-44]. Researchers discovered that a high dosage (1000 mg/kg) of Ephedra aqueous extract markedly raised the volume of salivary glands, the quantity of basophils in renal tubules, and the hypertrophy of acinar cells in both male and female F344 rats [43]. F344 rats exhibited muscle fiber degradation or even loss when *ephedrine and caffeine* were administered simultaneously [46]. Rats in a different set of animal tests experienced cardiac toxicity at high doses of ephedra or ephedrine (dosage corresponding to 12.5 to 50 mg/kg of ephedrine), which was positively connected with the dosage [48]. Researchers have examined the safety of ephedra extracts devoid of ephedra alkaloids since these compounds are the source of negative reactions to ephedra. *Ephedra extract (EHE)* and ephedra extract without *Ephedra alkaloids (EFE*) were employed by Takemoto et al. to assess mice's activity time, forced swimming time, and pentobarbital-induced sleep time in an open environment. They discovered that both could shorten the mice's time immobile during forced swimming, shorten their time sleeping during sleep tests, and boost their activity levels in the open environment. EFE may be employed as a side-effect-free alternative to EHE in the future, as evidenced by the fact that mice in the EFE group did not have arrhythmia when compared to mice in the EHE group [48]. In addition to reducing pain, Kobayashi discovered that EHE devoid of Ephedra alkaloids did not cause arrhythmia or sleep deprivation, two of its negative effects [49]. Therefore, based on the information above, we may state that a single herb has a lot of negative consequences, some of which can even be fatal if taken in excess. The following Table no.1 summarizes the herbs reported in the literature and their associated adverse effects [38].

Table 1: adverse effects of herbs

Herbs	**Adverse events**
Allium sativum (Garlic)	Blood pressure increased
Avena sativa (Oats)	Skin and subcutaneous tissue disorders
Camellia sinensis (Tea)	Heart rate increased
Cannabis sativa (Marijuana)	Psychiatric disorders and Social circumstances
Digitalis purpurea (Foxglove)	Cardiac disorders
Glycine max (Soybean)	Alanine aminotransferase increased
Hypericum perforatum (St John's Wort)	Paraesthesia, tremor, anxiety and depression
Linum usitatissimum (Flax)	Joint swelling
Medicago sativa (Alfalfa)	Diarrhoea and asthenia
Paullinia cupana (Guarana	Cardiac disorders
Phleum pretense (Timothy-grass)	Immune system disorders
Senna alexandrina (Senna)	Acute kidney injury, Confusional state, uninary retention, constipation, hypokalemia, respiratory failure, neutropenia
Taraxacum officinale (Dandelion)	Hepatobiliary disorders, dizziness
Vaccinium macrocarpon (Cranberry)	Urinary tract infection, constipation, sedation
Vaccinium myrtillus (European Blueberry)	Vomiting

Counselling Methods in PV for Herbal ADRs:

1. Patient Centered Communication: Use simple, non-technical language to explain herbal ADRs. Respect cultural beliefs and traditional use of herbs. Encourage open dialogue about all products used (herbal, Ayurvedic, home remedies, OTC, allopathic) [3].

2. Medication & Herb History Taking: Ask about all herbal products, teas, powders, oils, and supplements, document dose, frequency, duration, and source (home-prepared vs. marketed).Identify possible herb–drug interactions (e.g., *Ginkgo* with aspirin gives bleeding risk) [3].

3. Risk Benefit Counselling: Explain both therapeutic potential and risks of herbs. Inform patients about possible ADRs (allergic reactions, hepatotoxicity, nephrotoxicity).Highlight importance of quality, standardization, and regulatory-approved products [3].

4. ADR Reporting Awareness: Educate patients to report any unusual symptoms (rash, nausea, liver issues, bleeding).Encourage use of national PV programs (e.g., IPC PvPI in India, WHO VigiBase).Provide leaflets or digital resources for ADR reporting [70].

5. Safe Use Guidance: Avoid self-medication and overdosing of herbal remedies. Warn about combining herbs with prescription drugs without medical advice. Advise on pregnancy, lactation, children, elderly high risk groups [71].

