Herbal Harmony: Nurturing Safety through Pharmacovigilance – Insight, Risk, and Future Direction

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Abstract

Numerous patients utilize herbal supplements as an elective and or adjunct to their prescribed medicine. Herbal products are favoured by population, because they are natural. In addition, they are accepted to be "safe" and "have less side effects" than "synthetic drugs". On the other hand, plants contain a number of active ingredients that create physiological effect inside the body. In case herb/herbal product is claimed to have beneficial effect on a certain health condition, at the point it must be able to alter the physiological system; i.e., apply pharmacological response. Therefore, it may have side effects as well.

Broadly Utilized For therapeutic purposes herbal formulation pose challenges in safety recognition and monitoring. Dispelling the myth of universal safety, this survey underscores the require for custom-made pharmacovigilance practices it addresses complexities in naming, sourcing, and utilization of herbal medicines, emphasizing conquences of widespread self-medication

KEYWORD: Pharmacovigilance, Safety, Adverse Drug Reaction (ADR), Future, Challenges, Herbal Medicine.

Introduction

Pharmacovigilance is the science and activity relating to the collection, detection, assessment, monitoring, and prevention of adverse effects with pharmaceutical products.

The word "pharmacovigilance" is derived from pharmakon (drug in Greek) and vigil are (keep an eye on/monitor in Latin). As such, pharmacovigilance mainly focuses on adverse drug reactions (ADR), which are defined as any

response to a drug which is noxious and unintended, including lack of efficacy.

The worldwide development for the enhansment of patient safety is gaining momentum, so the subject of drug safety becomes even more unmistakable inside day present-day situation. In India moreover, pharmacovigilance practice is picking up pace in keeping with time.

These days, herbal medicines are being utilized by different communities all through the world. Herbal formulations have come to far reaching adequacy as therapeutic agents such as cough remedies, hepatoprotectives, and antidiabetics.

Herbal medicines are traditionally considered safe since these belong to natural sources. However, this is not genuine as there are a few case reports of adverse reactions of herbal drugs mentioned in published literature.

Although most traditional therapies are presumed to be safe, there is still the problem of how to assess and quantify the possibility of very rare adverse events. A genuine occasion is sufficient to tip the scales against the utilize of the alternative medicine therapy.

If the advantage for any alternative medicine therapy is modest or unproven, then the presence of even a very small increased risk for a serious event is sufficient to tip the scales against the use of the alternative medicine therapy. Increasing uses of these drugs are growing concerns about the safety of Ayurvedic medicines.

The safety of herbal medicines is a concern for regulatory authorities due to reports of serious effects like hepatotoxicity, renal failure, and allergic reactions recognizing the increasing use of herbal medicines worldwide.

The World Health organisation (WHO) developed guidelines to monitor herbal safety within the existing pharmacovigilance framework (WHO2004)

Modern medicine primarily targeted specific diseases based on their underlying causes, while many prevalent diseases such as cancer have multifactorial origins, prompting the exploration of multi- target drugs. Screening medicinal plants for anti-tumour agents began in the mid-20th century, leading to the isolation of vinca alkaloids like vinblastine and vincristine.

Over 60% of cancer therapeutics on the market or in testing is derived from natural products.

Traditional medical knowledge, often termed complementary or alternative medicine, serves two potential values: providing accessible and low-cost primary healthcare options and offering potential leads for drug development.

Patients may choose plant-based drugs due to limited access, high costs, and belief in natural safety. Challenges include potential interactions, identifying ingredients, and limited knowledge of adverse reactions

There is presently increasing awareness of the need to develop pharmacovigilance practices for herbal medicines, and the World Health Organization (WHO), for example, has produced guidelines.

Awareness has arisen not only because of the extensive use of herbal (and complementary) medicines, but also because of several high-profile safety concerns associated with herbal medicines that have had an impact on public health

Herbal medicines are known for helping with many chronic illnesses, and Ayurveda, a type of medicine from India, relies on herbs. Plants and their extracts have strong healing properties.

