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Pharmacovigilance of Herbal Medicines: Current Scenario and future Prospects

Divya Verma[1],Prof. (Dr) Mohd. Wasiullah[2], Piyush Yadav[3], Sushil Yadav[4]*
1. Dept. of Pharmacy, Prasad Institute of Technology, Jaunpur (222001) U.P, India.
2. Principal, Dept. of Pharmacy, Prasad Institute of Technology, Jaunpur (222001) U.P, India.
3. Principal, Dept.ofPharmacy, Prasad Polytechnic, Jaunpur (222001) U.P, India.
4. Assistant Professor, Dept. of Pharmacy, Prasad Institute of Technology, Jaunpur (222001) U.P, India.

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ABSTRACT:
Worldwide, herbal preparations are now widely accepted as effective treatments for conditions such as diabetes, arthritic pain, liver illness, cough and cold, memory improvement, and immune-stimulation. Herbs are generally thought to be safe, and more individuals are consuming them without a prescription. Due to a number of complex issues, such as products with multiple ingredients, poor standardization, a lack of clinical trials, variation in manufacturing processes, contamination, adulteration, and misidentification of herbs, for example, systematic data on the incidence of adverse effects associated with traditional medicine are not yet available. Herbal drug pharmacovigilance is still in its infancy, and keeping track of their safety presents special difficulties because they can be purchased from a variety of sources without the assistance of medical specialists. Additionally, there are regional differences in the legal status and approval process for herbal medicines.As a condition for worldwide harmonization, the World Health Organization has established particular rules for evaluating the safety, effectiveness, and quality of herbal medicines. The "yellow card" programme for ADR reporting has been introduced by the UK's medications and Healthcare Products Regulatory Agency in order to track the safety of herbal medications. Traditional herbal therapy has not yet been fully incorporated into all facets of the Indian healthcare system due to drug control. The Indian herbal regulatory system should employ herbal pharmacovigilance to access various ADR, delayed or acute toxicities, allergies, and other issues related to single herb and/or polyherbal formulations. This paper examines the complex issues surrounding herbal pharmacovigilance while taking into account recent developments and offers suggestions to enhance safety monitoring in the future.

KEYWORDS: Herbal medicine, Pharmacovigilance, Current Scenario, future Prospects, Artificial intelligence.

ABBREVIATIONS:WHO:World Health Organization; **NPA:**National Pharmacovigilance Advisory Committee;**PV**:Pharmacovigilance;**AI**:Artificial Intelligence; **ADR:**Adverse Drug Reactions, etc.

I. INTRODUCTION:

Herbal medicines have been used by many groups and civilizations worldwide since the Paleolithic era. Over the past few decades, the number of people using herbal medications without a prescription has increased. Herbal preparations, such as anti-diabetics, anti-arthritics, aphrodisiacs, hepatoprotective, cough cures, memory boosters, and adaptogens, have gained universal acceptance as medicinal agents. They are typically regarded as safe because they come from natural sources. The World Health Organization (WHO) has established particular recommendations for evaluating the quality, safety, and efficacy of herbal medications in this area. Pharmacovigilance, which is not only limited to chemical medications but also includes herbal, traditional, and complementary medicines, biologicals, vaccines, blood products, and medical technologies, is intended to detect, assess, and understand harmful effects as well as to prevent them. [1,2]

The WHO has praised the active involvement of national pharmacovigilance centers, drug regulatory agencies, and other parties in the creation of these recommendations. This has given these authorities a helpful place to start in order to improve communication, which will be necessary to assure advancement towards their shared objective—the safety of herbal medications. The suggested course of action is to incorporate herbal medications into the current national pharmacovigilance systems or, in the absence of

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such systems, to construct comprehensive national pharmacovigilance systems that cover herbal medicines.[3]

According to its definition, pharmacovigilance is "the study of the safety of marketed medications under the realistic circumstances of clinical usage in broad communities." The goal is to increase safety monitoring and identify pharmacological adverse events that had gone unrecognized in the past while being assessed in clinical trials. Although though these techniques were created for pharmaceutical drug monitoring, they are also used to assess the safety of other therapeutic items such as herbal remedies, blood products, vaccinations, and even medical gadgets.

The reports of suspected toxicity and adverse events have increased along with the usage of herbal medications. Such unintended effects may result from I side effects, which are typically detectable by pharmacodynamics and frequently predictable; (ii) reactions brought on by overdose, over duration, tolerance, dependence, and addiction; (iii) hypersensitivity, allergic, and idiosyncratic reactions; (iv) mid- and long-term toxic effects, including liver, renal, cardiac, and neurotoxicity; and (v) other reactions not listed above (detectable by in vitro and in vivo toxicological studies or by pharmacovigilance). Pharmacovigilance is crucial for spotting adverse responses because many herbal medications on the market haven't been extensively examined for their toxicity and pharmacology.[4] Also, there is a persistent issue with unexpected toxicity of herbal products as a result of concerns with quality, such as the use of subpar herbal material, incorrect or misidentified herbs, improper processing techniques, and the provision of adulterated or contaminated herbs or products. [5] The regulatory agencies are concerned about the safety of herbal medicines because they have been linked to major side effects like hepatotoxicity, renal failure, and allergic responses. [6]

