

Pharmacovigilance In Herbal Medicine: Insights, Risks and Future Direction

Pavan Pare, Ammar Ansari, Kshitij Bhadarge, Yash Sale, Om satpute, Pooja Rathi
Sayali Charitable Trust College of Pharmacy

Abstract: Herbal medicines are gaining popularity as treatments for various health conditions, including diabetes, arthritis, liver issues, coughs, memory loss, and stress. However, a common misconception persists: that herbal medicines are completely safe and don't require medical supervision. This has led to widespread self-medication, often resulting in disappointing outcomes, side effects, or unintended consequences. As a result, there is a growing recognition of the need for pharmacovigilance practices to monitor the safety of herbal medicines. However, current methods for monitoring drug safety were developed for synthetic drugs and may not be suitable for herbal medicines. Herbal medicines pose unique challenges due to differences in naming, perception, sourcing, and usage. To address these challenges, a tailored approach to pharmacovigilance is necessary.

• **Keywords-** Herbal medicine- Pharmacovigilance (monitoring drug safety)- Current situation- Future possibilities- Artificial intelligence.

• **Abbreviations-** WHO: World Health Organization
NPA: National Pharmacovigilance Advisory Committee- PV: Pharmacovigilance AI: Artificial Intelligence- ADR: Adverse Drug Reactions (bad reactions to drugs).

INTRODUCTION

Pharmacovigilance is the science of collecting, detecting, assessing, monitoring, and preventing adverse effects of pharmaceutical products, including herbal medicines. The term is derived from the Greek word "pharmakon" (drug) and the Latin "vigilare" (to keep an eye on). Pharmacovigilance primarily focuses on adverse drug reactions (ADRs). In India, pharmacovigilance practices are also evolving to keep pace with this trend. Herbal medicines are widely used globally, and their popularity stems from their perceived natural safety. However, there are documented cases of adverse reactions, and assessing rare adverse events remains a challenge. Even a small increased risk of serious events can outweigh the benefits of alternative medicine therapy. Regulatory authorities

are concerned about the safety of herbal medicines due to reports of serious effects like hepatotoxicity and allergic reactions. The World Health Organization (WHO) has developed guidelines to monitor herbal safety.

Traditional medical knowledge, including Ayurveda, has been used for centuries to treat various ailments. Plants and their extracts have strong healing properties, and many modern medicines are derived from natural products. However, challenges persist, including potential interactions, identifying ingredients, and limited knowledge of adverse reactions. There is a growing awareness of the need to develop pharmacovigilance practices for herbal medicines, and WHO has produced guidelines to address these concerns

Diabetes mellitus is a major global health concern, with a projected rise in prevalence. It's a degenerative disease affecting millions worldwide, and complementary and alternative medicine, including herbal supplements, are increasingly being used to manage the condition. Momordica charantia, or bitter melon, is a popular plant used to treat diabetes-related conditions, with potential antidiabetic and hypolipidemic properties.

PHARMACOVIGILANCE

It is a science dedicated to minimizing the risk of drug-related harm to consumers. It involves the collection, monitoring, assessment, and evaluation of information on adverse effects of medications, including herbal and traditional drugs. With the global movement towards improving patient safety gaining momentum, drug safety has become a prominent concern. In India, pharmacovigilance practices are also evolving to keep pace with this trend. The increasing use of herbal medicines worldwide has led to a growing need for pharmacovigilance in this area. While herbal medicines are often perceived as harmless due to their natural origins, there are documented cases of

adverse reactions. Assessing and quantifying rare adverse events remains a challenge, and even a small increased risk of serious events can outweigh the benefits of alternative medicine therapy, particularly if its benefits are modest or unproven.

- Functions of pharmacovigilance [as to WHO Guidelines 2000]

1. Drug Quality, Safety, and Effectiveness: Active monitoring and reporting.
2. Adverse Reactions: Identification and study.
3. Corrective Actions: Monitoring effects of measures taken.
4. Risk and Benefit Assessment: Measuring risk, effectiveness, and evaluating benefits and harms. Information Dissemination and Education
5. Disseminating Information: Educating on rational and safe use of medicines.
6. Early Warning System: Alerting stakeholders to potential safety concerns.
7. Informing Stakeholders: Educating consumers, practitioners, and regulators on effective drug use.

