

## Traditional and complementary medicines: Quality assessment strategies and safe usage

Khalid Hussain<sup>1</sup>, Muhammad Tahir Majeed<sup>2</sup>, Zhari Ismail<sup>1</sup>, Amirin Sadikun<sup>1</sup>,  
Pazilah Ibrahim<sup>1</sup>

<sup>1</sup>School of Pharmaceutical Sciences, Universiti Sains Malaysia, Minden Kampus Pulau Penang, 11800, Malaysia

<sup>2</sup>School of Health Sciences, Universiti Sains Malaysia, Kesihatan Kampus, Kubang Kerian, Kota Bharu, 16150, Malaysia

**Corresponding Author:** Khalid Hussain, Department of Pharmaceutical Chemistry, School of Pharmaceutical Sciences, Universiti Sains Malaysia, 11800, Penang, Malaysia. Email: hussain\_761@yahoo.com

### Introduction

Herbal medicines are also known as herbal remedies, herbal medicinal products, phytopharmaceuticals, phytotherapeutic agents and phytomedicines. Herbal medicines represent a vast array of therapies with proven benefits for the prevention and cure of different ailments. Nowadays, herbal medicines are being used along with modern medicine in many countries and this combination is playing an important role in health care. The increase in the popularity of herbal remedies is due to increase in the cost of treatment with modern medicine, fear of side effects of modern drugs and appreciation of natural remedies, which represent the alternative healthcare movement.

More than 80% of the population within developing countries relies on the use of herbal and other traditional medicines for their primary health care due to their lower cost and time-tested nature<sup>1</sup>. The World Health Organization (WHO) also encourages, recommends and promotes the use of traditional and herbal remedies in the National Health Care Program because these medicines are easily available at low cost, are comparatively safe and people have faith in such remedies<sup>2</sup>.

The actual global market size of herbal products is difficult to assess as the sale of herbal medicines is not regulated and that is why accurate statistics are not available. Until 1988, only 14 member countries of the WHO regulated the sales of herbal products and since then, 53 countries were added to the list,

with another 42 in the process of developing regulations by 2003<sup>3</sup>. According to the WHO, 75% of the world's population has therapeutic experience with herbal products<sup>4</sup>. According to a survey conducted in 2004, more than one third of American adults use alternative medicine<sup>3</sup> and this consumer-driven movement has expanded the market significantly in the United States (USA). The worldwide sale of the medicinal plants, crude extracts and finished products equated to 15 billion US dollars in 1999<sup>5</sup>, which increased to 32 billion US dollars in 2002<sup>6</sup>. According to the World Bank projection, with annual increases of 5 to 15%, the current market size of herbal products is about 60 billion US dollars per year<sup>3</sup>.

Maintaining quality of herbal products is challenging and it includes a strict set of processes which help to maintain consistency within the specified limits. In this article, we summarize the potential of natural flora in development of evidence based herbal medicines, various quality control strategies and role of retail pharmacist for their safe usage.

### Natural Flora and Traditional and complementary Medicines

The evidence of the use of natural products in therapeutics can be traced back at least 5000 years<sup>7</sup>. About 40% of new medications approved in North America during the period 1983-1994 were derived from natural compounds. Approximately 70% of newly reported chemical entities during the period 1981-2006 resulted from the study of

natural products<sup>8</sup>. The global documentation of 85,000 plants in medical use signifies the interest of scientists and medical professionals for these remedies as well as recognition of their true benefits<sup>6</sup>.

Many plants and plant-based products are being used as folk remedies in the form of fresh or dried plant materials and extracts. In spite of many developments in synthetic chemistry, cultivation and utilization of medicinal plants have been increased. A single plant contains a large number of compounds which can be used as starting material for the synthesis of novel drugs. However, only a small percentage of the 250,000 plant species have been investigated for bioactive compounds, indicating the potential of plants as a source of new drugs<sup>9</sup>.

The use of herbs varies from country to country. For example, products containing Echinacea or Ginkgo are popular in Germany. Feverfew, Garlic, Ginseng, Passiflora and Valerian are used more in the United Kingdom (UK). Tongkat Ali, Misai Kuching and Kacip Fatimah are popular in South East Asian countries. The use of these remedies is primarily for the management and prevention of age-related chronic diseases which thus improve the quality and longevity of life. The pathophysiology of these conditions is not completely known and presently available synthetic drugs are rarely preventive or curative<sup>10</sup>.