The guidelines were developed with the view that, within the current pharmacovigilance systems, monitoring of the safety of medicines should be enhanced and broadened in ways that will allow the successful monitoring of herbal medicines. The inclusion of herbal medicines in pharmacovigilance systems is becoming increasingly important given the growing use of herbal products and herbal medicines globally. For example, in the United States of America, some US$ 17 billion were spent by more than 158 million Americans in 2000. Furthermore, a recent study indicated that more than 70% of the German population reported using “natural medicines” and that, for most of them, herbal medicinal products were the first choice in the treatment of minor diseases or disorders. The worldwide consumption of herbal medicines today is enormous, so that, in terms of population exposure alone, it is essential to identify the risks associated with their use. Safety of herbal medicines is therefore an important public health issue. Herbal medicines are frequently used in conjunction with other medicines, and it is essential to understand the consequences of such combined use and monitor whether any adverse effects are arising. Despite the growing interest in the safety of herbal medicines, national surveillance systems to monitor and evaluate adverse reactions associated with herbal medicines are rare, even among the more than 70 Member States participating in the WHO International Drug Monitoring Program. Moreover, there is a lack of effective communication on this subject at all levels, from international to local. A recent WHO survey showed that around 90 countries, less than half of WHO’s Member States, currently regulate herbal medicines, and an even smaller proportion has systems in place for the regulation/ qualification of providers of herbal medicines. Moreover, there are disparities in regulation between different countries, and this has serious implications for international access to and distribution of such products.[7]

PHARMACOVIGILANCE:

Pharmacovigilance, a French term referring to identifying side effects of drugs, their treatment, documentation, reportage, and regulatory decisions based on them, is a well-established science in the developed world. Pharmacovigilance is the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems, particularly long term and short-term side effects of medicines. Generally speaking, pharmacovigilance is the science of collecting, monitoring, researching, assessing and evaluating information from healthcare providers and patients on the adverse effects of medications, biological products, herbalism and traditional medicines. Safety and efficacy are the two major concerns about any drug. While the efficacy of a drug can be detected with relative ease, the same cannot be said about safety because the adverse effect of a drug may be uncommon but very serious, and many

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patients may be affected or subjected to a potential risk before the relationship with the drug is established. This gave birth to a new branch of pharmacology called pharmacovigilance. Recently, its concerns have been widened to include herbals, traditional and complementary medicines, blood products, biologicals, medical devices and vaccines.[8]

FUNCTIONS OF PHARMACOVIGILANCE:

Functions of pharmacovigilance, as to WHO Guidelines (2000), include:

- Drug quality, safety, and effectiveness are all actively monitored and reported on.
- Adverse responses are also found and studied.
- Monitoring the effects of any corrective actions taken.
- Measuring risk.
- Measuring effectiveness.
- Evaluating benefits and harms.
- Disseminating information, education v Early warning v Rational and safe use of medicines.
- Informing consumers, practitioners, and regulators on the effective use of drugs.
- Creating programs and procedures for gathering and analyzing reports from patients and clinical.

SCOPE OF PHARMACOVIGILENCE:

Since the WHO technical report from 1972, the field of pharmacovigilance has advanced significantly, and it continues to be an active one on the clinical and scientific fronts. Meeting the challenges posed by the expanding variety and potency of pharmacological and biological therapies, including vaccinations, which contain an inescapable and occasionally unanticipated potential for harm, has been crucial. Yet, there is a lower chance of danger when drugs are used by healthcare professionals who are knowledgeable and by people who are aware of and accountable for their medications.

