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PHARMACOVIGILANCE TOWARDS SAFETY APPROACH FOR AYURVEDIC DRUGS: A NARRATIVE OVERVIEW

Sachin S. Mali*[1], Poonam V. Patil[1], Prasad V. Patrekar[1], Amita A. Ahir[1], Shweta S. Nazare[1], Sachin S. Salunkhe[2]

[1]Department of Pharmaceutics, Adarsh Institute of Pharmacy, Vita, 415 311, Maharashtra, India.
[2]Department of Quality Assurance, Bharati Vidyapeeth College of Pharmacy, Kolhapur, 416 013, Maharashtra, India.

***Correspondence for Author: Sachin S. Mali**

Department of Pharmaceutics, Adarsh Institute of Pharmacy, Vita, 415 311, Maharashtra, India.

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ABSTRACT

India is the largest country in the world where more amount of ayurvedic system is used traditionally. The tendency of population towards ayurveda is straight forward that is ayurveda medicine doesn't have any harmful effect on animal or human body. So by seeing this approach towards ayurveda it is necessary to incorporate new system towards safety which is known as Pharmacovigilance (PV). There will be the need of improvement of awareness towards safety use of ayurvedic formulations. PV is a demanding science offering great opportunities for reducing harm to patients and costs to healthcare systems. From small beginnings, with the right knowledge and skills, PV can make an important contribution to the health of the nation. Adverse drug interactions (ADR) reporting is an important aspect of post marketing surveillance. In this review we have focused on the ADR from herbals, also Indian status for PV, Need of PV, PV method and Home message. Recently we have invented the GREEN CARD which is new concept in PV in India for reporting any adverse effect from ayurvedic formulation. This report we made independently which will ideal for every PV centres in India.

KEY WORDS: PV, ADRs, PV methods, GREEN CARD etc.

INTRODUCTION

"PHARMACOVIGILANCE" The science and activities relating to the detection, evaluation, understanding and prevention of adverse drug reactions or any other drug-related problems.[1]

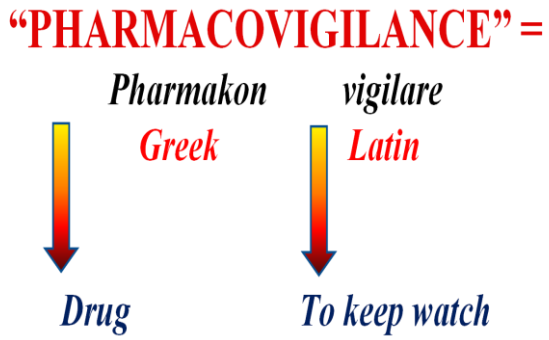


Fig.1. PV

The purpose of Pharmacovigilance is to detect, assess, and understand, and to prevent the adverse effects chemical drugs, but extended to herbal, traditional, and complementary medicines, biologicals, vaccines, blood products. India is the largest country in the world where more amount of ayurvedic system is used traditionally.

The tendency of population towards ayurveda is straight forward that is ayurveda medicine doesn't have any harmful effect on animal or human body. So by seeing this approach towards ayurveda it is necessary to incorporate new system towards safety which is known as PV. There will be the need of improvement of awareness towards safety use of ayurvedic formulations.

More and More Countries are Regulating Herbal Medicines.[1]

Fig.2. Countries those Regulates Herbal Medicines

Aim of PV[1,2,3]

- To improve patient care and safety in relation to the use of medicines, and all medical and paramedical interventions
- To improve public health and safety in relation to the use of medicines
- To contribute to the assessment of benefit, harm, effectiveness and risk of medicines, encouraging their safe, rational and more effective use
- To promote understanding, education and clinical training in Pharmacovigilance and its effective communication to health professionals and the public.