## **Quality of Traditional and Complementary Medicines**

Apart from the potential outlined previously, there are many reports of severe side effects due to the ingestion of herbal products<sup>11</sup>. Similarly, presence of heavy metals in Ayurvedic and Traditional Chinese Medicine is a clear indication of the poor quality of many herbal products<sup>12, 13</sup>. These products are sold at different outlets as medicinal products and food supplements with or without therapeutic claims. Hence, despite well documented benefits, the quality and safety of herbal medicines are still a question mark.

The WHO has conducted a number of surveys about regulatory issues regarding herbal products<sup>14, 9</sup>. A global survey in 2005 has taken into account the regulatory findings of 141 countries indicating that

many countries have started establishing regulatory authorities for the assessment of safety and efficacy of herbal medicines<sup>15</sup>. The WHO has also specified guidelines for improving consumer information, pharmacovigilance and good agriculture and collection practices for herbal medicines<sup>16, 17, 18</sup>.

## **Standardization of Traditional and Herbal Medicines**

Standardized herbal medicines have several advantages as compared to un-standardized extracts because they assure the identification "that the herb is what it is claimed to be". Moreover, herbal products of well-defined constituents are also a prerequisite for use in clinical trials. Advances in chemical and biological techniques over the past 50 years have resulted in scientific support to substantiate the use of herbal products. These techniques have enabled manufacturers to produce evidence-based standardized products<sup>19</sup>.

Standardization is a process which maintains consistency in the claimed efficacy of a product and its batch-to-batch reproducibility. The major challenges in terms of scientific standardization to adhere to industry norms are variation in the source, lack of safety evaluations and difficulty in quality control<sup>20</sup>. Standardization of herbal medicines is also difficult as synthetic drugs have well known constituents while many herbs have unknown active components.

Standardization of herbal products can be divided into two categories: first, an active constituent extract, where biochemical principles are known and have therapeutic values, and second, a marker extract, where the active principle is not known and a characteristic compound is used as a marker to assess the presence of other therapeutic biochemical compounds<sup>21</sup>. In active constituent extracts, the known biochemical compound is isolated to be used in standardization. This type of standardization has limitations because only isolated compounds are considered, ignoring the whole constituents of the herb, which may have synergistic or buffering activities to reduce the side effects. In the marker extract, where the active principle is not known, partly known or the preparation contains many crude drugs or extracts, the whole formulation is considered active in the presence of all plant constituents. In this case, a

single isolated compound would not be used as a marker because it is not unique to any one plant. With this in mind, it is fair to suggest that the standardization of herbal medicines is not merely an analytical operation which ends with the identification and assay of the active principle. Rather, it embodies the total information and controls which are necessary to ensure consistency in composition by employing relevant modern analytical tools.

### Quality Assurance Strategies

The first step to ensure therapeutic efficacy of a herbal medicine is to confirm the composition of the products using authenticated pharmacognostic methods. This may include identification by scientific nomenclature, knowledge of the parts used and the percentage of those parts. The metabolites of the herbs vary due to ontogenetic, ecotypic, genotypic and chemotypic factors. Growth conditions, age of the plant, time of harvesting, drying methods, and storage conditions are some other contributing factors. These factors may be controlled by applying good agriculture and collection practices (GACP) to obtain standardized raw materials.

The evaluation of physicochemical properties such as color, odor, microscopic examination, loss on drying, moisture contents and ash values of herbal materials is the important for quality control of raw materials. Heavy metal testing is of prime importance because poisoning has been reported following the ingestion of herbal remedies<sup>22, 23, 24</sup>. Nevertheless, the residues of fertilizers, pesticides and herbicides should also be monitored by using well accepted methods. Fourier Transform Infra red (FTIR) or Attenuated Transform Infra red (ATIR) spectroscopy is an important non-destructive quality assessment tool which facilitates the analysis of crude powders on solid matrix. The comparison of FTIR spectra of the sample with the reference is a powerful tool for the acceptance or rejection of samples.