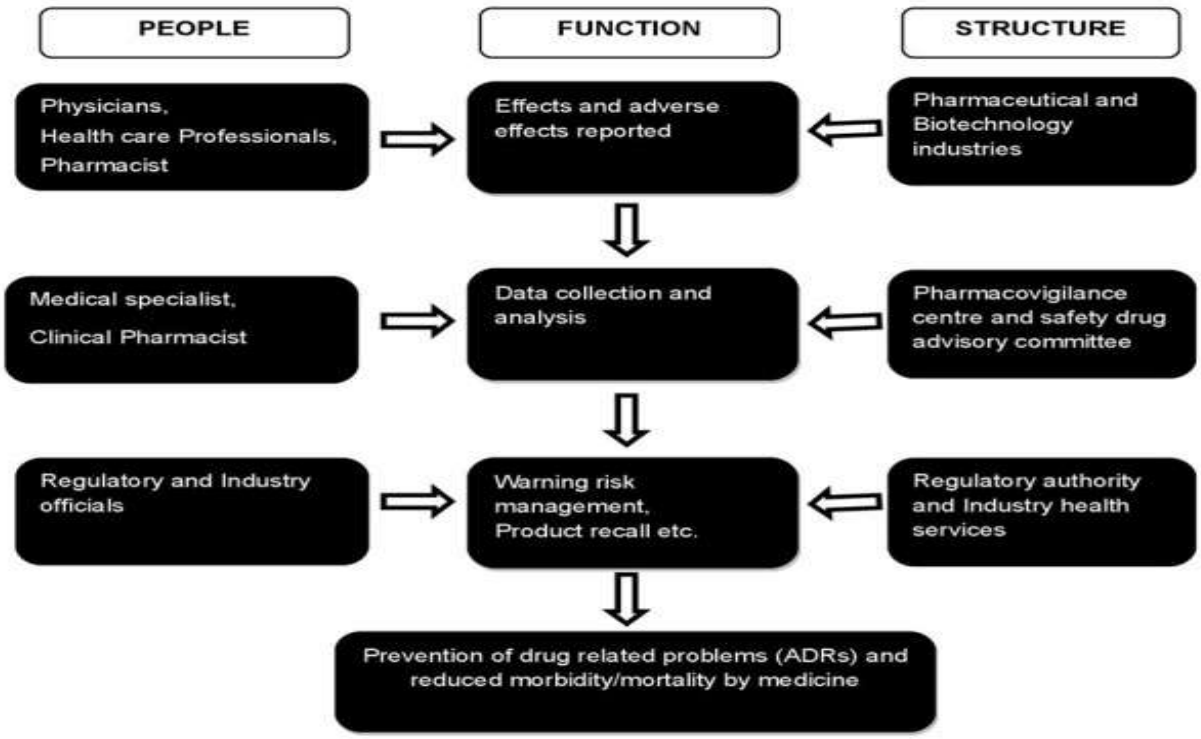

Fig. 1: Atypical pharmacovigilance setup.

PHARMACOVIGILANCE IN INDIA:

India is a nation having a population in excess of one billion. India's population uses a variety of modern medical systems, including Allopathy, Homoeopathy, Ayurveda, Siddha, etc. Without a monitoring and review process, drug interactions, bad effects, and misuse can wreak havoc on the nation's healthcare system. In India,

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ADR monitoring programs are not new. For the purpose of monitoring ADRs nationally, the Drug Controller General of India established five facilities in 1982. With its multi-institutional study, the Indian Council for Medical Research gathered over 58,000 ADR cases in 1987; however, in a short period of time, all of them ceased to exist for a variety of reasons, including a lack of funding and lack of motivation. A large number of medications have been taken off the market in the past two decades. The Cox-II inhibitor and anti-inflammatory medicine Rofecoxib, which has reportedly resulted in 93,000 heart attacks among users globally, was recently banned in India due to serious cardiovascular side effects after the manufacturer withdrew the drug from the market. In November 2004, the Central Drugs Standard Control Organization (CDSCO), Ministry of Health and Family Welfare, Government of India, introduced the National Pharmacovigilance Program (NPP), recognising the significance and advantages of pharmacovigilance. It is based in large part on the guidelines provided in the WHO document Safety Monitoring of Medicinal Products - Guidelines for Setting Up and Operating a Pharmacovigilance Center. For operational efficiency, this scheme divides the entire nation into zones and regions.The WHO-sponsored and World Bank-funded NPP for India started operating on January 1, 2005. The Program seeks to promote the culture of reporting adverse drug events and subsequently seeks to:

- Generate extensive ADR data on the Indian population and disseminate the information to the global health care community through WHO-UMC (Uppsala Monitoring Center).
- Ensure the highest level of product safety for drugs sold in the Indian market.
- Offer technical expertise for assessing statutory adverse event reports provided by Sponsors conducting clinical trials in India.

It is governed by the National Pharmacovigilance Advisory Committee (NPAC). The member secretary of the Committee is the Drug Controller General of India. Information is gathered from all over the nation and sent to the Committee as well as the UMC in Sweden by two zonal centers, the South-West zonal center (located at the Department of Clinical Pharmacology, Seth GS Medical College and KEM Hospital, Mumbai) and the North-East zonal center (located at the Department of Pharmacology, AIIMS, New Delhi). Two regional centers are subordinate to the New Delhi center, and three to the Mumbai center. Many auxiliary centers report to each regional center in turn. There are 24 peripheral centersat the moment. The CDSCO website (www.cdsco.nic.in) has a complete list of the centers. Only healthcare professionals (doctors, including dentists, nurses, and pharmacists) may send ADR reports to the nearest pharmacovigilance center. ADR reporting is available online at some facilities, including JIPMER in Pondicherry and AIMS in Kochi. The international database of ADR reports received from various National Centers is maintained by the WHO-UMC in Sweden. 3.5 million ADR reports were in the database as of September 2005, and 78 nations were taking part in the initiative. [9]

PHARMACOVIGILANCE FOR HERBAL MEDICINAL PRODUCTS IN OTHER COUNTRIES:

In many underdeveloped nations, herbal remedies are the go-to form of treatment for a variety of illnesses. In the United States, herbal products can currently only be advertised as food supplements, and without FDA approval, a manufacturer or distributor of herbs cannot make any particular health claims. Herbal medicines are not subject to the premarketing regulatory clearance required for medications because they are regulated as dietary supplements under the Dietary Supplement Health and Education Act (DSHEA) of 1994.