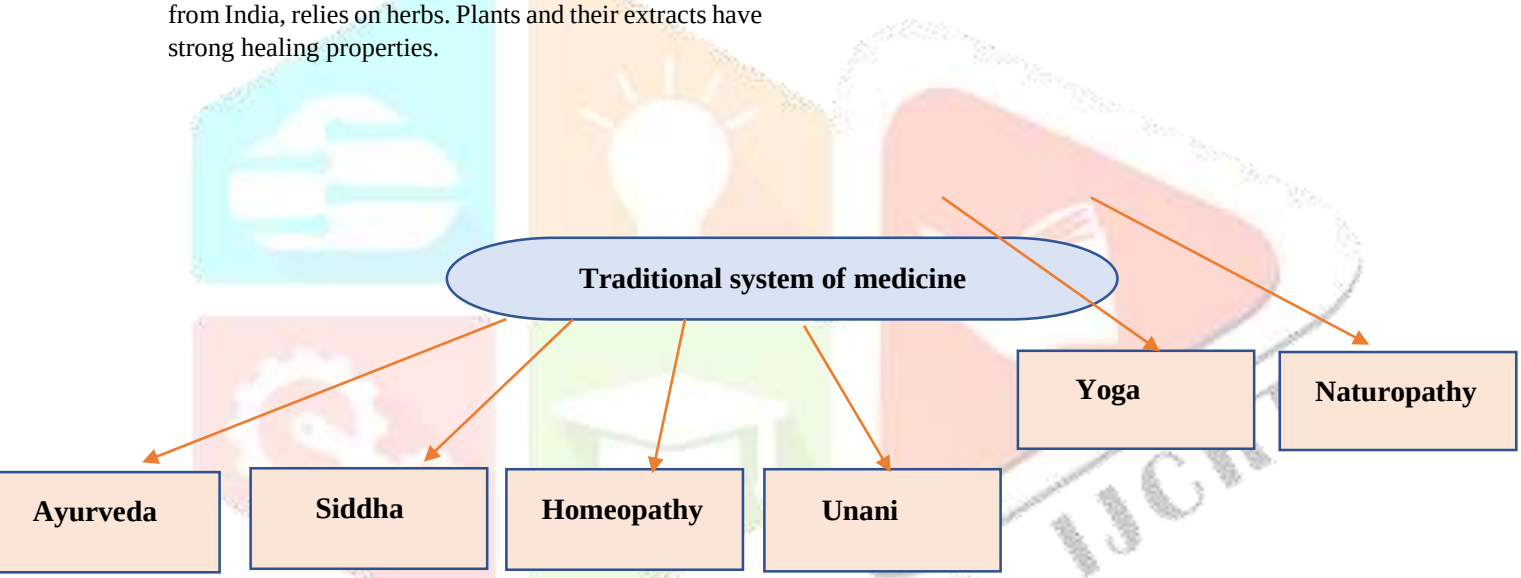

FIGURE 1: Traditional system of medicine

Even though modern medicine is popular, many people still trust herbal remedies. They use them for everything from a simple cold to serious illnesses because they think they're safer than synthetic drugs.

But just because something is natural doesn't always mean it's safe. Using herbs the wrong way, taking too much, or mixing them with other medicines can cause problems.

Plants can also have things like dirt or germs on them, which can make you sick if you eat them. That's why it's important to test herbal medicines to make sure they're safe and work well.

Pharmacovigilance is all about keeping an eye on medicines to prevent bad side effects, including those from herbal remedies.

It's important to check how safe herbal drugs are. While many traditional medicines come from plants, herbal medicines are made only from plants.

The history of using herbs as medication is as ancient as human history itself. Some authors claim that the first recorded use of herbs for medical purposes dates back over 4000 years, originating in China and India.

Traditional Indian medicine, dating back to 3000 BC, includes Ayurvedic medicine as one of its forms.

The traditional system of medicine includes Ayurveda, Siddha, Homeopathy, Unani, Yoga, and Naturopathy

Table1: Herbal product from different cultures

Type of herbal medication	Natural sources	Origins
Ayurvedic	P.A.M	India
Chinese	P.A.M.	China
Indusynunic	P.A.M	Pakistan
Islamic	P.A.M.	Middle east
Aromatherapy	P.	European
Herbalism	P.	European
Homeopathy	P.	European
Botanical	P,	European

