**PHARMACOVIGILIANCE OF HERBAL & TRADITIONAL SYSTEM**

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Pharmacovigilance is an important & integral part of clinical research. Pharmacovigilance is defined as a the pharmacological sciences relating to detection , assessment ,understanding & prevention of adverse effects particularly long term & short term adverse effects of medicine . Pharmacovigilance is the process of monitoring the safety of medicines.

Global Pharmacovigilance of herbal medicines Pharmacovigilance monitors and acts in case of adverse reactions related to drugs or medicines in the market (Fig. 3). Different agencies in different countries work in Pharmacovigilance. Today, when we have so many communication facilities, we must report the benefits and harmful effects of the treatments given by health practitioners. There are certain portals worldwide where reporting can be done to bring the side effects or adverse reactions. To encourage appropriate monitoring of drugs, the World Health Organization (WHO), US Food and Drug Administration (FDA), and European Medicines Agency (EMA) developed Pharmacovigilance laws 29, 35,36. FDA launched a national electronic system named “Sentinel Initiative” in May 2008 to monitor the safety of FDA-regulated products including pharmaceuticals, vaccines, biopharmaceuticals, and healthcare products. Pharmacovigilance of herbal medicine is also a section in the overall Pharmacovigilance of medicines

**The important purpose of Pharmacovigilance programme are:**

* To patient care
* To provide medicines & all medical and paramedical services staff.
* To improve public health services.
* To support understanding, educating & clinical training in Pharmacovigilance
* To asses benefit, risk & effectiveness of medicines.
* To support effective communication to health care professionals & the public.

There are various methods to identify the problem related to use of medicines. The prescription events monitoring & careful review of adverse drug reaction in hospitalization patients & patients discharge from the hospital covered under the active Pharmacovigilance.

Passive Pharmacovigilance depends mainly on spontaneous reporting. During clinical practice the heath care professionals are supposed to report the adverse reaction to Pharmacovigilance.

**The major and well known limitation of spontaneous reporting are :**

Under reporting

Lack of information

Biased reporting

With all these limitation this methods still used throughout the word because it has relevance on suspicion of ADRs sent by clinicians & substituent analysis of the reports by physicians ,clinical pharmacologist ,practicing pharmacist.

Herbs are part of the plants which are used for their flavor fragrance, dietary supplements, and

Therapeutic purposes. People can obtain them either prescribed by a healthcare provider or over the counter. Nowadays, online purchases in the form of powders, capsules, extracts, dip sachets, and direct parts of the plant in the form of dried or fresh parts are also available. For therapeutic purposes or dietary supplements, people have used a variety of flora present in their geographical conditions for different ailments in the past and made these herbs an integral part of their lifestyle.

The World health organization (WHO) has suggested moving towards traditional medicinal

Practice that primarily involving herbs or plants, or mineral products. These suggestions have inspired most developing countries to explore traditional practices, and recently such practices have increased tremendously. The WHO launched the 13th General Program of Work (GPW13) to ensure healthy lives and promote well-being for all age groups with the help of traditional and complementary medicine.

**The system of managing a healthy lifestyle & the treatment**

The traditional system of medicine (TSM) includes Ayurveda, Siddha, Homeopathy,Unani, Yoga, and Naturopathy. Ayurveda has been practiced worldwide.

**Traditional system follow**

 **Traditional system of**

 **medicines**

 **Ayurveda**

 **Siddha**

**Naturopathy**

 **Yoga**

 **Homeopathy**

 **Unani**

Herbs are used commonly in Ayurveda and it is an ancient system of a healthy lifestyle in India by following natural ways.

**Food is medicine interventions**

Food is medicine interventions include medically tailored meals (also called therapeutic meals), medically tailored groceries (sometimes known as food “farmacies” or healthy food prescriptions), and produce prescriptions. Various spices and flavouring agents from plants are incorporated into Indian cooking. Like ginger, which is added to impart flavour to food, also improves cardiovascular health by providing antioxidant, Antinflammatory, and rheumatologic benefits. Garlic helps to regulate cholesterol, improves blood circulation, and has antimicrobial properties. Similarly, ginger is considered for treating gastrointestinal disorders, and helps to minimize cardiovascular diseases and diabetic risks.