The U.S. Food and Drug Administration has the burden of proving that a dietary supplement is dangerous. Pharmaceutical medications, on the other hand, cannot be approved until the maker has shown their safety and efficacy. Australia has created a two-tiered system for regulating therapeutic goods. Essentially, this is predicated on risk, where listed medications are thought to have a smaller danger than fully registered medications. Before being put on the market, each registered medicine is tested for quality, safety, and efficacy. The Therapeutic Goods Administration examines each of the listed medications for legal compliance on an individual basis; they are not reviewed prior to release. Just symptomatic alleviation of mild diseases, health maintenance, health improvement, and risk reduction may be the only uses and benefits listed for herbal medications.Low risk herbal medicines are given early market access under Australian risk management standards, and the necessary post-market regulatory activities is encouraged. Patent herbal treatments made of whole, dried, and powdered herbs or herb extracts

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are frequently used in therapy in Japan, China, Korea, and India.

The State Administration of Traditional Chinese Medicine, which is in charge of managing traditional herbs, is the foundation of Chinese medicine. Traditional medicines from Japanese folklore are included in kampo, the traditional medicine of Japan. Kampo is comparable to and historically descended from Chinese medicine. Kampo medication quality control and manufacturing procedures were created by the Japanese herbal medicine industry in 1988. The Japanese government's Rules for Manufacturing Control and Quality Control of Medicines are complied with by these rules. Moves are being made in India.[10]

PHARMACOVIGILANCE FOR HERBALS:

Herbal medicines are widely used in health-care in both developed and developing countries. Pharmacovigilance for herbal medicines is, in many respects, in its infancy and monitoring the safety of herbal medicines presents unique challenges. The associated safety risks for some herbal medicines are believed to be low but the collated knowledge on the relative safety of herbal medicines remains poor.

To promote pharmacovigilance for herbal products, manufacturers should follow good manufacturing practices and conduct clinical trials to assess the safety and efficacy of their products. Healthcare providers should be encouraged to report any adverse effects associated with the use of herbal products to their respective regulatory authorities. Consumers should also be educated about the potential risks associated with herbal products and advised to consult with a healthcare provider before using any herbal products, especially if they are taking other medications.

CHALLENGES OF HERBAL PHARMACOVIGILANCE:

Herbal pharmacovigilance is the monitoring of the safety and efficacy of herbal medicines. While herbal medicines have been used for centuries, they are not without risks, and there are several challenges associated with herbal pharmacovigilance, including:

- **Lack of standardization:**

Herbal medicines are often not standardized, meaning that the active ingredients and their concentrations can vary widely between different batches of the same product or between different products. This makes it difficult to assess the safety and efficacy of these medicines.

- **Difficulty in identifying adverse events:**

Adverse events associated with herbal medicines are often underreported or not recognized because they are not well-known or not well understood. This can be particularly challenging in populations that may use herbal medicines in conjunction with conventional medicine, as it can be difficult to determine the cause of adverse events.

- **Cultural and linguistic barriers:**

Herbal medicines are often used in traditional medicine systems that are specific to certain cultures, and the terminology used to describe these medicines may not be easily translatable or recognizable to those outside of the culture. This can make it difficult to collect and interpret data on the safety and efficacy of herbal medicines.

- **Limited regulation:**

Herbal medicines are often classified as dietary supplements rather than drugs, and therefore are subject to less stringent regulation than pharmaceutical drugs. This can make it difficult to ensure the safety and efficacy of these products.

- **Lack of standardized reporting:**

There is no standardized system for reporting adverse events associated with herbal medicines. This can make it difficult to collect and analyze data on the safety and efficacy of these products.Overall, herbal pharmacovigilance requires a multidisciplinary approach and collaboration between different stakeholders, including researchers, healthcare providers, regulatory agencies, and the public.

METHODS IN PHARMACOVIGILANCE:

1. **Passive Surveillance.**
2. **Stimulated Reporting.**
3. **Active Surveillance.**
4. **Comparative Observational Studies.**
5. **Targeted Clinical Investigations.**
6. **Descriptive studies.**

1. **Passive Surveillance:**

- **Spontaneous Reporting:**

The primary method of collecting data for international pharmacovigilance is spontaneous

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reporting, which relies on healthcare practitioners to recognize and report any suspected adverse drug reactions (ADRs) to their national pharmacovigilance center or to the manufacturer. The majority of the time, spontaneous reports are provided voluntarily. Following the launch of a medicine, spontaneous reports are crucial in identifying safety flags. Unexpected reports provide warnings of uncommon adverse occurrences that were missed by prior clinical trials or other pre-marketing investigations. Additionally, it offers crucial details on risk groups, risk factors, and clinical traits of recognized significant ADRs. [11,12]

Case series:

A case report is a warning from a professional about a patient who has a problem that is thought to be caused by drugs. It can be a warning indicator when numerous clinicians independently report the same unanticipated adverse medication reactions. Anaphylaxis, aplastic anemia, toxic epidermal necrolysis, and Stevens-Johnson syndrome are only a few of the different side effects that are known to be more frequently linked to medication therapy.

