



A Framework for Promoting Safety Monitoring of Herbal Medicines: The International Society of Pharmacovigilance Special Interest Group on Herbal and Traditional Medicines

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1 Introduction

Herbal products are used globally for different purposes (e.g., therapeutic, cosmetic, etc.) and are easy to obtain as in most cases they do not require a prescription. Herbal and traditional medicines (H&TMs) have been used for generations and are part of the culture of many communities. Furthermore, in many countries, their introduction into the market is not yet fully regulated [1]. This calls for more safety monitoring for these products. In fact, there is a continuous progress in pharmacovigilance (PV) of herbal medicines (HMs) or “phytovigilance” in the context of regulations, terminologies for coding, etc. [2].

Hitherto, phytovigilance still faces many challenges, the most notable of which is underreporting of herbal medicines’ adverse reactions (ARs) [3]. There is a notion among the public that H&TMs are safe because of their natural origin [4]. Also, healthcare professionals (HCPs), in some cases, find complexity to distinguish between whether these

ARs are caused by herbal products or whether these are consequence symptoms of the comorbid conditions or even interactions between HMs and conventional drugs [5]. Over and above that, sometimes they have no idea that H&TMs can cause unexpected and serious ARs (e.g., hepatic disorders, renal disorders, carcinogenic effects, etc.) [6]. This is due to the absence of a curriculum on PV in general and phytovigilance in particular within their undergraduate studies [7, 8].

In addition, some may not realize that the origin of the herbal products, the way of extraction, their source, and the method of storage are aspects that must be considered, otherwise they will become contributing factors for the appearance of ARs or increase in severity and seriousness of these ARs [9]. Such perceptions hinder the spontaneous reporting of ARs and result in difficulty in the detection, assessment, and understanding processes [10]. Accordingly, it will be difficult to take the necessary measures to minimize the risks of H&TMs. Addressing these challenges that face the PV activities demands multidisciplinary collaborations between the different stakeholders of phytovigilance.

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2 ISoP Special Interest Group on Herbal and Traditional Medicines (H&TMs SIG)

The International Society of Pharmacovigilance (ISoP) is a professional, independent, nonprofit society, open to anyone with an interest in the safe and effective use of medicinal products. The main goal is the better knowledge and understanding of the safe and effective use of medicines, pre- and postmarketing. Special interest groups (SIGs), which are considered a fundamental part of the ISoP operational strategy, are loops of ISoP members that cover several areas of interest on PV.

In that sense, ISoP has included in its scope the verification of best practices in the production, use, and follow-up effects of H&TMs.

2.1 Sharing Knowledge of Natural Health Products Around the Globe

The ISoP Special Interest Group on Herbal and Traditional Medicines (H&TMs SIG) was launched at the 17th Annual Meeting of ISoP in Liverpool in October 2017 [11].

Since 2022, the group has been under the leadership of Professor Souad Skalli from the Faculty of Science University Mohammed V in Rabat (Morocco), with a specific interest and expertise in the PV of H&TMs. The deputy Lead is Dr Florence van Hunsel from Netherlands Pharmacovigilance Centre “Lareb,” and the Project Manager is Professor Jia-bo Wang, School of Traditional Chinese Medicine, Capital Medical University, Beijing, China.

The H&TMs SIG objectives are aligned with and expand on the World Health Organization (WHO) Herbal and Traditional Medicines with the following goals [12]:

- Address safety and PV issues in H&TMs.
- Raise awareness among relevant organizations and patients about the safety of H&TMs and PV.
- Support HCPs and organizations with scientific evaluation of ARs to HMs.
- Promote and develop education on all aspects of phytovigilance.
- Communicate activities and provide a forum for discussion and generation of new research and ideas, utilizing social media and other platforms.
- Facilitate collaboration for ISoP members on H&TMs research and projects.
- Advocate for the unique characteristics of H&TMs and the need for adapted PV tools.
- Share news, research, regulatory actions, and other relevant information on HMs issues.
- Expand membership in the H&TMs SIG.
- Build relationships with other ISoP groups and chapters.
- Collaborate with external organizations on phytovigilance initiatives.

The H&TMs SIG is made up of 31 members coming from various countries belonging to different partners of the HMs PV system as outlined in Table 1. The year 2023 was particularly the year for new memberships with ten new members. This distribution of the different members of the group shows that most continents are represented as are all categories of countries both economically and in terms of the development and regulation of phytovigilance in these countries [13, 14].