Reporting and Analysis Gathering and Analysing Reports: Creating programs and procedures for collecting and examining reports from patients and clinician

- Scope of Pharmacovigilance Pharmacovigilance has evolved significantly since the WHO's 1972 technical report. Its scope continues to expand, addressing challenges posed by: - 1.Increasing variety and potency of pharmacological therapies

2Biological therapies, including vaccinations

3.Potential harm associated with these therapies

4.Importance of Healthcare Professional and Patient Awareness

5. The risk of harm is reduced when Healthcare professionals are knowledgeable and informed And Patients are aware

PHARMACOVIGILANCE IN INDIA

India has a population of over 1 billion people. These people use different types of medicine, including:

1. Allopathy: Western medicine, commonly used in hospitals and clinics.
2. Homoeopathy: A system of medicine that uses natural remedies.

3. Ayurveda: An ancient Indian system of medicine that uses natural herbs and plants.

4. Siddha: A traditional system of medicine that originated in South India.

- In India, people have many options when it comes to choosing a type of medicine. This can be helpful, but it also means that there are many different approaches to healthcare. India's healthcare system faces challenges due to inadequate monitoring and review processes, leading to drug interactions, adverse effects and misuse. To address this, the country has implemented various initiatives.

- Pharmacovigilance Programs National Pharmacovigilance Program (NPP): Launched in 2004 by the Central Drugs Standard Control Organization (CDSCO), this program aims to promote reporting of adverse drug events and monitor drug - WHO-sponsored and World Bank-funded NPP: Operational since January 1, 2005, this program divides the country into zones and regions for efficient monitoring.

Objectives

1.Promote Adverse Drug Reaction (ADR) reporting: Encourage healthcare professionals to report adverse events and side effects.

2.Monitor drug safety: Identify potential safety issues and take corrective actions. 3.Improve patient care: Enhance healthcare services by minimizing harm from medications.

Challenges and Progress

- Insufficient funding and motivation: Previous ADR monitoring programs faced challenges, but the NPP has made significant progress.

- Banning of hazardous drugs

- Improved healthcare infrastructure: India's healthcare system is evolving, with increased government spending and initiatives like Ayushman Bharat .

- The National Pharmacovigilance Program (NPP) in India has three main goals:

1. Collect and Share Data; Gather information on adverse drug reactions (ADRs) in India. Share this data with the global healthcare community through the WHO-UMC (Uppsala Monitoring Centre).
2. Ensure Drug Safety- Monitor the safety of drugs

sold in India. Take steps to prevent harm from medications.

3. Provide Expertise- Help sponsors of clinical trials in India assess adverse event reports. Provide technical support to ensure compliance with safety regulations.

India's pharmacovigilance system is overseen by the National Pharmacovigilance Advisory Committee (NPAC), with the Drug Controller General of India serving as its member secretary. The system collects adverse drug reaction (ADR) reports from across the country through :

- Two Zonal Centres :

1.South-West zonal centre at Seth GS Medical College and KEM Hospital in Mumbai.

2.North-East zonal centre at the Department of Pharmacology, AIIMS in New Delhi.

These zonal centres receive reports from:

- Regional Centres : Two under New Delhi and three under Mumbai.

- Auxiliary Centres : Multiple centres reporting to each regional centre.

- Peripheral Centres : 24 centres currently collecting ADR reports.

• Reporting ADRs

Only healthcare professionals, including doctors, dentists, nurses and pharmacists, can submit ADR reports to the nearest pharmacovigilance centre. Some facilities, like JIPMER in Pondicherry and AIMS in Kochi, offer online ADR reporting.

• Global Collaboration

The WHO-UMC in Sweden maintains an international database of ADR reports, with 3.5 million reports from 78 countries as of September 2005. This collaboration enables global monitoring of drug safety and facilitates sharing of information to protect public health .