**Natural remedies for the treatment of infectious and non-infectious disorders**

Saponin is also useful for the treatment of tumour. A mix of these medicines is also used in combinatorial therapy by combining these drugs in different doses. Nigella sativa inhibits the warfarin metabolism and when taken together, they can have potential food drug interactions.

**Preparation and formulation of herbal medicine**

Ayurvedic preparations are nature-based and prepared from herbal or medicinal plants. Natural compounds beneficial for therapeutic purposes can also possess heavy metal ions. These ions pose nephrotoxic risks. For example, different plants like Artemisia herbaalba, Glycyrrhiza glabra, Euphorbia paralias, and Aloe vera used for treatments are involved in nephrotoxicity.

**Scope of Pharmacovigilance**

Interaction of medicines

Adverse drug reaction reaction

Lack of efficacy

Medication error

Substandard medicines

Pharmacovigilance

Abuse misuse of medicines

Pharmacovigilance covers not only the conventional medicines but beyond these. These include herbal medicine other complementary product, biological product, vaccines,& possible medical devices.

**Product covered by Pharmacovigilance**

MEDICINES

Traditional & complementary

Herbals

Biological

Blood product

Medical devices

 Vaccines

**What is to be monitored?**

 Adverse reactions.

Medication error.

Case reports of acute and chronic poisoning (toxicity).

 Abuse and misuse of medicines.

Adverse interactions of medicines with chemicals, other medicines and food.

**Pharmacovigilance system**

With the purpose of developing a set of indicators to monitor or evaluate Pharmacovigilance system it is essential to understand its operation. As on date the spontaneous reporting system is considered as the basic of global Pharmacovigilance. For the purpose the systematic collection analysis of the report of suspected ADRs are required

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**What information should be in the report?**

Any suspected adverse drug reactions (ADRs)/adverse events (AEs) associated with the use of herbal/traditional medicines and other factors affecting product safety should be reported.

The report should contain information on the following elements:

**Patient information:**

Identification of the patient/consumer with appropriate confidentiality needs to be provided in order to avoid duplications and to facilitate follow-up.

Age, sex and a brief medical history.

Risk factors,e.g. age, impaired renal function, previous exposure to the herbal medicine(s) concerned, previous allergies, drug misuse or abuse.

**Product information:**

Details of suspected herbal/traditional medicine products if known: species name (Latin binomial name and common vernacular name of medicinal plant) and/or brand or ingredient name(s), part of medicinal plant used, preparation methods; manufacturer, country of origin, batch number, expiry date and provider.

Administration details: dose and quantity supplied, dosage form, route, start/stop dates, and indication or reason for use.

All other medicines used (including self-medication), with administration details.

**Adverse drug reaction/adverse events information**: Date of onset (or duration from first administration to onset of event), description with symptoms and signs, severity and seriousness, results of clinical investigations and tests, course and outcome, and

 **Reporter information:** Name and address (to be considered confidential and to be used only for data verification, completion and case follow-up)

**What does PV centre do after receiving the report?**

Conduct individual case safety report (ICSRs) assessment while classifying its severity and suggesting regulatory actions and feedback to the reporter.

Conduct signal detection by analyzing and assessing the case report in its database and assessment (case series).

 Propose risk minimization tools, if needed.

 Do risk communication at national and international level, when signal is detected.

 The causality assessment can be carried out using any appropriate assessment method for herbal and traditional medicine products.

Categorize ICSRs into non-serious and serious categories. The serious adverse drug reactions (ADRs) and adverse events (AEs) will be further subcategorized such as death, life-threatening, hospitalization or prolongation of existing hospitalization, persistent or significant disability/incapacity, or congenital anomaly/birth defect

After detecting signal, PV centre has to inform the concerned National Regulatory Authority (NRA) to take appropriate regulatory action including risk management and communication such as withdrawing products from the market, adding warnings, amending labeling or packaging, restricting prescribing criteria or use as per the evidences received.

**Communication network of Pharmacovigilance (PV)**

MASS MEDIA

CONSUMERS/PATIENTS

NATIONAL REGULATORY AUTHORITY

 OTHER

**NATIONAL PHARMACOVIGILANCES CENTRE**

MANUFACTUR

**Why is it challenging to do pharmacovigilance for traditional medicine products?**

Complexity of herbal product:

 (1) Lack of clinical trial data: Unlike conventional medicines, systematic clinical trial data for many herbal and traditional medicine products is not always available. A license can be issued based on the history of medicinal use. It is difficult to obtain safety and efficacy data on the herbal product.