6. Follow-up & Monitoring:

Regularly follow up for herb safety, efficacy, and tolerance. Monitor lab values if herbs with known organ toxicity are used (e.g., liver/kidney tests).Modify or discontinue herbal use if ADRs occur [72].

7. Educational Tools: Use pamphlets, posters, apps, or group counselling in hospitals/clinics. Provide community awareness sessions on herbal ADR risks centered communication awareness sessions on herbal ADR risks [72].

Future Perspectives of Herbal Pharmacovigilance:

Herbal medicines and traditional remedies continue to play important roles in global healthcare. As the worldwide demand for natural remedies grows, the necessity of herbal pharmacovigilance, also known as herbovigilance, is becoming more recognised. Unlike synthetic medications, herbal formulations frequently contain complicated mixes, varied preparations, and diverse sources, making their safety assessment difficult. In this context, the future of herbal pharmacovigilance calls for a multidimensional approach that includes regulatory reforms, technological innovations, clinical awareness, patient participation, and global collaboration [50]. Future pharmacovigilance systems will move towards higher harmonisation and tougher frameworks, according to regulatory expectations. Herbal items continue to be governed inconsistently, with some being categorised as dietary supplements and others as medications. Moving ahead, clearer registration, labelling, quality control, and post-marketing surveillance standards will be implemented. In adverse drug reaction (ADR) reports, regulatory authorities are likely to require the inclusion of product identity (botanical names, batch numbers, and production data. This would ensure that safety alerts can be linked back to specific preparations rather than being broadly associated with a "herbal product" [50].

Clinically, healthcare experts and chemists will take on a more active role. Herbal treatments are widely used in conjunction with conventional therapies, which increases the danger of herb-drug interactions and organ toxicity. Future systems would encourage regular reporting of herbal usage in patient records, aided by electronic health record (EHR) templates and clinical decision-support technologies that alert to potential interactions. Continuous professional education will prepare doctors to recognise, report, and counsel patients about potential side effects [54]. The industrial perspective is also crucial. Manufacturers must maintain transparency and traceability by implementing modern quality control techniques such as QR codes or digital IDs that link herbal goods to batch analysis and chemo profiles. Companies that make standardised extracts or innovative herbal formulations may be required to file post-marketing safety plans,

comparable to pharmacovigilance requirements for synthetic pharmaceuticals. This adjustment will promote accountability and increase consumer trust [53].

In terms of patient and public health, accessibility and awareness will shape the future. One of the most significant challenges in herbal pharmacovigilance is the failure to report the adverse events. As a result, user-friendly mobile apps, internet portals, and pharmacy-based reporting systems will most likely be introduced. Public health initiatives will try to improve patient literacy by encouraging users to disclose their herbal intake to clinicians and promptly report unpleasant occurrences [53]. The scientific and technology approach is quite promising. Advances in DNA barcoding and metabolomic analysis are expected to improve herbal product authentication by distinguishing genuine materials from adulterated or contaminated ones. Simultaneously, pharmacovigilance databases will progressively incorporate artificial intelligence (AI), machine learning (ML), and natural language processing. These techniques will enable real-time mining of spontaneous reports, EHRs, and even social media posts to spot emergent safety signals much more quickly than existing methods [52, 54]. Finally, the global perspective emphasises teamwork. Herbal items frequently cross borders as part of international commerce. To detect infrequent but serious adverse responses, interoperable pharmacovigilance networks, anonymised safety data exchange, and the use of uniform case definitions will be required. Organisations such as the World Health Organisation and the International Society of Pharmacovigilance (ISoP) have already begun to develop frameworks for improving international herbovigilance. The long-term goal is to create a federated global system that can offer timely alarms and coordinated reactions, improving the safety of herbal medicine use around the world [51 -53].

In conclusion, the future of herbal pharmacovigilance lies in combining regulatory stringency, clinical vigilance, manufacturer responsibility, patient engagement, technology innovation, and global cooperation. By bridging these dimensions, pharmacovigilance systems will be better able to verify that herbal medications provide benefits while minimising hazards. The changing picture reflects both the increased reliance on traditional medicine and the global commitment to protecting public health through science-based monitoring.