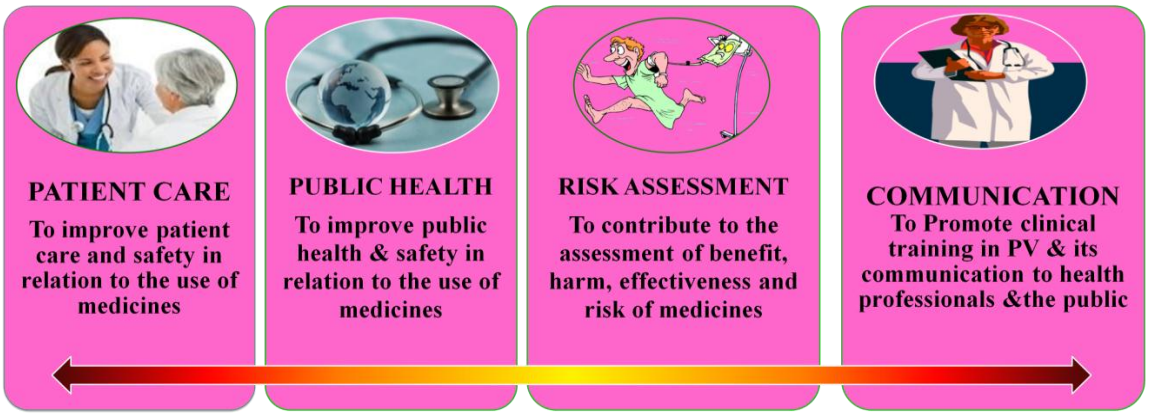


Fig. 3. Aim & Objectives for Pv

Challenges in introducing PV[1,2]

Herbal medicines in Europe come from all traditions including Chinese, Indian, north and south American and African systems as well as that of European systems. This diversity adds to the challenges of herbal pharmacovigilance including basic questions such as defining the most appropriate herb naming system (botanical, common, pharmaceutical name or herbal drug name) and validation of the botanical identity of the herbal ingredients.

- NPP encouraged reporting of all suspected ADRs, But number of reports related to Ayurvedic /herbal drugs are abnormally low.
- Concept & terminologies related to ADR monitoring are not covered in the Ayurvedic curriculum.
- Methods to study drug safety problems have not evolved adequately in Ayurveda.
- Information related to medicines are in the form of slokas in the texts, it is not easily available for general public.
- Signal detection is difficult because of inherent belief that Ayurvedic medicines are safe.
- Patients often use medicines from different systems of medicine concomitantly - difficulty in assigning causality.
- Lack of quality assurance and control in manufacture of Ayurvedic medicine.
- Most Ayurvedic formulations are multi-ingredient.

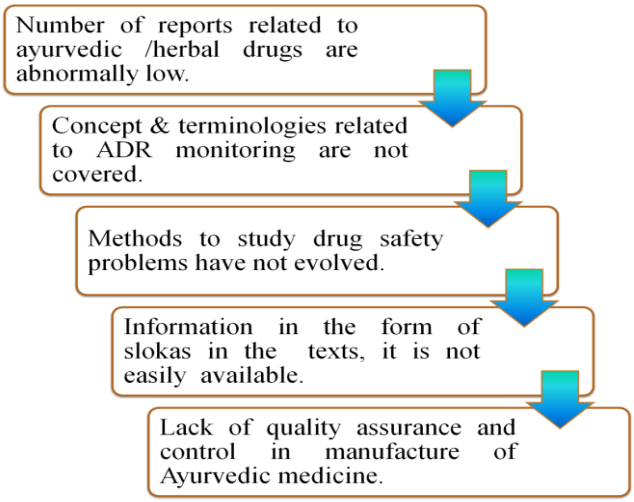


Fig. 4. Challenges in introducing PV

Adverse Drug Reactions (ADRs)[4,5,6]

Any response to a drug which is noxious and unintended and which occurs at doses used in man for prophylaxis, diagnosis or therapy.