P Medicinal plant M minerals A Animal source

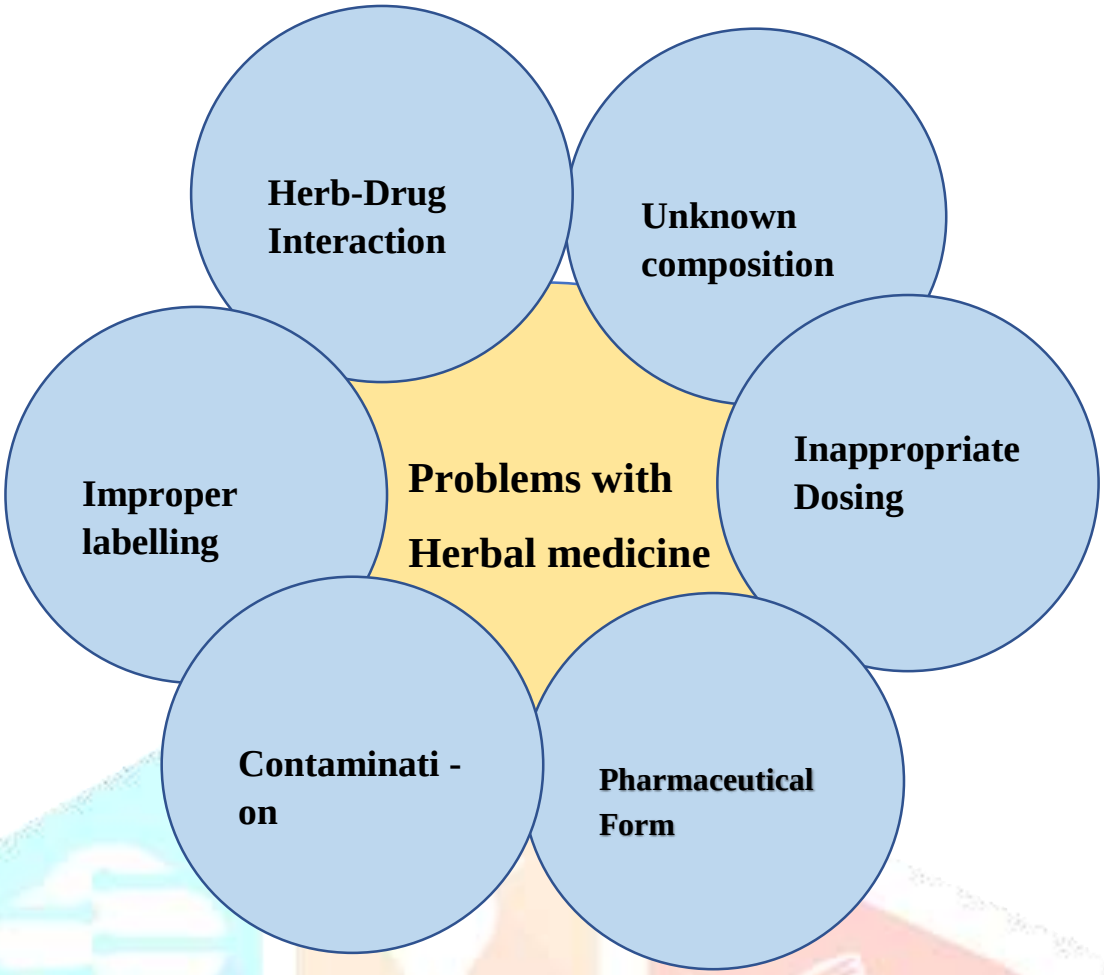

Figure 2: Problems with herbal product

Particular difficulties

Herbal medicines, unlike synthetic medicines, are chemically rich and complex products rather than isolated single components.

Many factors can have an effect on the qualitative and quantitative chemical profile, including:

• Geographic origin - climate, soil, and photoperiod.

• The genotype. • Plant parts such as leaves, stems, roots, root bark, and so on.

• Harvesting circumstances (year, season, and time of day).

• Preservation, processing, and extraction.

• Herb combinations and/or the preparing of mixed herbs as medicines.

Adverse drug reaction (ADR)

Adverse drug reactions (ADR) are unintended and undesirable impact which which occurs as result of drug treatment.