• In other countries

-United States ;Herbal products are considered dietary supplements, not medications. Manufacturers can't make health claims without FDA approval. The FDA must prove a supplement is dangerous before taking action.

-Australia A two-tiered system regulates therapeutic goods based on risk. Registered medicines are tested for quality, safety, and efficacy.

-Other Countries; Japan, China, Korea, and India use herbal treatments in traditional medicine. Each country has its own regulations and quality control measures...

PHARMACOVIGILANCE IN HERBAL MEDICINE

TRADITIONAL SYSTEM OF MEDICINES

1.Ayurveda

2.siddha

3.homeopathy

4.unani

5.yoga

• The Importance of Pharmacovigilance for Herbal Remedies Herbal Remedies Are Popular worldwide Many people trust herbal remedies for their natural origin. They are used to treat various health issues, from common colds to serious illnesses.

Risks Associated with Herbal Remedies, 1.Safety concerns 2.Incorrect usage 3.Contamination

The Need for Testing and Monitoring for Testing for safety and efficacy: Ensuring herbal medicines are safe and effective. Herbal remedies can be beneficial, but they can also pose risks if not used correctly. testing and monitoring are crucial to ensure the safety and efficacy.

• Problems with Herbal Medicines; cause liver and kidney damage, interact with other medicines Often contain multiple ingredients, making it hard to identify the cause of harm, Lack of clinical trials means we rely on reports of adverse reactions to understand safety concerns

• Importance of Monitoring Safety: The World Health Organization (WHO) has a database of over 16,000 suspected herbal medicine-related adverse reactions.

• Pharmacovigilance Methods for Herbal Drugs: To ensure consistency and accuracy in monitoring adverse reactions (ADRs) to herbal drugs, the World Health Organization (WHO) recommends:

1. Standardized naming conventions: Use scientific binomial names for herbs in ADR reports.

2. Detailed product information: Include label, manufacturer, ingredients, and dose details in published case reports

3. Product analysis: Conduct tests for contamination, adulteration, or incorrect species identification.

•Pharmacovigilance Methods

1. Passive surveillance: Spontaneous reporting and stimulated reporting of ADRs.

2. Active surveillance: Monitoring sentinel sites for ADRs.

3. Drug event monitoring: Tracking ADRs

4. Registries: Maintaining databases of ADR reports.

5. Comparative observational studies: Survey studies, case-control studies, and cohort studies. 6. Targeted clinical investigations drug-drug interactions, food-drug interactions, and other specific concern.

Detection of adverse reaction in herbal medicine

Herbal drug	Adverse effects
1.Ginkgo biloba	Bleeding
2.St. John's wort	Gastrointestinal disturbances, allergic reactions, fatigue, dizziness, confusion, dry mouth, photosensitivity
3.Aristolochia sp. (Found use in Chinese medicine)	Kidney toxicity, Carcinogenicity.
4.Ephedra (Ma Huang)	Hypertension, insomnia, arrhythmia, nervousness, tremor, headache, seizure, cerebrovascular event, myocardial infarction, kidney stones.

TABLE1. ADVERSE DRUG REACTIONCHALLENGES OF HERBAL PHARMACOVIGILANCE:

1.LACK OF STARDARDIZATION Herbal medicines can be unpredictable due to several factors. The amount of active ingredients in these products can vary greatly, and different batches of the same product can have different compositions. Furthermore, different products can have varying

ingredients and strengths, making it challenging to determine their safety and effectiveness.

2.Cultural and Language Barriers. Language barriers can hinder understanding and communication about these medicines, leading to potential misinterpretation or misuse.

3. Limited Regulation Herbal medicines are often regulated as food supplements rather than pharmaceutical drugs, which means they are subject to less stringent regulatory oversight.

4.No Standard Reporting System There's no uniform way to report problems with herbal medicines.

5,Collaboration It is Key To ensure herbal medicine safety, we need teamwork between: Researchers, Healthcare providers, Regulatory agencies.