Examples of highly toxic herbs include

Fig. 5. *Datura stramonium*

Datura stramonium is a highly effective treatment for asthma symptoms when smoked, because it contains atropine, which acts as an antispasmodic in the lungs. However, overdoses of the tropane alkaloids in it can result in hospitalization or death.[1,2]

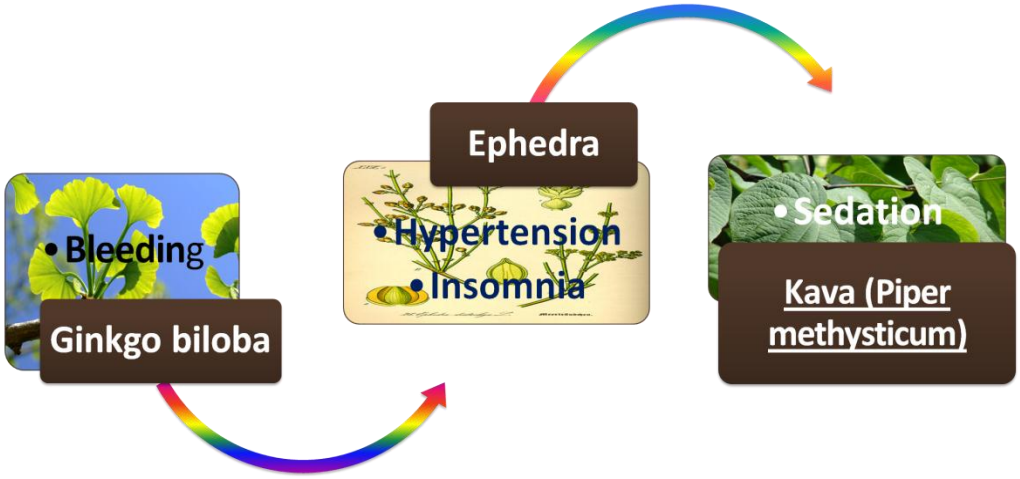


Fig. 6. Toxic herbs

- Poison hemlock and nightshade. They are not marketed to the public as herbs, because the risks are well known, partly due to a long and colorful history in Europe, associated with "sorcery", "magic" and intrigue.
- A case of major potassium depletion has been attributed to chronic liquorice ingestion., and consequently professional herbalists avoid the use of liquorice
- Black cohosh has been implicated in a case of liver failure.
- Examples of herbs where a high degree of confidence of a risk long term adverse effects can be asserted include ginseng, which is unpopular among herbalists for this reason, the endangered herb goldenseal, milk thistle, senna, against which herbalists generally advise and rarely use, aloe vera juice, buckthorn bark and berry, cascara sagrada bark, saw palmetto, valerian, kava, which is banned in the European Union, St. John's wort, Khat, Betel nut, the restricted herb Ephedra, and Guarana.

Who Reports PV Centre's?[1,6,7]

- Physicians
- Pharmacists
- Pharmaceutical companies qualified persons – (Pharmacovigilance/Regulatory manager)
- Investigational products (clinical trials)
- Post-approval reporting – Individual Case Safety Report (ICSR), Periodic Safety Update Report (PSUR)
- In many countries patients are encouraged (but not obligated) to report side effects

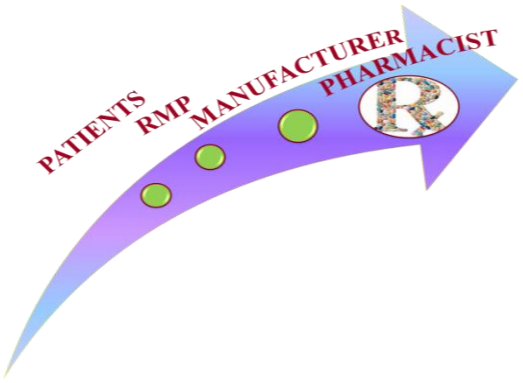


Fig. 7. Flow chart for reporting PV

What to Report[1,7,8]

- It is important to report serious unexpected ADRs.
- Most cases of unexpected ADRs are associated with medicines newly introduced on the market.
- All suspected adverse reactions.
- Every single problem related to the use of a drug.
- ADRs associated with radiology contrast media, vaccines, diagnostics, drugs used in traditional medicine, herbal remedies, cosmetics, medical devices and equipment.

WHAT HAPPENS TO SUBMITTED PV Reports[1,8,9]

The information in the form shall be handled in confidentiality. Peripheral Pharmacovigilance Centres shall forward the form to the respective Regional Pharmacovigilance Centres who will carry out the causality analysis. This information shall be forwarded to the National Pharmacovigilance Resource Centre. The data will be statistically analysed and forwarded to the Dept. of AYUSH, Govt. of India.