Projects and Industries Related to Herbal Pharmacovigilance in India

1. Industries Involved:

The herbal and AYUSH sector in India is experiencing significant growth, with numerous stakeholders playing a role in herbal pharmacovigilance. Leading domestic herbal market players, including Dabur, Himalaya, Zandu, and Patanjali, are increasingly mandated to establish pharmacovigilance systems to comply with both national and international regulations [55].Additionally, pharmaceutical and nutraceutical firms that manufacture phytopharmaceuticals, botanical extracts, and dietary supplements are also required to engage in post-marketing safety monitoring [56]. Furthermore, research entities like the Central Council for Research in Ayurvedic Sciences (CCRAS) and associated organizations offer standardization, preclinical safety assessments, and toxicity evaluations to enhance the safety of herbal medications [57]. AYUSH hospitals and clinical centers act as reporting centers for adverse drug reactions (ADRs), supplying real-world data for further analysis. Regulatory bodies such as the Ministry of AYUSH and the Pharmacopoeial Commission for Indian Medicine & Homoeopathy (PCIM&H) manage the reporting process through the National Pharmacovigilance Programme for ASU&H drugs [51,58].

2. Project Models in Herbal Pharmacovigilance :

Pharmacovigilance initiatives within the herbal and AYUSH sectors are being implemented throughout India to tackle the specific challenges posed by herbal medicines. A key focus of these initiatives is the creation of Adverse Drug Reaction (ADR) surveillance programs in AYUSH hospitals and dispensaries. The goal of these projects is to gather and analyze real world data on adverse events reported by patients using Ayurvedic, Siddha, Unani, and homeopathic treatments. Practitioners receive training to utilize standardized forms, such as the WHO-UMC case report format, to systematically document ADRs. By aggregating these reports at both regional and national centers, these initiatives yield useful thoughts into the safety profiles of traditional medicines. Such efforts not only facilitate the early detection of safety signals but also promote a culture of ongoing monitoring among AYUSH practitioners [55,56]. Additionally, another significant area of focus is herb–drug interaction (HDI) studies, given the increasing number of patients in India who are using herbal remedies in conjunction with allopathic medications. Projects in this domain are structured to observe potential interactions between frequently used herbs like *Ashwagandha*, *Giloy*, and *Turmeric* and medications such as antidiabetics, anticoagulants, or antihypertensives. These studies are typically conducted through prospective observational research in hospitals where both medical systems are utilized. The results from these projects offer evidence-based recommendations for healthcare providers and assist in enhancing labeling practices for herbal products, ultimately improving patient safety [56,51]. Some initiatives aim to connect product quality with pharmacovigilance data. This includes analytical testing of marketed herbal products to assess their purity, authenticity, and the absence of contaminants like heavy metals, pesticides, or adulterants. The results from these quality tests are then compared with reports of adverse drug reactions to determine if certain adverse events are linked to substandard or adulterated batches. Such initiatives hold particular significance in India, where standardization of products poses a significant challenge, and they frequently inform regulatory actions such as recalls or enhanced quality inspections [57,51].

With the rise of digital health, a new model has emerged that utilizes digital platforms and mobile applications for reporting pharmacovigilance. Initiatives like the “Ayush Suraksha” portal and other mobile-based programs motivate both healthcare practitioners and consumers to report adverse events associated with herbal medicines directly. These digital reporting systems are typically connected to central databases overseen by the Pharmacopoeial Commission for Indian Medicine & Homoeopathy (PCIM&H). Evidence suggests that such projects can greatly decrease under-reporting, improve transparency, and enhance the accessibility of pharmacovigilance for both rural and urban communities [58]. Moreover, community-based pharmacovigilance initiatives have been established to raise awareness among pharmacists, community health workers, and the general public. These initiatives encompass educational sessions, safety campaigns, and pharmacist-led efforts to disseminate knowledge regarding the safe usage of herbal medicines. By promoting spontaneous reporting at the grassroots level, these projects expand the pharmacovigilance network and ensure that adverse drug reaction signals are detected beyond hospital environments [55,57].