CASE STUDY OF HERBAL DRUG

• MOMARDICA CHARANTINA [BITTER GUARD]

USED AS ANTIDIABETIC DRUG

DIABETUS MELITUS

Diabetes is a condition that happens when your blood sugar (glucose) is too high. It develops when your pancreas doesn't make enough insulin or any at all, or when your body isn't responding to the effects of insulin properly. Diabetes affects people of all ages. Most forms of diabetes are chronic (lifelong), and all forms are manageable with medications and/or lifestyle changes

A Growing Global Health Concern; Diabetes is one of the top causes of death worldwide. It's a serious metabolic disorder that's spreading rapidly.

171 million people had diabetes in 2000, Expected to rise to 366 million by 2030.Diabetes is a condition where the body's metabolism goes haywire, often due to genetics and lifestyle. This leads to High blood sugar levels, Degenerative damage to the body.

The Impact of Diabetes

- Affects 200 million people worldwide.
- Third leading cause of death globally.
- Most common endocrine disorder.

Alternative Treatments. Some people turn to complementary and alternative medicine, using

herbs and supplements instead of traditional Western medicine. Many Diabetes Patients Turn to Alternative Medicine A recent study found that: Up to 30% of people with diabetes use complementary and alternative medicine, This means nearly 1 in 3 diabetes patients try alternative treatments alongside conventional medicine.

Medicinal Plants: Ancient Remedies for Modern Ailments, Plants and plant-based products have been used for centuries to treat various health issues, including diabetes. Many traditional medicines are derived from: Medicinal plants Minerals, Organic matter

A Wealth of Medicinal Plants.

The World Health Organization (WHO) has identified:

- 21,000 plants used for medicinal purposes worldwide.
- 150 species commercially used on a large scale.

These plants offer a treasure trove of potential remedies for various health conditions.

Bitter gourd: A Natural Remedy for Diabetes.

Bitter gourd also known as *Momordica charantia*, is a plant used in many cultures to treat diabetes. Its fruit has a strong bitter taste and has been shown to have anti-diabetic properties.

Bitter gourd Works Studies have found that bitter Guardcan:

- Lower blood sugar levels.
- Reduce complications from diabetes, such as nerve damage and kidney disease

•Nutrient Profile of Bitter Melon

Bitter melon is a nutrient-rich plant packed with: Vitamins: C, A, E, B1, B2, B3, and folate Minerals: potassium, calcium, zinc, magnesium, phosphorus, and iron Dietary fiber Antioxidants: phenols, flavonoids, isoflavones, terpenes, anthroquinone, and glucosinolates Caloric Value Leaves: 213.26 Kcal/100g Fruits: 241.66 Kcal/100g Seeds: 176.61 Kcal/100g The high antioxidant properties and diverse nutrient profile make bitter melon a valuable plant for: Treating various illnesses Supporting overall health and well-being.

Test name	result
1.Molish's Test Add Molisch reagent + concentrate H2SO to extract	Violet ring show presence of carbohydrate which contribute in glucose activity
2.Benedict's test Add Benedict's reagent to extract heat	Green ppt show presence of saponin group for hypoglycemic effect
3.Foam Test Shake extract with water in test tube	Foam formation show presence of phenolic compound
4.Test For Alkaloids (Wagner's)	Presence of alkaloids
5.Flavonoid Test (NaOH Test)	Presence of flavonoids

Table 2 chemical test for bitter guard

By performing test conclude the presence of compound which role in antidiabetic agent



Figure 1 chemical test for bitter guard

Adverse effect of bitter guard

Momordica charantia, also known as bitter melon, is generally considered safe when consumed in moderation. However, it can cause some adverse effects, particularly when taken in large quantities or in certain forms:

Common Adverse Effects

1. Gastrointestinal issues: Diarrhea, stomach pain, bloating, and gas

2. Hypoglycemia: Bitter melon can lower blood sugar levels, which may be problematic for people with diabetes taking medications