These reactions occur due to self-medication or due to intake of over dose of medicine without prescription. This prescribed drug may produce undesirable effect along with main effect which leads to adverse drug reaction

Most of the adverse drug reactions are preventable. Hence in order to avoid to adverse drug reaction one should take only properly prescribe drug

Any undesirable effect of a drug beyond its anticipated therapeutic effect occurring during clinical use

Medical substance are used because of their ability to affect biological processes in the body using such substances always carries a certain risk of unwanted or unintended effects

Classification of adverse drug reaction (ADR)

1) Type A

2) Type B

3) Type C

4) Type D

5) Type E

6) Type F

1) Type A (Augmented)

Reaction result from an exaggeration of a drug's normal pharmacological action when give at the usual therapeutic dose

Type A is a dose dependent

Example: respiratory depression with opioids or bleeding with warfarin.

2) Type B (Bizarre)

Reaction is novel responses that are not expected from the known pharmacological action of the drug.

Type B is a dose independent

Example: anaphylaxis with penicillin or skin rashes with antibiotics

3) Type C (Continuous drug use)

Type C or continuous reaction persist for a relatively long time

Example: Osteonecrosis of the jaw with bispthosphonates occurs as a result of continuous drug use

4) Type D (Delayed)

Type D or Delayed reaction become apparent sometimes after the use of medicine

Example: corneal opacities after thioridazine, ophthalmopathy after chloroquine

5) Type E (End of dose)

Type E or End of dose reaction are associated with the withdrawal of a medicine

Example: Insomnia; anxiety and perceptual disturbances following the withdrawal of benzodiazepines

6) Type F (Failure of therapy)

Result from the ineffective treatment

Example: accelerated hypertension because of inefficient control

- **Detection of Adverse Reactions to Ayurvedic Medicine**

  The belief among the doctors and prescribers that ayurvedic drugs are safe presents a major challenge in detecting adverse reaction to this medicine. From obtaining a correct medical history to diagnosis and pinpointing the casual medicine, the process is riddled with obstacles including

- The absence of concept and terminologies related to adverse reaction monitoring in the ayurvedic curriculum hinders the accurate identification of adverse reaction
- Methods to study drug safety problems have not evolved adequately in Ayurveda
- Information related to medicine exist in the stanza in the ancient treatises of Ayurveda it is not easily accessible
- Detecting signals is challenging because many people believe ayurvedic medication are safe resulting in under reporting and a lack of collected reports on any formulation
- patient frequently use medication from various medical systems simultaneously making it challenging to determine causality
- The absence of quality assurance and control in ayurvedic medicine manufacturing complicates the diagnosis of adverse reaction
- the large informal sector involved in manufacturing and selling ayurvedic drug on a small scale often makes it impossible to identify the specific medicine causing the adverse reaction
- the issue of counterfeit and spurious drugs is significant
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Importance of pharmacovigilance for herbal medicine

- Increased self-medication worldwide underscores the need for awareness and pharmacovigilance for herbal medicines.

- Herbal medicines' natural perception often overlooks safety concerns, necessitating pharmacovigilance to identify, assess, and prevent adverse effects.

- Monitoring is vital to address issues like incorrect plant species, interactions with other medications, and contamination risks.

- Healthcare providers must monitor interactions between herbal and prescription drugs.

- The WHO's International Drug Monitoring Program guides the establishment of pharmacovigilance centers and advocates for scientific plant names in medicines.

- Accessible international pharmacovigilance databases should contain label details, manufacturer information, and case reports of contamination.

- National regulations vary, affecting access and distribution of herbal medicines.

- Quality assurance, safety monitoring, and record-keeping are critical for regulating herbal medicines.

- Safety and quality are maintained through research, regulatory control, pharmacovigilance, and awareness campaigns.

- Compliance with global regulations is ensured through comprehensive audits.

- Reliable data collection is essential for developing safety guidelines for herbal medicines.

- Scientific information and toxicological investigations support systematic pharmacovigilance.

- Education and training in pharmacovigilance are essential for healthcare professionals, students, and consumers.

- Patient and healthcare provider feedback is vital for detecting pharmacovigilance signals and improving safety measures.