In summary, these varied initiatives spanning ADR surveillance, herb–drug interaction research, quality monitoring, digital reporting, and community involvement demonstrate India’s organized efforts to establish a strong framework for herbal pharmacovigilance. They tackle the specific safety issues associated with herbal medicines while also enhancing the global acknowledgment of India’s traditional medicine system as safe, trustworthy, and grounded in evidence.

3. Industry Benefits

a) Regulatory compliance

For the herbal and AYUSH sectors, adhering to pharmacovigilance standards guarantees that their products align with both Indian and global safety regulations. Following the pharmacovigilance guidelines established by the Ministry of AYUSH, PCIM&H, and WHO aids industries in avoiding legal complications and eases the process of obtaining approvals in international markets. This compliance is particularly crucial for businesses looking to export their products, as importing nations frequently require comprehensive safety data. By implementing pharmacovigilance systems, industries can showcase their accountability and scientific integrity. Ultimately, this enhances the global reputation of Indian herbal medicines [56,58].

b) Market credibility

Pharmacovigilance bolsters the image of herbal industries by proving that safety and consumer welfare are top priorities. When companies commit to post-marketing surveillance and safety reporting, it fosters consumer confidence in their offerings. Openness in revealing adverse effects or safety protocols reassures both patients and healthcare professionals regarding the dependability of herbal products. This credibility not only boosts acceptance within the domestic market but also enhances competitiveness on the international stage. Consequently, herbal companies secure a lasting advantage through safety-focused branding [55,57].

c) Risk management

Pharmacovigilance serves as an early-warning mechanism for industries, enabling the detection of safety issues before they develop into significant crises. By consistently monitoring adverse drug reactions (ADRs), companies can pinpoint potentially dangerous products, ingredients, or interactions. This forward-thinking approach to risk management aids in averting extensive recalls that could lead to financial setbacks and harm to brand reputation. It also empowers industries to implement corrective measures, such as reformulating unsafe products or revising dosage guidelines. Consequently, pharmacovigilance plays an important part in ensuring both business stability and consumer safety [56].

d) Evidence based labeling

Pharmacovigilance data is invaluable for industries when creating precise product labels, dosage instructions, and safety warnings. The evidence gathered from ADR monitoring and studies on herb–drug interactions allows companies to offer scientifically supported guidance to consumers. Well-defined labeling minimizes product misuse and bolsters patient safety, especially when herbal formulations are used in conjunction with allopathic medicines. Moreover, this level of transparency mitigates liability concerns for industries. Ultimately, evidence-based labeling elevates herbal products to a status of professionalism, trustworthiness, and comparability with modern pharmaceuticals [56,51].

e) Innovation and Product Development

Pharmacovigilance fosters innovation by producing safety profiles that assist industries in crafting new and enhanced formulations. Insights from pharmacovigilance initiatives indicate which herbs are the safest, which need reformulation, and how combinations can be optimized. This encourages industries to channel resources into research and development to build standardized, globally competitive herbal medicines. Additionally, safer and scientifically validated products pave the way for new markets and partnerships with international pharmaceutical companies. Thus, pharmacovigilance emerges not only as a regulatory requirement but also as a catalyst for innovation [55,57,58].

GROWTH OF HERBAL INDUSTRIES WORLDWIDE:

There is a growing global shift from synthetic drugs to herbal medicines, often termed a “Return to Nature.” India, known as the “Medicinal Garden of the World,” holds a unique position with systems like Ayurveda, Siddha, Unani, Homeopathy, Yoga, and Naturopathy. Herbal products are gaining popularity worldwide

due to the belief that they are safe, affordable, and have fewer side effects, driving demand for plant-based medicines, supplements, cosmetics, and health products in both developed and developing nations [59].