Fig. 8. SUBMITTED PV Reports

PPC: Peripheral Pharmacovigilance Centre's
RPC: Regional Pharmacovigilance Centre's
NPRC: National Pharmacovigilance Resource Centre
AYUSH: Ayurveda, Yoga & Naturopathy, Unani, Siddha & Sowarigpa and Homeopathy.

RESPONSIBILITIES OF CENTRE'S[9,10,11]

- To collect ADR reporting
- To fill in the ADR form properly
- To forward duly-filled in ADR forms to next higher level centre
- To maintain a log of all ADR notification forms (blank or filled)
- To identify, induce PPC / RPC (with concurrence of NPRC - ASU), provide them with general technical support,coordinate and monitor their functioning
- To identify and deploy a pharmacologist for management of pharmacovigilance tasks
- To identify and deploy a data manager for data management
- To carry out (or review) causality analysis of all ADR forms or review such analysis by the RPC
- To forward all duly-filled ADR forms as per pre-determined time line i.e. first week of every month Information of all serious ADR's must be conveyed to the NPRC within 2 working days by fax, email, telephone, courier as per stipulated guideline
- To report all serious adverse reactions within 24 Hrs.
- To forward periodic reports to next higher centre in first week of every month.
- To liaison with healthcare professionals order to inculcate / foster the culture of ADR reporting
  1. Acknowledge the cooperation of the notifier
  2. Share with notifier relevant feedback from higher centres
- To orgnize and attend training programs/ interactive meetings for all lower level centres
- Organize the public campaigns

Pharmacovigilance in India[11,12,13]

Perceptive of the importance of Pharmacovigilance, Institute for Post Graduate Teaching and Research In Ayurveda, Jamnagar has already conducted a two days workshop on 3rd & 4th December 2007, on "Pharmacovigilance for Ayurvedic Drugs: Scope, Limitations & Methods of Implementation", funded by WHO, Country Office for India, New Delhi. Based on the recommendations of the workshop, a Pharmacovigilance Cell PV Cell), first of its kind in India for Ayurveda, has been established and a Reporting Form for Suspected Adverse Reactions of Ayurvedic Formulations has been developed and distributed among the faculty members / research scholars / physicians under intimation to the Department of AYUSH, Ministry of Health and F.W., Govt. of India.

- PV was established since 2003 under the control of Central Drug Standard Control Association (CDSCO) under the aegis of Ministry of H & FW, DGHS (Directorate General of Health Service) New Delhi.
- WHO emphasized that it should include Traditional medicines in PV system and has published guidelines on safety monitoring of herbal medicines in PV systems in 2004.
- The first National Consultative meet of National Pharmacovigilance Programme for ASU Drugs was organized at Dept. of AYUSH, Ministry of Health & FW, New Delhi on August 2008, sponsored by WHO
- Based on the recommendations Reporting Form for Suspected ADRs of Ayurvedic Formulations has been developed.[1,3]

To put pharmacovigilance for ASU drugs in proper place in India, formation of a National Pharmacovigilance Centre for ASU Drugs, under the control of Department of AYUSH, is highly essential which would monitor the programme centrally. This programme aims to provide adverse drug reaction data related to various drugs of herbal, mineral, metallic, animal and other origin available in the country. Sponsored and coordinated by the country's National Pharmacovigilance Resource Centre (NPRC) for ASU drugs to establish and manage a data base of ADRs for making uniformed regulatory decisions regarding marketing authorisation of drugs in India for ensuring safety of drugs.