3. Allergic reactions: Rare cases of allergic reactions, such as hives, itching, and swelling

Less Common Adverse Effects

1. Headache: Some people may experience headaches due to bitter melon consumption

2. Liver damage: High doses or prolonged use may potentially cause liver damage

Special Precautions

1. Pregnancy and breastfeeding: Bitter melon may stimulate uterine contractions, so pregnant women should consult their healthcare provider before using it

2. Diabetes medications: Bitter melon may interact with diabetes medications, increasing the risk of hypoglycemia

Forms-Specific Adverse Effects

1. Supplements: High doses or concentrated extracts may increase the risk of adverse effects

2. Raw or unripe fruit: May be more likely to cause gastrointestinal issues due to higher concentrations of bioactive compounds

FUTURE PROSPECTIVE

• Future Plans for Herbal Medicine Safety 1. Integrate herbal therapy into healthcare: Offer herbal therapies in hospitals and clinics, and cover them under health insurance.

2. Register and regulate herbal products: Make sure all herbal products and providers are registered and follow rules.

3 Strategies for a Successful Pharmacovigilance Program

a. Educate patients: Teach patients how to use herbal remedies safely and effectively. b. Update product information: Regularly review and update product information to ensure safety and effectiveness.

c. Standardize herbal medicine classification: Create a standardized system for classifying and coding herbal medicines.

d. Conduct research: Study the effects of herbal medicines on different people and populations. e. Train staff and improve facilities

• Artificial intelligence (ai) in pharmacovigilance AI is the ability of machines to perform tasks that typically require human intelligence. In pharmacovigilance, AI helps:

1. Improve clinical trials: AI makes it easier to randomize patients and increases the success rate of clinical trials.

2. Enhance disease detection and treatment: AI improves early detection, mitigation, and treatment of diseases like diabetes, cancer, and retinopathy.

3. Analyze pharmacovigilance data: AI improves the accuracy and quality of pharmacovigilance data, which confirms the safety of medical devices.

4 Categories of AI

1. Rule-based static systems: AI follows predefined rules.

2. AI-based static systems: AI learns from data.

3. Dynamic rule-based systems: AI updates rules with new data.

• Roles of AI in Pharmacovigilance

1. Detect adverse drug reactions-

-Electronic health records

- Social media

- Scientific studies

2.Improvedata analysis: AI analyzes large amounts of data efficiently.

3. Enhance signal detection: AI identifies potential safety signals from data.

4. Support regulatory decision-making: AI provides insights for regulatory agencies.

5.signal detection Analyze large amounts of data - Identify potential safety issues that might be missed by traditional methods

6.AI Helps Assess Drug Risks - Analyze data to understand potential drug risks - Identify groups of people who may be more likely to experience harm from a drug susceptible to harm

CONCLUSION

Identify potential harm from herbal, conventional, and complementary treatments- Understand and prevent these harms. Gather data on potential adverse reactions to herbal medicines. Provide safer and more effective treatment options for patients. Momordica charantia, or bitter melon, has been used for centuries as a dietary supplement and ethnomedicine to relieve symptoms of diabetes. The plant is rich in medicinal properties and contains over 225 different compounds that may contribute to its therapeutic effects. Specifically, charantin, insulin-like peptide, and alkaloid-like extracts have been found to possess hypoglycaemic properties, exerting their beneficial effects through various mechanisms to control and treat diabetes mellitus. While biochemical and animal studies support the potential benefits of M. charantia, clinical data are often limited by small sample sizes, lack of control, and poor study designs. Therefore, better-designed clinical trials are needed to confirm the efficacy of M. charantia as a natural nutritional treatment for diabetes. Despite these limitations, M. charantia may be a feasible option for ethnic minorities who prefer natural products according to their cultural beliefs, particularly given the high prevalence of diabetes in these populations. Using AI for Better Safety AI helps pharmacovigilance by: Detecting adverse drug reactions more accurately and efficiently, Improving patient safety.