Table 1 Special interest group on herbal and traditional medicines members: country, number, and disciplines

Member countries	Member number	Member disciplines
Asia (10 members)		
China	3	Health professionals
Indonesia	1	Health professional
India	1	Academic sector (university)
Italy	1	Health professional
Japan	1	Academic sector (university)
Oman	1	Regulatory
South Korea	1	Health professional
Thailand	1	Academic sector (university)
Europe (7 members)		
Netherlands	2	Health professional (LAREB)
New Zealand	3	Academic sector (University); Health professional
Serbia	1	Industry
Sweden	1	Uppsala Monitoring Center
Switzerland	2	Health professional
Africa (6 members)		
Burkina Faso	1	Regulatory
Egypt	1	Health professional
Ethiopia	1	Regulatory
Morocco	1	Academic sector (University)
Nigeria	1	Academic sector (University)
Uganda	1	Health professional
North America (5 members)		
Mexico	3	Industry
USA	2	Industry
Australia (1 member)		
Australia	1	Academic sector (University)

2.2 Communicating for the Safe Use of H&TMs

Unlike conventional medicines, PV of H&TMs is not as developed, and this can be noticed at different levels in the WHO member countries for the international PV program. This ranges from the absence of PV of H&TMs in the country to fairly even developed PV [13, 14].

Phytovigilance must develop much further to ensure the safe use of H&TMs. In the daily healthcare sector, it remains a challenge and requires strong collaboration across regulatory agencies, pharmaceutical industries, HCPs, academics, traditional practitioners, herbalists, and patients who today expect to discuss with their HCPs and to participate in reporting, as well as to have their say in their treatment [15]. This collaboration must inevitably involve communication which may at times be challenging

for phytovigilance specialists who are first of all dedicated to the collection and assessment of data on adverse reactions. Effective communication is required between all phytovigilance partners where H&TMs is concerned, and safety information must be shared and accessible to all [16].

The H&TMs SIG can leverage its members' expertise by involving them in relevant lectures and communications at various meetings, including those organized or cosponsored by ISoP.

2.3 Promoting Phytovigilance to the Public

The H&TMs SIG continues to actively promote the exchange of safety information and science to enhance public awareness of phytovigilance. This is done through supporting the publication of phytovigilance related books and articles based on the translation of international educational phytovigilance textbooks and bibliographies. Such an example is *Pharmacovigilance for Herbal and Traditional Medicines Advances—Challenges and International Perspective* [17], a recently published book where the active members of the SIG were invited to write several of the chapters of which constitute the book. At the ISoP annual meeting 2023 in Bali, a proposal was put forward to use social media outlets for effective communication to disseminate information, real time warnings, and the latest news in relation to H&TMs.

2.4 Supporting Education and Research

Improvements in the education of all HCPs is required regarding the principles and practice of phytovigilance. The addition of such a subject to the curriculum of both conventional (medical) and alternative (naturopathic and chiropractic) schools and universities would inform these practitioners of the importance of discussing the use of H&TMs with their patients, as well as how to recognize and report ARs. The inclusion of information on H&TMs as a potential therapy should be included in academic programs. Pharmacological aspects of phytotherapy and phytovigilance should be included in the regular medical and pharmacy curriculum. This is already the case in Morocco, which, since 2017, has introduced a university curriculum for the pharmacovigilance of herbal medicines [18].

Phytovigilance training and education that involves national pharmacovigilance centers, national medicines regulatory affairs (NMRAs), as well as academia, is needed. The Moroccan experience may be replicated nationally and internationally. This experience and those of Switzerland were presented during ISoP 2023 in the preconference course dedicated to H&TMs. This half-day session was organized and conducted by the lead of the ISoP H&TMs SIG.

In the field of research, many members of the SIG have extensive experience in the field and participate in research projects of great scientific contribution. The results of these projects are published and even recognized and awarded by their peers.

We can mention the latest distinctions awarded to Souad Skalli from Morocco for her abstract: "Poster-300: DNA Barcoding as a Tool to Overcome the Challenges of phytovigilance of Natural Health Products Quality: The Example of Safran," third poster prize during the twenty-first ISoP annual meeting in September 2022, Verona, Italy [19]. Of particular interest is the challenge of counterfeit natural products. The article by Jia-bo Wang et al. has been selected as one of the top ten advances in traditional Chinese medicine (TCM) research in China [20]. In addition, Kampadilemba Ouoba from Burkina Faso was awarded the 2023 International Prize for the proper use of medicines for his research into the PV of traditional medicines in West Africa. This prize was awarded by the French National Academy of Pharmacy, in partnership with Les Entreprises du Médicament (Leem).