Indian herbal trade in world scenario:

The Indian herbal drug industry is expanding rapidly, with an annual turnover of about ₹2,300 crore and a growth rate of 15%. India is a major global exporter of medicinal plants, ranking second in castor seed production and exporting products like *isabgol, senna, vinca, cinchona alkaloids, menthol, and sandalwood oil* [60]. The domestic herbal market is valued at nearly USD 1 billion, while crude herbal extract exports contribute around USD 80 million annually [61]. To strengthen safety monitoring and international credibility, the Ministry of AYUSH has established a structured pharmacovigilance framework with a National Coordination Centre at the All India Institute of Ayurveda, New Delhi, supported by regional, peripheral, and intermediary centers located at major national institutes in Jaipur, Bangalore, Chennai, and Kolkata. This organizational framework, schematically represented in figure 2, depicts the systematic reporting of adverse drug reactions in Ayurveda, Unani, Siddha, and Homoeopathy.

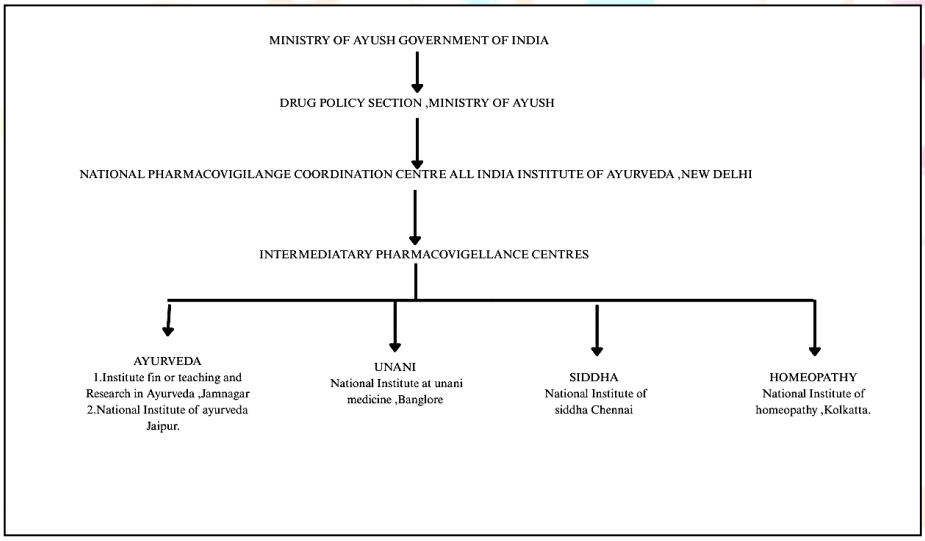

fig.2 pharmacovigilance framework for ayurveda, unani, siddha, and homoeopathy (ayush) medicines in India

INNOVATIVE APPROACHES FOR HERBAL PHARMACOVIGELLANCE :

Modern approaches include:

1. **Artificial intelligence data mining for ADR signals : [3]**

i. Digital Reporting Systems: Use of mobile apps and online tools for real-time adverse event reporting.

ii. Big Data Analytics: Mining health records, clinical data, and social media for safety signal detection.

iii. Traditional Knowledge Integration: Incorporating ethno medicinal knowledge into monitoring frameworks.

iv. Multi-Stakeholder Platforms: Collaboration among regulators, manufacturers, healthcare providers, and patients.

v. Community-Based Surveillance: Empowering local communities to report adverse reactions in underserved regions.

vi. Advanced Analytical Techniques: Application of LC-MS and NMR to detect adulterants and ensure product quality.

vii. Regulatory Harmonization: Establishing unified global standards for herbal medicine safety monitoring.

viii. Pharmacogenetics and Genomic Research: Using genetic data to predict individual responses and risks.

2. Blockchain ensuring supply chain transparency: [62]

i. A blockchain-based informative platform, HerBChain, was established for the herbal industry.

ii. Plantation base, processing factory, manufacturer, testing laboratory, distributor and retailer are recorded.

iii. The traceability and reliability of herbal products can be ensured.