2. Stimulated Reporting:

Stimulated reporting is a technique used to encourage and facilitate the reporting of adverse events by health professionals based on a pre-designed methodology in particular circumstances (for example, in-hospital settings) for new goods or for brief periods of time. Online reporting of negative incidents is one of these approaches.

Early Post-Marketing period Vigilance, or EPPV in Japan, is an example of how firms can employ stimulated adverse event reporting in the early post-marketing period to inform healthcare professionals about new medications and offer safety information before the general public uses them.

3. Active Surveillance:

Active surveillance, as opposed to passive surveillance, uses an ongoing, pre-planned method to fully identify the number of undesirable events. Active surveillance refers to the monitoring of patients receiving a certain medication as part of a risk management strategy.

- **Sentinel sites:**

In order to ensure complete and reliable data on reported adverse events from these sites, active monitoring can be performed by reviewing medical records or questioning patients and/or clinicians in a sample of sentinel sites. When compared to a passive spontaneous reporting method, the chosen sites can offer information data from certain patient groupings.

Sentinel sites have many drawbacks, including selection bias issues, patient shortages, and higher expenses. For those medications used mostly in institutional settings, such as hospitals, nursing homes, dialysis facilities, etc., active surveillance with sentinel locations is most effective.

- **Drug event monitoring:**

Patients are typically identified in medication event monitoring via electronic prescription data or automatically generated health insurance claims. a follow-up survey emailed to each prescribing doctor or patient at certain intervals to gather information on the results.

The questionnaire can ask about patient demographics, treatment indications, therapy duration, dose, clinical events, and reasons for discontinuation. This allows for the collection of more comprehensive data on adverse occurrences from a large number of doctors and/or patients.

- **Registries:**

A registry is a list of patients who share a certain characteristic or characteristics. A disease (disease registry) or a particular exposure (drug registry) can both fit this description. These registries can be used to prospectively gather a variety of data using standardized questionnaires. Drug exposure information can be gathered through disease registries for conditions like blood dyscrasias, severe cutaneous reactions, and congenital deformities.

4. Comparative Observational Studies:

An important aspect of the evaluation of adverse events is the use of conventional epidemiologic methodologies. It is possible to validate signals from unprompted reports or case series using a variety of observational study approaches.

Cross-sectional studies, case-control studies, and cohort studies (both retrospective and prospective) are the main varieties of these designs.

- **Cross-sectional study (survey):**

A cross-sectional study is one that gathers information on a group of patients at one point in time (or interval of time), regardless of exposure or

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disease condition. These investigations are typically conducted to collect information for surveys or ecological analyses.

- **Case-control study:**

Case-control studies are particularly useful when the goal is to investigate whether there is an association between a drug and one specific rare adverse event, as well as to identify risk factors for adverse events.

- **Cohort study:**

When it is necessary to understand the incidence rates of adverse events in addition to the relative risks of adverse events, cohort studies can be helpful. In a cohort study, many adverse events may also be researched utilizing the same data source. A cohort study tracks the development of the disease through time in a group that is at risk for it. Each patient's follow-up period includes the collection of exposure status data, which is used to determine incidence rates.

5. Targeted Clinical Investigations:

Targeted clinical studies can be carried out to look into possible drug-drug and food-drug interactions based on the pharmacological characteristics and predicted use of the drug in general practise. These studies consist of medication concentration monitoring in patients and healthy volunteers as well as population pharmacokinetic research.

Due to small sample sizes or the absence of certain patient subpopulations from these clinical studies, it is sometimes possible to identify potential hazards or unexpected benefits in certain populations from pre-approval clinical trials, although these effects cannot always be properly quantified. Drugs may be metabolized differently in children, the elderly, and patients with co-morbid diseases than in patients who are generally included in clinical trials. Additional clinical trials could be used to gauge the size of the risk (or benefit) in such populations..

6. Descriptive studies:

Descriptive studies are a crucial part of pharmacovigilance, but they cannot be used to identify or confirm adverse events linked to medication exposure.

These studies are generally used to establish the prevalence of drug use in particular communities as well as the background rate of outcome occurrences.

- **Natural disease history:**

Epidemiology was once primarily concerned with determining the incidence and prevalence of prospective outcomes of interest, as well as the natural history of disease, including the characteristics of ill people and the distribution of disease in certain groups.