2.5 Collaborating with Others for a Multidisciplinary Network

The H&TMs SIG, by devoting itself to building strong connections with other organizations (Regulatory, academic, researchers, HCPs, and public) in tackling challenges relating to the safety and effectiveness of HMs, promotes phytovigilance and H&TMs risk management knowledge during ISoP meetings and to provide a platform for researchers to interact and learn. In addition, the tradition is not only to organize meetings and to discuss with the participants but also to schedule exclusive meetings with the group members. This contributes to strengthening the ties between the participants and the group members. Moreover, exchanges of ideas and perspectives are better done face to face. Other external meetings may be organized in collaboration with the ISoP where the members of the group are actively involved in the discussion about H&TMs. An example of this was the conference held at the Royal Botanic Gardens at Kew, London, UK, from 13 to 14 April 2023, entitled *Advances in Pharmacovigilance for HMs* [21]. ISoP was a partner in arranging this conference, and several members of the ISoP H&TMs SIG gave invited presentations.

2.6 Boosting Active Dialogue Between ISoP Members Who are Interested in H&TMs

H&TMs SIG is a focal point for ISoP members who are interested in phytovigilance to share and provide information on relevant issues and developments and to support H&TMs

pharmacovigilance. With its main mission to provide a forum for members to share experiences to suggest and discuss best practices and policy in the field of H&TMs monitoring and safety surveillance. Besides raising awareness of H&TMs pharmacovigilance issues among HCPs and the public, the ISoP H&TMs SIG is a valuable resource for anyone interested in the safe and effective use of H&TMs.

3 A Framework for Strengthen Phytovigilance and Boosting Patient Safety

Participation in domestic and international events concerned with patient safety issues is one of the ISoP's strategies to foster PV worldwide [22]. These strategies are adopted through ISoP national and regional chapters along with ISoP SIGs or by individual members. Such events enhance the culture of medication safety in all aspects (e.g., World Patient Safety Day, MedSafetyWeek, etc.).

The Egyptian chapter of the ISoP received an invitation to participate in the tenth Volatile Oile Gallery (VOG). The VOG is an annual symposium that was established in 2014 by the pharmacognosy department of the Faculty of Pharmacy Ain Shams University (FOPASU), Cairo, Egypt [23]. It provides a scientific platform where students can present their work on the use of volatile oils in medicine. Every year, the students have the opportunity to show the importance of essential oils in the wellbeing of human life through transforming what they have learned in the lecture halls into life applications and present this information in a simplified way. There is a cultural character to the event where the international students attend in their folk costumes with the herbs for which their countries are famous.

It was an indispensable chance for the ISoP to highlight the importance of phytovigilance. Accordingly, a collaboration took place between the Egyptian Chapter and H&TMs SIG to develop a framework to promote the safety of HMs.

At the FOPASU campus, many stakeholders from different health sectors (e.g., NMRAs, nonprofit organizations, pharmaceutical companies, patients, hospitals, etc.) were invited to attend with their booths and the postgraduate students of the pharmacognosy department to present their scientific posters.

During the preparation for the event, the Egypt chapter provided a proposal to the organizers to be addendum to the VOG's agenda. The proposal included several items, including:

1. Printing flyers with two different contents about the safety of HMs. One designated for medical students,

2. Providing scientific trainings before the event for students about PV and its broader scope, which includes not only medicines but also vaccines and HMs. The training consists of pivotal details about the safety of HMs. After these trainings, students will be able to give a focused message about phytovigilance while distributing the flyers.

The concept of these two points is to spread our message as widely as possible, by engaging the community in field activities through making the audience participate in disseminating information instead of being mere recipients. This strategy boosts deeper levels of community engagement.

The deliverables of adapting this approach are:

1. Debunking myths and infodemic about the unrealistic benefits of herbal products without considering their safety.
2. Giving an example of an executable framework for effective outreach.
3. Establishing a strong nexus between the different PV stakeholders to promote the safety monitoring of H&TMs.
4. Providing a forum to listen to the safety anecdotes about H&TMs from patients.
5. Increasing the awareness among the HCPs about other sources from which adverse effects may occur.
6. Engaging the community will allow PV stakeholders to recruit new allies and work under a common protocol.
7. Shedding light on the importance of updating the educational programs of undergraduate studies to integrate phytovigilance within the medical student curriculum.

Integrating the culture of safety of herbal products into the routine life of the community and creating a network between the PV stakeholders will help overcome all the barriers that face phytovigilance being consolidated within healthcare systems. It will facilitate the detection of new risks and the rapid development of phytovigilance to enable optimum measures to minimize these risks.

4 Conclusions

Adapting innovative approaches for opening new channels to the public to promote phytovigilance awareness is one of the strategies of the ISoP H&TMs SIG as a significant percentage of the community depends on H&TMs for many purposes, including healthcare. The public must be

aware of the potential risks, just as it itself is aware of its benefits, to be able to evaluate all different treatment options, including H&TMs. Furthermore, PV stakeholders must develop communications tools for promoting the safer use of H&TMs. ISoP, as a nonprofit international professional organization, continues to provide support to all countries for fostering the science of PV to ensure the safe and proper use of medicines, and this includes H&TMs.

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Declarations

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