BLOCKCHAIN :

Blockchain, with features like decentralization [62], immutability [63], time stamping [65], and cryptographic security [66], provides high potential for pharmacovigilance by guaranteeing secure, transparent, and tamper-proof recording of adverse medication reactions (ADRs). Consortium-based models such as Herbchain [64] can be adapted to herbal PV, enabling validated and traceable data sharing among stakeholders.

Mobile apps enabling real time patient reporting:

Mobile app–based pharmacovigilance (PV) systems represent an innovative approach to improving the safety monitoring of herbal medicines. Professional and regulatory-oriented tools such as Herb Safe, Green Pharma Vigil, Phyto Vigil, VigiHerb (modeled on VigiBase), Herb Med Report, and Herbal Watch can strengthen structured ADR reporting for regulators and healthcare providers. Patient-friendly apps like MyHerbReport, NatureCare Report, Trust Herb, Safe Herbs, and Herbal Alert enhance accessibility and encourage public participation in herbovigilance. Meanwhile, globally integrative options such as PhytoTrack, VigiNature, Herb Aware, Herba Safety Net, and Natural Med Watch provide cross-border relevance, fostering international collaboration. Such digital platforms can address underreporting, ensure traceability, and support evidence-based integration of herbal medicine into healthcare systems [67].

Integration with telemedicine linking pharmacovigilance with digital health

"Digital health" covers a broad range of applications. Digital health encompasses any use of communications and information technology to improve health and well-being. Below is a discussion of a few important applications [67].

1. Telemedicine:

The practice of providing healthcare using telecommunications technology is known as telemedicine. Despite not being a distinct field, notable for using a variety of technology to deliver conventional medical treatments from a distance.It is a wide notion that encompasses a number of different areas, including teleradiology, teleconsultation, telenursing, tele -ICU, and tele- surgery [69]. In India, where more than 75% of the population lives in rural areas and more than 75% of the country's healthcare infrastructure is concentrated in urban areas, telemedicine can be an especially helpful tool to enhance treatment outcomes.

More people could have access to healthcare thanks to telemedicine, which could successfully close the gap between the patient and the physician [69].

2. Digital health technologies:

i. Artificial Intelligence (AI): Helps identify patterns in large datasets, enabling faster diagnosis, clinical documentation, risk factor detection, and personalized treatment. AI also accelerates drug and vaccine development [68].

ii. Intelligent Manufacturing: Uses automation, data, and digital tools to improve pharmaceutical supply chains and drug production efficiency [68].

iii. Internet of Medical Things (IoMT): Networked devices like remote monitoring sensors, cardiac implants, and smart ambulances enhance patient safety, medication compliance, and quality of care [70].

iv. Mobile Health (mHealth): Wearables and mobile apps support chronic disease management, monitoring, and communication, while ensuring compliance with privacy regulations (e.g., HIPAA)[84].

v. EMR & Blockchain: Blockchain-based electronic records improve data security, privacy, scalability, and interoperability, protecting sensitive healthcare data from cyber-attacks [69].

vi. Augmented Reality (AR): Enhances medical training, surgical planning, and patient experience through immersive digital overlays [68].

vii. Big Data: Enables analysis of vast healthcare datasets (structured/unstructured) using AI and analytics, driving smarter decisions and advancing value-based care [68].

DISCUSSION:

The challenges facing herbovigilance are significant, but they are not insurmountable. The path forward lies in a strategic integration of traditional knowledge with current technology, a harmonization of global regulations, and a concerted effort to increase awareness and collaboration among all stakeholders. The future of herbal safety will be defined by its embrace of innovation and a commitment to evidence-based practice.The first and most critical step is the adoption of advanced digital technologies to transform the pharmacovigilance ecosystem from a reactive to a proactive model. The current reliance on spontaneous reporting is a cornerstone of PV, but it is inherently passive and slow [77]. Artificial Intelligence (AI), particularly machine learning (ML) and natural language processing (NLP), offers a game-changing solution. By leveraging these technologies, regulators and researchers can sort through massive volumes of unstructured data from a variety of sources, including electronic health records (EHRs), patient forums, social media, and online marketplaces, to identify subtle patterns and early signals of adverse events [69-78]. For example, an AI algorithm could analyse millions of patient comments on a public forum to detect a rising trend of a specific symptom, like liver enzyme elevation, associated with a particular herbal supplement, triggering an investigation before a critical mass of cases is reached [85]. This predictive capability is a significant leap forward from the current retrospective analysis model. The WHO is already exploring the potential of AI to enhance global health, and its application to pharmacovigilance is a natural and vital next step.Another transformative technology is blockchain, which can address the fundamental issue of supply chain opacity and product traceability [70]. The herbal industry's fragmented supply chain makes it vulnerable to fraud and adulteration. A decentralized, immutable ledger created by blockchain can track a herbal product at every step of its journey, from the farm where the plant is cultivated to the consumer's hand [70]. This transparent record provides irrefutable proof of a product's origin, identity, and