- **Drug utilization study:**

Drug usage studies (DUS) evaluate a drug's marketing, prescribing, and use in a community and how these aspects affect clinical, social, and financial results. These studies include information on certain groups of people, such as the elderly, kids, or those with hepatic or renal impairment, and are frequently stratified by age, gender, concurrent medications, and other factors.

WHO GUIDELINES ON SAFETY MONITORING OF HERBAL MEDICINES IN PHARMACOVIGILANCE SYSTEMS:

Herbal medicine safety is a significant public health concern. The policy emphasizes: l The necessity of procedures for pharmacovigilance systems to monitor the safety of herbal medicines; l Standard definitions of words used in pharmacovigilance and safety monitoring of herbal medicines. 1 Difficulties in assessing the efficacy of herbal remedies Effective safety monitoring requires effective communication. With the help of these recommendations, member states can more easily regulate herbal medicines and other goods used in traditional medicine. The following topics are covered: classification of herbal medicines; minimal standards for evaluating their safety; minimal standards for evaluating their effectiveness; quality assurance of herbal medicinal products; pharmacovigilance of herbal medicinal products; and regulation of their marketing. The recommendation helps governments establish requirements for the registration and regulation of herbal medicines by acting as a guide. The current pharmacovigilance models and techniques were created in connection to synthetic drug use. Modifications to current methods, patient reporting, and increased consideration of pharmacogenetics and pharmacogenomics in maximizing the safety of herbal medications are all potential improvements in safety monitoring of herbal medicines. For the purpose of ensuring the quality, safety, and efficacy of traditional medicine, there aren't any widely accepted standards of quality control or suitable evaluation techniques. The following actions can be

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taken to put in place an efficient pharmacovigilance system.

Step 1: Planning the Pharmacovigilance Phase Step.
Step 2: Establishing a culture of notification.
Step 3: Debriefing, interaction, and training.
Step 4: Establishment of reporting methods.
Step 5: Documenting and identifying the composition of herbal medications.
Step 6: Examining the case reports.
Step 7: Data analysis.
Step 8: Data handling.
Step 9: Last reporting to advisory or regulatory committee.
Step 10: Data upkeep.
Step 11: Reporters receive feedback.
Step 12: Sharing risk information among reports, pharmacovigilance canters, UMCs, and the general public.
Step 13: Information Publication As significant safety information becomes available and milestones are met, the pharmacovigilance plan should be updated often. [13]

CURRENT SCENARIO:

Pharmacovigilance in India was reinitiated by the Government of India by launching the National Programme of Pharmacovigilance (NPP) with the support of the World Bank in November 2004, and started functioning 1 January 2005. The National Pharmacovigilance Center (NPC) at the Central Drugs Standard Control Organization (CDSCO) coordinated the countrywide pharmacovigilance programme under the aegis of the Ministry of Health and Family Welfare, New Delhi, and the programme was directed by the National Pharmacovigilance Advisory Committee (NPAC). The programme had three main objectives: to foster a reporting culture, to involve a large number of HCPs in the system for the dissemination of information, and to be a benchmark for global drug monitoring [14]. Two zonal, 26 peripheral and five regional centers were established. These canters were responsible for collating the information about adverse drug events from all over the country. The zonal centers submitted these reports to the CDSCO as well as to the UMC in Sweden [15]. However, the programme did not meet expectations, and in 2009, it was temporarily suspended, as the support from the World Bank was discontinued [16]. The need for a robust pharmacovigilance system for safeguarding public health was soon realized by the regulatory authorities, and the NPP was renamed the Pharmacovigilance Programme of India (PvPI), which started functioning 14 July 2010, with the All-India Institute of Medical Sciences (AIIMS), New Delhi, as the National Coordination Centre (NCC). In order to monitor ADRs all over India, the programme had 22 ADR monitoring centers (AMCs), including AIIMS, New Delhi. The NCC was later shifted from AIIMS to the Indian Pharmacopoeia Commission (IPC), Ghaziabad, on 15 April 2011, for effective implementation of the programme, with the main aim of generating independent data on the safety of drugs to match the global drug safety monitoring standards. Because pharmacovigilance was considered to be a programme that monitors prescriptions for adverse drug events and medication errors, some clinicians were apprehensive about it, as they felt that their capabilities were being doubted [17]. The PvPI is striving hard to overcome this challenge of apprehension and to eliminate the reasons for underreporting [18] by way of conducting several continued medical education, awareness and training programmes for HCPs on a regular basis to educate them on and inculcate the habit of reporting of ADRs.

The HCPs have been made aware that no legal action is implicated in reporting ADRs. s. The following are the objectives of the programme [19]:

- To create a nationwide system for patient safety reporting.
- To identify and analyse new signals from the reported cases.
- To analyse the benefit–risk balance of marketed medications.
- To generate evidence-based information on the safety of medicines.
- To support regulatory agencies in the decision-making process on the use of medications.