Ayurvedic concept of PV[13-16]

- Term PV does not feature in Ayurvedic texts.
- Rational drug use are recurrent themes of Ayurvedic pharmacology (DRB) and therapeutics (chikitsa).
- Along with descriptions related to actions & benefits of medicines, Ayurvedic pharmacology describes detailed adverse reactions & also how to deal with ways to minimize adverse effect such as

1. Precaution in manufacture techniques.
2. Time of drug administration.
3. Compliment diet and life style and so on.

- सम्यक्प्रयोगनिमित्ता हि सर्वकर्मणां सिध्दिरिष्टा, व्यापच्चासम्यक्प्रयोगनिमित्ता.....//(Ca.Su. 15/4)
- *Effectiveness of all actions depends on proper administratoin, Conversely failure is the result of improper administration.*

- अथ खलु द्रव्याणि नात्युपयुञ्जीताधिकमन्येभ्यो द्रव्येभ्यः, तद्यथा- पिप्पलि, क्षारः, लवणमिति // (Ca. Vi. 1/15)
- *Of all the substances, one should not resort too much to the 3, Pippali, Kshara, Salt*

Need of PV for Ayurvedic Medicines[1]

In ancient times, physicians prepared medicines for their patients themselves. Today production and sale of Ayurveda drugs is formalized into a thriving industry. (25000 thousands ayurvedic formulation available, 1.5 millions RMP, 7800 Mfg. Units Available)

Ayurvedic medicines –

1. Classical Ayurvedic formulations.
2. Patent and proprietry formulations.

This industrialization has brought many challenges about safe use of Ayurvedic medicines.[1,2]

Pharmacovigilance Method[1]

It is used for monitoring herbal safety but require modification to address specific challenges such as botanical nomenclature, quality, adulteration, labelling issues, prescriber/reporter.

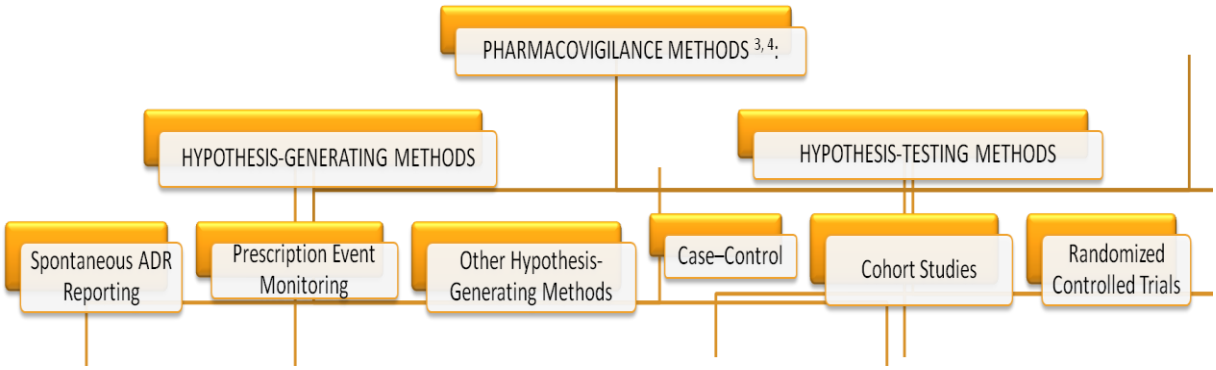


Fig. 9. Pharmacovigilance Method

SPONTANEOUS REPORTS[1,3,17,18]

- Safety of medicines is commonly monitored.
- Standardised forms are used for reporting of suspected ADR.
- In the UK spontaneous reporting is referred as the *'yellow card'* scheme. The Yellow Card Scheme is the main ADR reporting scheme in the UK and was introduced in 1964 after the thalidomide tragedy highlighted the urgent need for routine monitoring of medicines. It receives more than 20,000 reports of possible side effects each year.