The instrumental techniques used for the analysis of extracts and finished products are spectroscopic methods such as FTIR/ATIR, nuclear magnetic resonance (NMR), and chromatography such as high performance thin layer chromatography (HPTLC), high performance liquid chromatography (HPLC), gas chromatography (GC) and gas

chromatography/liquid and chromatography-mass spectroscopy (GC/LC-MS). All these instrumental techniques are helpful for both qualitative and quantitative analysis.

### Pharmacist and Herbal Medicines

Studies carried out in the UK, USA and Australia has indicated the frequent involvement of the pharmacist in the supply of herbal medicines<sup>25, 26, 27, 28</sup>. The consumers are influenced by irrational claims through different means to use herbal medicines alone or in combination with other medicines which may lead to clinical complications. The pharmacist, being an expert on drugs can play an important role in public health by stimulating awareness about the proper use of herbal medicines. The pharmacist should be able to advise the consumer about the rational and safe use of these medicines<sup>29, 30, 31</sup>.

However to advice in a proper manner, pharmacist must have information about the safety, toxicology, antidotes, side effects and potential interactions of herbal medicines with other modern medicines. There should be a joint effort between the pharmacists, the herbal industry and the regulatory authorities to include necessary information with the products regarding the composition, safety, dose, dosing interval, mechanism of action and interactions with other herbs and pharmaceuticals. In addition, access to reliable data regarding these products is equally important. The importance of information regarding quality, safety and efficacy has been emphasized in many studies<sup>32, 33, 34</sup>. The interference of herbal medicines with diagnostic markers may lead to false assessment of disease which clearly indicates the importance of data about the herbal medicine with respect to therapeutic drug monitoring.

### Concluding Remarks

The necessary data about herbal medicine is scarce as compared to pharmaceuticals because these medicines are based on several indigenous treatment systems such as Traditional Chinese Medicine (TCM), Unani, Islamic Tib, Sidha and Ayurveda<sup>34</sup>. Scientifically and clinically documented accounts of herbs, covering their botany, chemistry, pharmacology, ethno-pharmacology, toxicology and

clinical properties are essential for the promotion and safe use of herbal medicines. However, these treatment systems have limitations due to lack of proper documentation, which is indeed necessary for scientific validity.

In this context, it is relevant to mention that a number of information on phytomedicines have been published in both Europe and the USA<sup>35</sup>. Other initiatives include; the British Herbal Compendium, the Indian Herbal Pharmacopoeia, the Hamdard Pharmacopoeia, the (European Scientific Cooperative on Phytotherapy), the German E. Commission Monographs and the British Herbal Pharmacopoeia<sup>36</sup>. From present discussion, it is evident that good quality and safe herbal medicines can be produced by applying suitable analytical and biological techniques and case reports outlining the use of herbal medicine will be increasingly helpful to ensure patient safety.