processing history, thereby ensuring quality and preventing counterfeiting [77]. A consumer could simply scan a QR code on the packaging to access this information, which would include the plant's species, the date of harvest, and any quality control test results [77]. In the event of an adverse reaction, this technology would allow for a rapid and precise recall of the problematic batch, saving lives and resources.Beyond data management and supply chain integrity, DNA barcoding is a powerful scientific tool for quality control and species verification. As mentioned earlier, the misidentification of plants is a serious risk, leading to cases of toxicity from look-alike species [79]. DNA barcoding provides a reliable and objective method to identify plant material, even in processed forms where morphological features have been lost [80]. By analyzing a short, standardized DNA sequence, researchers can confirm the authenticity of the plant species used in a product, even in powdered or processed forms [80]. This technology is particularly valuable for complex polyherbal formulations, where multiple species are combined, and can be used to screen for unwanted adulterants or contaminants [81].The integration of these technologies must be accompanied by regulatory and policy reforms. The current patchwork of national regulations is a hindrance to global safety monitoring. There is a pressing need for the harmonization of guidelines for herbal product manufacturing, quality control, and adverse event reporting. International bodies like the WHO, in collaboration with national agencies, must lead the charge in establishing a universal framework that allows for seamless data sharing and cross-border collaboration [80]. A centralized, global database for herbal ADRs would be invaluable, enabling researchers and regulators to identify safety signals that might be too subtle to detect within a single country's data set. The International Society of Pharmacovigilance (ISoP) is a key player in promoting such collaboration and scientific exchange [82].

Finally, the success of herbovigilance depends on community-level engagement and education. It is essential to break down the “natural equals safe” myth through targeted public awareness campaigns. Patients need to be empowered to report side effects without fear or hesitation, and mobile applications can be developed to make the reporting process as simple and user-friendly as possible [69]. Concurrently, healthcare professionals require continuous education and training on herbal medicine safety. Pharmacists are uniquely positioned at the front lines of patient care and can play a vital role in taking a comprehensive medication history that includes herbal supplements and counselling patients on potential risks and herb-drug interactions [86]. By fostering a culture of open communication and shared responsibility, we can build a more robust and responsive safety system for the herbal industry.

CONCLUSION:

The journey of herbal medicine, from ancient healing traditions to a global billion-dollar industry, now demands a parallel evolution in its safety oversight. We have shown that the challenges facing this field, including a lack of standardization, the widespread problem of underreporting, and fragmented international policies, are significant and have led to preventable harm. Yet, these challenges are not insurmountable. The solution lies not in abandoning tradition, but in fortifying it with the power of modern innovation. Our comprehensive review has laid out a clear, forward-looking path. By strategically implementing AI for real-time surveillance, we can move from a reactive to a proactive safety model, catching subtle signals before they become crises. By adopting block chain technology, we can create an unbreakable chain of trust from the farm to the consumer, eradicating the risk of adulteration. And by embracing DNA barcoding, we can ensure product authenticity with scientific certainty. The herbal industry’s prospects hinges on a unified global commitment to these rigorous, evidence-based practices. This is the moment to bridge the distance between ancient wisdom and cutting-edge technology, ensuring that the legacy of nature’s remedies is not only preserved but also protected for all.

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