Fig. 10. Yellow Card

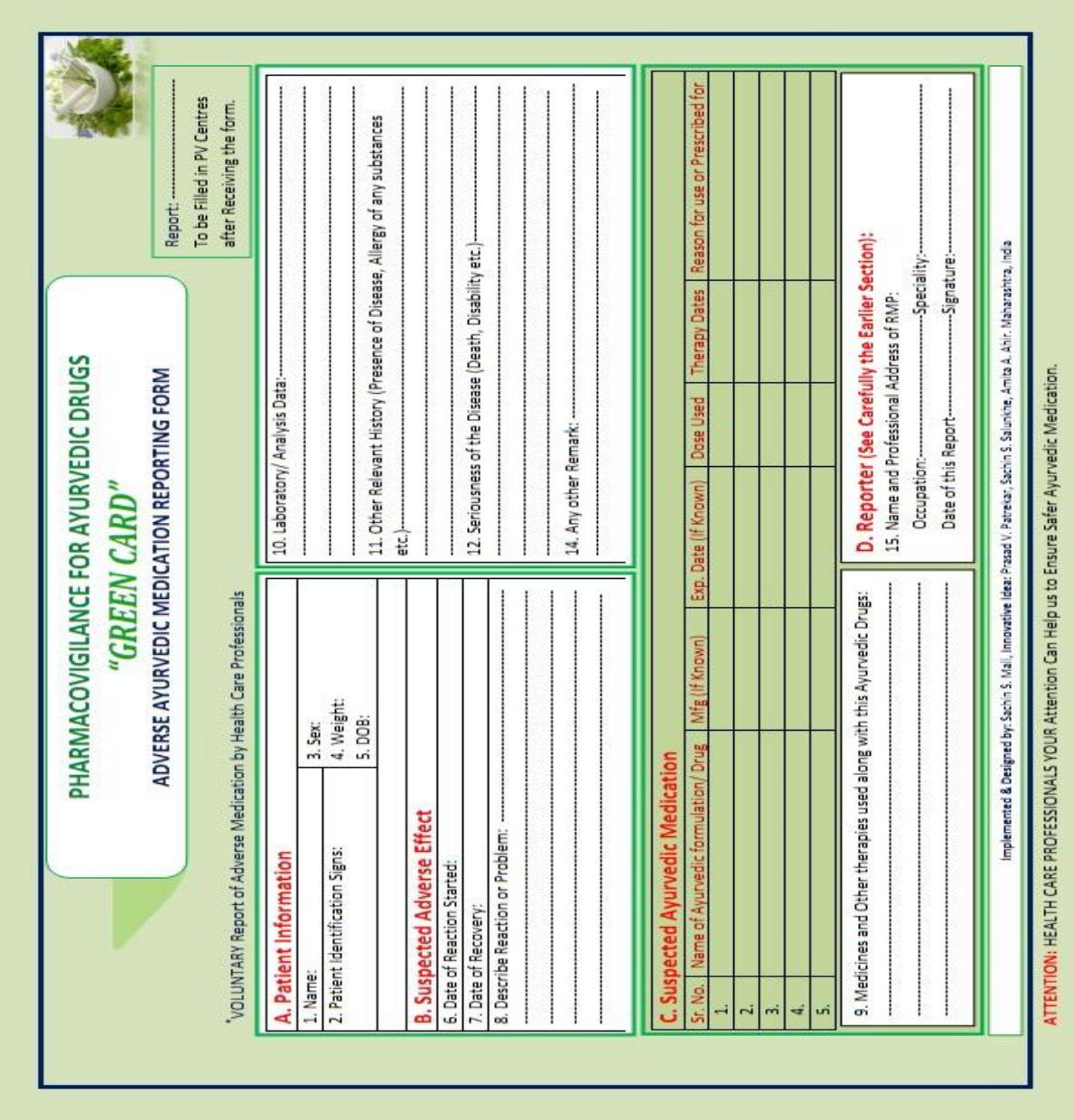
- Herb–drug interactions.
- Post Marketing safety Monitoring.

Take Home Message

- Natural Doesn't Mean Absolute Safe.
- Need for Post Marketing Surveillance.

- Need to develop 'GREEN CARD' scheme.

Recently we have invented the new concept in PV in India for reporting any adverse effect from ayurvedic formulation. This report we made independently which will ideal for every PV centres in India. The format i have invented and implemented as follow.



- Need of Patient Education.
- To improve National PV Program for Ayurveda.
- Need of Standardization and QC.

CONCLUSION

Invented GREEN CARD concept in PV which will ideal for every PV centres in India. It is expected that 50 – 75 % of medical errors are preventable. Think less about drug safety: more about patient safety. By incorporating PV, we will be able to prepare medicines with good efficacy, quality, safety and minimum harmful effect. By incoperating PV, we will be able to prepare medicines with good efficacy,,quality, safety and minimum harmful effect. In all, Pharmacovigilance will promote: Systematic and rational use of medicines Boost confidence for safety.

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