The programme resurged within a span of 5 years and exhibited impressive performance at the international level, including ADR reporting and providing skill development. During 2017, the PvPI conducted six skill development programmes; around 276 HCPs have acquired basic knowledge and adequate skills in pharmacovigilance. The participants were pharmacists (70%), doctors (10%) and regulators and nurses (20%). At present, about 250 AMCs have been established in government and private hospitals, medical colleges and pharmacy colleges all over India, establishing a

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framework of pharmacovigilance and developing a culture of reporting in India [20]

FUTURE STRATEGIES:

India needs to integrate traditional herbal medicine into its national healthcare system. Traditional herbal therapy is acknowledged formally and integrated into all facets of healthcare delivery in an integrative system. This means that traditional herbal therapies should be offered at hospitals and clinics (both public and private), and that treatment with traditional herbal therapies should be covered by health insurance. It also means that all herbal medicine providers and products must be registered and regulated. The following tactics can be developed for the execution of a successful pharmacovigilance programme for herbal and conventional medicines:

1. The bearer of the Traditional Herbal Registration must teach patients on the safest and most efficient ways to use traditional herbal remedies. In order to decide what steps, if any, are required to improve the safe use of medicines, regulatory agencies will be able to assess the risks and benefits of medications with the aid of this data.
2. Holders of Traditional Herbal Registrations should include a concise description of the pertinent facts as well as a critical assessment of the product's risk-benefit ratio in light of new or evolving information. This assessment will determine whether additional research is necessary and whether the registration and product information need to be updated.
3. Standard words and definitions should be created for a classification and/or coding system for herbal medications.
4. To fully understand the pharmacogenetics and pharmacoepidemiology of herbal medications, pertinent study must be conducted. Grants for research and financial incentives will promote education in the area of conventional herbal medicine.
5. To increase capacity for monitoring herbal medicines at national pharmacovigilance centers, staff must be trained in pertinent technical areas, facilities for product analysis must be made available, and access to trustworthy information must be made available.

ROLE OF ARTIFICIAL INTELLIGENCE IN PHARMACOVIGILANCE:

The capacity of a machine to accomplish tasks that need human intelligence is known as artificial intelligence (AI). AI is the use of machines to solve problems that will happen in the future by introducing learning technologies to the machines with the aid of data gathered in the past. Randomization of patients is made easier by AI, which also improves the success rate of clinical trials. The three biggest global health burdens—diabetes, cancer, and retinopathy—have all been improved by AI in terms of early detection, mitigation, and treatment. PV data is crucial in confirming the safety of currently available medicinal devices. It is anticipated that the PV data would be of higher accuracy and quality once AI has implemented it.

Three categories can be used to categorize AI: rule-based static systems, AI-based static systems, and rule-based static systems with automated outcomes (supervised machine learning, natural language processing). c) Dynamic rule-based system: New updated data (New ICSRs) for future use. The PV validation framework's validation framework was based on rules, and the GMP validation framework was based on AI. The intelligent automation system had to be categorized due to the inadequate validation framework of existing technologies. AI is employed to enhance human intellect on the basis of a rule-based static system [21].

The use of AI in pharmacovigilance has become increasingly important in recent years, as it can provide more accurate and efficient ways of detecting adverse drug reactions (ADRs) and other drug-related problems.

Here are some of the roles of AI in pharmacovigilance:

1. **Detection of ADRs**: AI can analyze large volumes of data from various sources, such as electronic health records, social media, and scientific literature, to identify potential ADRs. This can help pharmacovigilance teams to detect ADRs more quickly and accurately, and take appropriate actions to mitigate risks associated with the use of the drug.
2. **Signal detection**: AI algorithms can help identify potential safety signals from large datasets, which may otherwise go unnoticed using traditional pharmacovigilance methods. This can help pharmacovigilance teams to prioritize their investigations and take proactive measures to minimize the potential harm caused by a drug.

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3. **Risk assessment**: AI can assist in the risk assessment of drugs by providing valuable insights into the potential harm associated with a drug. It can also help in identifying high-risk populations who may be more susceptible to adverse events.
4. **Post-marketing surveillance**: AI can be used to monitor drugs after they have been approved for marketing. This can help identify any emerging safety concerns and enable pharmacovigilance teams to take appropriate actions to mitigate risks associated with the use of the drug.
5. **Pharmacovigilance automation**: AI can automate many of the manual processes involved in pharmacovigilance, such as data entry, data cleaning, and case processing. This can save time and reduce the risk of errors, allowing pharmacovigilance teams to focus on more critical tasks.

Overall, AI has the potential to transform the field of pharmacovigilance by providing more accurate, efficient, and timely detection and assessment of ADRs and other drug-related problems.

Fig. 2: Role of Artificial Intelligence in Pharmacovigilance.