Table 2: List of herbs with suspected or known adverse effect

Herbal drug	Adverse effect
Ginkgo biloba	Bleeding
St. John's wort	Gastrointestinal disturbance, allergic reaction, fatigue, dizziness, confusion, dry mouth, photosensitivity
Ephedra (Ma- hung)	Hypertension, insomnia, tremor, headache, seizure, kidney stone, myocardial infraction, nervousness
Kava (Piper methysticum)	Sedation, torticollis, oral and lingual dyskinesia, oculogyric crisis
Aristolochia. sp (found use in Chinese medicine)	Kidney stone, carcinogenicity

Table 3: List of specific herbal drugs and their adverse interactions

Herb	Drug	Adverse effect
Ginkgo biloba	Drug such as aspirin, warfarin, dipyridamole, garlic, vitamin E	With aspirin- retards aspirin, absorption
Psyllium seed	Coumarin derivatives	Retaeds absorption of drug
Ephedra	Caffeine, decongestants, stimulant	Maybe additives in nature
Feverefew	Aspirin	Additive effects

Minimum requirements for reporting adverse drug reactions (ADRs)

involving herbal medicines include:

- Patient demographics and medical history.
- Symptoms experienced and relevant laboratory results.
- Details of the herbal medicine, including product name, producer, batch number, extract type, concentration, and standardized constituents for manufactured herbal products.
- Botanical identification, including the Latin scientific name, plant parts used, and preparation methods.
- Additional information on the identity of the herbal medicine as per the label/prescription.
- Processing details, such as stir frying in Chinese medicine, which can impact chemical profiles.
- Information on the reason for use and diagnosis by the herbal practitioner, based on supportive information.
- Involvement of the herbal practitioner in assessing suspected adverse reactions.
- Accurate reporting to identify real adverse events, provide appropriate warnings, and prevent incorrect restrictions on safe herbs.
- Effective pharmacovigilance to gather reliable safety information for diverse patient populations and develop guidelines for safe and effective herbal use as herbal medicine use expands globally.

The future for pharmacovigilance of herbal medicine

- **Directive Impact on Research**: The herbal medicines directive may shift research focus from discovering pharmacological activities towards investigating safety, as manufacturers are not mandated to demonstrate efficacy beyond traditional use.

- **Unregulated Sector:** Currently, the herbal medicinal products sector in the UK is largely unregulated, allowing the sale of products

without demonstrating evidence of quality, safety, and efficacy to the licensing authority.

- **Post-Thalidomide Parallel:** Similar to the lack of a formal regulatory system before the thalidomide disaster, the herbal medicines sector remains largely unregulated, raising concerns about safety.

- **Expected Improvements:** Implementation of the proposed EU directive for traditional herbal medicinal pro ducts is expected to improve safety and pharmacovigilance by requiring adherence to quality standards, safety evidence, and compliance with regulatory provisions.

- **Safety Concerns:** Recent high-profile safety concerns, such as renal failure and urothelial cancer linked to Aristolochia species, drug interactions with St John's wort, and hepatotoxicity associated with kava-kava, highlight the need for monitoring the safety of herbal medicines.

- **Future Safety Monitoring Tool:** Potential tools for monitoring herbal medicine safety include pharmacy-record linkage, a common electronic health record, and involvement of consumers and patients in pharmacovigilance through recognized reporting schemes and data collection.

- **Role of Pharmacogenetics and Pharmacogenomics:** The future safety of herbal medicines may involve exploring pharmacogenetics and pharmacogenomics to optimize treatment based on individual genetic factors, reducing the potential for adverse drug reactions (ADRs).

Unapproved Ayurvedic Products

List of unapproved Ayurvedic products

List of the unapproved Ayurvedic medicinal products found on the Canadian showcase in this way distant which have been analyzed by Health Canada and found to contain high levels of mercury, lead, and arsenic, are as follows:

1) Karela tablets, produced by Shriji Herbal Products, India

2) Karela capsules, produced by Himalaya Drug, India

3) Karela capsules, produced by Charantia, UK (specifically batch #12011)

4) Maha Sudarshan Churna powder, produced by Zandu Pharmaceuticals, Mumbai, India

5) Maha Sudarshan Churna powder, D and K Pharmacy, Bhavnagar, India

6) Maha Sudarshan Churna powder, produced by Chhatrisha, Lalpur, India

7) Maha Sudarshan Churna powder, produced by Dabur India, New Delhi, India

8) Safi liquid, produced by Hamdard-WAKF-Pakistan

9) Safi liquid, produced by Hamdard-WAKF-India

10) Yograj Guggul tablets, produced by Zandu Pharmaceuticals, Mumbai, India

11) Sudarshan tablets, produced by Zandu Pharmaceuticals, Mumbai, India

12) Shilajit capsules, produced by Dabur India, New Delhi, India

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