(2) Chemical complexity: Herbal and traditional medicine remedies and preparations are chemically rich complex mixtures comprising several hundreds of constituents. The effects are likely to be attributed to a group of related constituents rather than a single constituent.

(3) Non-uniformity (products not standardized): The profile of constituents is often not uniform throughout a plant and certain parts of the plant can be toxic. The precise profile of constituents is likely to vary between different batches of herbal materials, and factors such as environment, time of harvesting, storage, processing and drying can affect their variability. This makes it difficult to determine pharmacokinetics, pharmacodynamics and toxicology, and to establish which ingredient causes a safety concern.

(4) Quality assurance and control: Unlike conventional pharmaceutical products, herbal and traditional medicines are prepared from materials of herbal origin which are often obtained from various geographical and commercial sources, resulting in uncertain condition. Furthermore, procedures and techniques used in its manufacturing and quality control measure are often very different from those used for conventional medicines.

 (5) Lack of technical expertise and facilities and manpower to analyse the problem, particularly in identifying substandard, adulterated and contaminated, wrong medicinal plants, which is a common problem with traditional medicine products.

(6) Possible interaction between different traditional medicine products and with allopathic medicines and foodstuffs.

 **Difference in product regulation** on categorizations of herbal/traditional medicine.For instance, a herbal product in one country can be classified as a dietary/food supplement in another without any health claim.

 **Insufficient information and lack of access to reliable information** support such as product name, part use, etc., for analyzing the products concerned.

**Botanical nomenclature:** The nomenclature of crude plants is not consistent. In many texts the names are in Latin, consisting of two parts, one related to the scientific name and the other indicating the plant part, e.g. digitalis folium. Misleading and inconsistent names are commonly used.

**Safety monitoring:** Many health-care providers are not trained on safety monitoring of medicines including traditional medicine(Pharmacovigilance methods),which results in underreporting or zero report.

**How can Pharmacovigilance for herbal and traditional medicine be improved?**

* Networking should cover health facilities (traditional medicine practitioners), manufacturer, drug store (pharmacists) and consumer.
* Harmonize regulations for herbal/traditional medicine products among Member States.
* Proactive Pharmacovigilance through the product life cycle is the way forward and the future direction for drug safety. For instance, the regulatory system should have a mechanism to collect safety data before marketing approval and after marketing. !
* TRM practitioners should participate in causality assessment process and they should be trained on causality assessment. ! PV should be integrated into curriculum of medical education.
* PV should be integrated into good pharmacy practices (GPP) in community pharmacy.
* Use of modern technology and its development through IT facilities and mobile application tools should be encouraged.
* The exact scientific name of the plant, the plant part used and the name of the manufacturer should be included in the ADR report on herbal medicines.
* Regular training programmers for strengthening national capacity in monitoring the safety of traditional medicine products and for promoting awareness should be encouraged.
* It would be better to start early with the professional training of health-care students to create a culture of reporting ADRs.
* National quality specification and standard for herbal materials (selection, sampling, testing of plant material, stability studies), GMP, labeling, and licensing schemes for manufacturing, imports and marketing should be mandatory.

List of the unapproved Ayurvedic medicinal products found on the Canadian market thus far, which have been analyzed by Health Canada and found to contain high levels of lead, mercury, and arsenic, are as follows:

* Karela tablets, produced by Shriji Herbal Products, India
* Karela capsules, produced by Himalaya Drug, India
* Karela capsules, produced by Charantia, UK (specifically batch #12011)
* Maha Sudarshan Churna powder, produced by Zandu Pharmaceuticals, Mumbai, India
* Maha Sudarshan Churna powder, D and K Pharmacy, Bhavnagar, India
* Maha Sudarshan Churna powder, produced by Chhatrisha, Lalpur, India
* Maha Sudarshan Churna powder, produced by Dabur India, New Delhi, India
* Safi liquid, produced by Hamdard-WAKF-Pakistan
* Safi liquid, produced by Hamdard-WAKF-India
* Yograj Guggul tablets, produced by Zandu Pharmaceuticals, Mumbai, India
* Sudarshan tablets, produced by Zandu Pharmaceuticals, Mumbai, India
* Shilajit capsules, produced by Dabur India, New Delhi, India