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## References

1. Evans WC. Trease and Evans's Pharmacognosy. 15<sup>th</sup> edn. London: WB Saunders; 2001.
2. Wani MS. Herbal medicine and its standardization. *Pharmaceutical Reviews* 2007; 5(6).
3. Voigt K. Our look at global burgeoning Asian herbal industry. *The Wall Street Journal* 2006; June 11.
4. Dubey NK, Kumar R, Tripathi P. Global promotion of herbal medicine: India's opportunity. *Current Science* 2004; 86: 37-41.
5. Raskin I, Ribnicky DM, Komamytsky S, Ilic N, Poulev A, Borisjuk N et al. Plants and human health in the twenty first century. *Trends in Biotechnology* 2002; 20: 522-531.
6. Balunas MJ, Kingerhorm AD. Drug discovery from medicinal plants. *Life Sciences* 2005; 78: 431-441.
7. Goldman P. Herbal medicine today and roots of modern pharmacology. *Annals of Internal Medicine* 2001; 135: 594-600.
8. Newman DG, Cragg GM. Natural products sources of new drugs over the last 25 years. *Journal of Natural Products* 2007; 70: 461-477.
9. Prance GT. Floristic Inventory of the tropics: Where do we stand? *Annals of Missouri Botanical Garden* 1997; 64: 659-684.
10. Mitscher LA, Pilla S, Shankel DM. Some transpacific thoughts on the regulatory need for standardization of herbal medicine. *Journal of Food and Drug Analysis* 2000; 8: 229-234.
11. O'Sullivan HM, Lum K. The poisoning of awa: the non traditional use of an ancient remedy. *Pacific Health Dialog* 2004; 11(2): 211-215.
12. Ernst E. Contamination of herbal medicines. *The Pharmaceutical Journal* 2005; 275: 67-168.
13. De Smet PAGM. Health risks of herbal remedies: an update. *Clinical Pharmacology and Therapeutics* 2004; 76(1):1-17.
14. WHO. Regulatory situation of herbal medicine. A worldwide review, Geneva, 1998.
15. WHO. National policy on traditional medicine and regulation of herbal medicines. Report of a WHO global survey, 2005.
16. WHO. WHO guidelines for developing consumer information on proper use of traditional medicines and complementary/alternative medicine. Geneva, 2004a.
17. WHO. WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance system. Geneva, 2004b.
18. WHO. WHO guidelines on Good Agriculture and Collection Practices (GACP) for medicinal plants. Geneva, 2003.
19. Phillipson JD. Fifty years of medicinal plant research-every progress in methodology is a progress in science. *Planta Medica* 2003; 69: 491-495.
20. Wang ZG, Ren J. Current status and future direction of Chinese herbal medicine. *Trends in Pharmacological Sciences* 2002; 23: 347-348.
21. Tierra M. Founding Member of the American Herbalists Guild. <http://www.surfnetusa.com/planetherbs/articles/STANDARDIZED%20edited%203.html> (Feb 25, 2009)

22. Handa SS. Medicinal Plants- Priorities in Indian Medicines Diverse Studies and Implications. In: Handa SS, Kakul MK. (eds). Supplement to Cultivation and Utilization of Medicinal Plants. Jammu Tawi: Regional Research Laboratory Council of Scientific and Industrial Research; 1996. p 33-51.
23. Baer R, Ackerman A. Toxic Mexican folk remedies for the treatment of empacho: the case of azarcon, greta, and albayalde. *Journal of Ethnopharmacology* 1998; 24: 29-31.
24. Abu Melah A, Ahmad NA, Hassan AYEI. Traditional remedies and lead intoxication. *Tropical and Geographical Medicine* 1987; 39(1): 100-103.
25. Barnes J, Abbor NC. Experience with complementary remedies: a survey of community pharmacists. *The Pharmaceutical Journal* 1999; 263: R37-R43.
26. Kayne S. A helping hand? *Chemist and Druggist* 2002; 12: 26-28.
27. Naido S, Wilkinson JM, Simpson MD. Attitudes of Australian Pharmacists toward complementary and alternative medicines. *The Annals of Pharmacotherapy* 2005; 39:1456-1461.
28. Welna EM, Hadsall RS, Schommer JC. Pharmacists's personal use, professional practice behavior, and perception regarding herbal and other natural products. *Journal of the American Pharmacists Association* 2003; 43(5): 602-611.
29. Shrivastava S, Dubey D, Kapoor S, Dubey P. The Pharmacist's Role in Herbal Care. *Medscape Pharmacists* 2007.
30. Leaders FE. Incorporating botanical products into MCO formularies. *Drug Benefit Trends* 1998; 10: 34-43.
31. Meinhardt RA, Richardson C, Ohlinger P. Alternative medicine and pharmacist counseling obligations. *Drug Benefit Trends*.1998; 10: 24-28.
32. Ernst E. Complementary medicine pharmacist. *The Pharmaceutical Journal* 2004; 273: 197-198.
33. Ernst E. Recommended information sources. *The Pharmaceutical Journal* 2005; 275: 348.
34. Nathan JP, Cicero LA, Koumis T, Rosenberg JMR, Feifer S, Maltz F. Availability and attitudes toward resources on alternative medicine products in the community pharmacy setting. *Journal of the American Pharmacists Association* 2005; 45(6): 734-739.
35. Patwardhan B. Indian Drugs, Ayurveda: the designer medicine-a review of ethno-pharmacology and bioprospecting research. *Indian Drugs* 2000; 37(5): 213-227.
36. Narayana DBA, Dobriyal M. How green are Indian and US pharmacopoeias. *The Eastern Pharmacist* 2000; 43(514): 21-24.