REFERENCE

- [1] <https://www.sciencedirect.com/science/article/pii/S0378874112000645.com>
- [2] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3159283/.com>
- [3] <https://www.sciencedirect.com/science/article/abs/pii/S221080331500007X.com>
- [4] <https://content.iospress.com/doi/10.3233/JRS-150643.com>
- [5] <https://www.sciencedirect.com/science/article/pii/S0378874112000645.com>
- [6] https://www.walshmedicalmedia.com/open-access/pharmacovigilance-of-herbal-medicine-herbavigilance-2167-1052_1000208.pdf.com
- [7] <https://greenpharmacy.info/index.php/ijgp/article/download/610/519.com>
- [8] Pharmacovigilance Programme of India. Introduction & functions. 2017. <http://www.ipc.gov.in/PvPI/about.html>. Accessed Dec 2017.
- [9] WHO Guidelines on safety monitoring of herbal medicines in pharmacovigilance, https://apps.who.int/iris/bitstream/handle/10665/43034/9241592214_eng.pdf
- [10] WHO., World Health Organization. WHO Traditional medicine strategy 2002-2005. Geneva, 2002.
- [11] Adithan, C., National pharmacovigilance programme. Indian Journal of pharmacology, 2005, 37(6):347. Joseph B, Jini D. Insight into the hypoglycaemic effect of traditional Indian herbs used in the treatment of diabetes. Res J Med Plant 2011a; 5(4): 352-376.
- [12] Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010; 87: 4-14.
- [13] Patel DK, Prasad SK, Kumar R, Hemelatha S. An overview on antidiabetic medicinal plants having insulin mimetic property. Asian Pac J Trop Biomed 2012; 2: 320-330.
- [14] Ogbonnia SO, Odimegu JI, Enwuru VN. Evaluation of hypoglycemic and hypolipidemic effects of ethanolic extracts of Treculia africana Decne and Bryopyllum pinnatum Lam. And their mixture on streptozotocin (STZ)- induced diabetic rats. Afr J Biotech 2008; 7(15): 2535-2539.
- [15] Sharma AK, Aggarwal A, Singhal VK. Treatment of diabetes mellitus with indian herbal Drugs. IJARPB 2012; 1(2): 145-153.
- [16] Raman BV, Krishna NV, Rao NB, Saradhi PM, Rao BMV. Plants with antidiabetic activities and their medicinal values. Int Res J Pharm 2012; 3(3): 11-15.
- [17] Joseph B, Raj SJ. Phytopharmacological properties of Ficus racemosa Linn – And overview. Int J Pharm Sci Rev Res 2010b; 3(2): 134-138.
- [18] Singh U, Singh S, Kochhar A. Therapeutic potential of antidiabetic nutraceuticals. Phytopharmacol 2012; 2(1): 144-169.
- [19] Zohary D, Hopf M. Domestication of plants in the old world. Oxford: Oxford University Press; 2000, p. 122.
- [20] Cefalu WT, Ye J, Wang ZQ. Efficacy of dietary supplementation with botanicals on carbohydrate metabolism in humans. Endoc Metab Immune Disord Drug Targets 2008; 8: 78-81.
- [21] Lee SY, Eom SH, Kim YK, Park NI, Park SU. Cucurbitane-type triterpenoids in Momordica charantia Linn. J Med Plants Res 2009; 3(13): 1264-1269.

- [22] Bakare RI, Magbagbeola OA, Akinwande AI, Okunowo OW. Nutritional and chemical evaluation of *Momordica charantia*. *J Med Plant Res* 2010; 4(21): 2189-2193.
- [23] Snee LS, Nerurkar VR, Dooley DA, Efird JT, Shovic AC, Nerurkar PV. Strategies to improve palatability and increase consumption intentions for *Momordica charantia* (bitter melon): A vegetable commonly used for diabetes management. *Nutr J* 2011; 10: 78.
- [24] Saeed MK, Shahzadi I, Ahmad I, Ahmad R, Shahzad K, Ashraf M, et al. Nutritional analysis and antioxidant activity of bitter gourd (*Momordica charantia*) from Pakistan. *Pharmacologyonline* 2010; 1:252-260.
- [25] Basile AO, Yahi A, Tatonetti NP. Artificial intelligence for drug toxicity and safety. *Trends Pharmacol Sci.* 2019;40(9):624–35