BENEFITS OF APPLYING ARTIFICIAL INTELLIGENCE TECHNIQUES IN PHARMACOVIGILANCE:

- In terms of machine learning (ML), supervised learning, which is used in PV for ICSR processing, can teach ML algorithms where the ground truth is a human-annotated answer file, whereas unsupervised learning, which has no ground truth, is used for signal management.
- Improve searcher comprehension using semantic search.
- Identify text in scanned documents using optical character recognition (OCR), which can also be used to check handwriting on text.
- Chabot: Use NLP to perform human conservation through text or audio methods.
- Text mining is the process of structuring unstructured text to analyse acquired data from resources as evidence.

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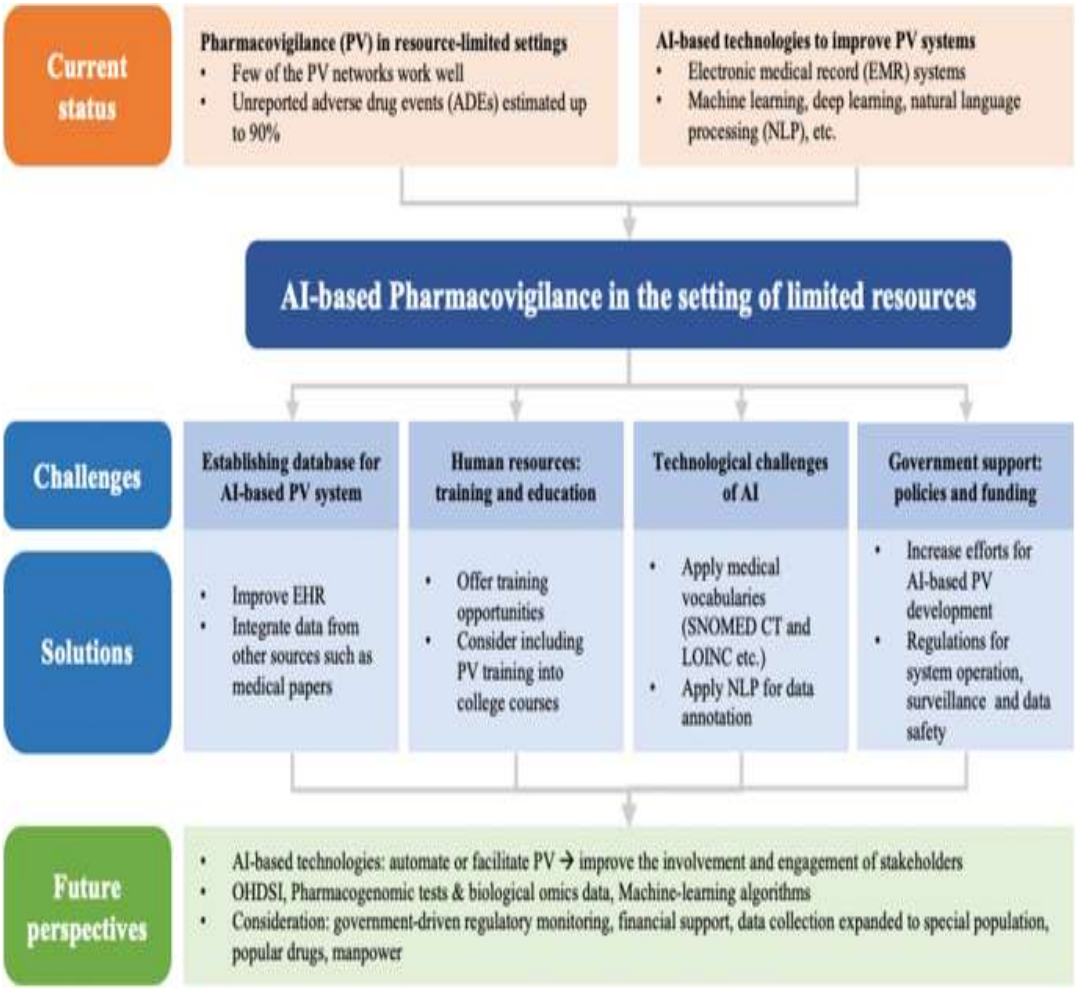

Fig. 3: The key points of ArtificialIntelligence (AI)based pharmacovigilancein resource-limited settings.

II. CONCLUSION:

Pharmacovigilance's goal is to identify, evaluate, and comprehend any negative effects or other potential drug-related issues associated with herbal, conventional, and complementary treatments in order to prevent them. To gather data on potential adverse drug reactions (ADRs) associated with herbal medications, modified spontaneous reporting forms are to be created using the WHO template. The ultimate goal is to provide patients with safer and more effective treatment options. This review seeks to offer a thorough and critical overview of the state of pharmacovigilance for herbal medications at the local, national, and international levels. This paper examines the complex issues surrounding herbal pharmacovigilance while taking into account recent developments and offers suggestions to enhance safety monitoring in the future The use of AI in pharmacovigilance has become increasingly important in recent years, as it can provide more accurate and efficient ways of detecting adverse drug reactions (ADRs).

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