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Review Article

IMPORTANCE OF STANDARDIZATION OF HERBAL DRUGS – AN UPDATED OVERVIEW

J. Karthi[1], M.Purushothaman*[2]

[1]Alwar College of Pharmacy, Sun Rise University, Alwar, Rajasthan – 301030, India

[2] Vasavi Institute of Pharmaceutical Sciences, Kadapa-516247, India

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ABSTRACT

Ayurveda emphasize the relationship between man and plants throughout the development of human culture. The increased need by developed and developing country for herbal medicine, led to sudden increase in the number of herbal drug manufacturers. The practices continue today because of its biomedical benefits as well as place in cultural beliefs in many parts of world and have made a great contribution towards maintaining human health. The quality control of crude drugs and herbal formulations are paramount importance in justifying their acceptability in modern system of medicine. However, one of the major problems faced by the herbal drug industry is non-availability of rigid quality control profile for herbal material and their formulation. The task of lying down standards for quality control of herbal crude and their formulations involved biological evaluation for a particular disease area, chemical profiling of the material and lying down specification for the finished products. The importance of this study is to review the methods of standardization of raw and finished herbal products and to know about the updated importance of the standardization of herbal drugs.

INTRODUCTION

The Indian herbal industry is growing in a tremendous rate. More number of herbal products is arrived in the market. The safety and efficacy of herbal products are dependent upon the standardization of these herbal drugs. Standardized herbal products of consistent quality and containing well-defined constituents are required for reliable clinical trials and to provide consistent beneficial therapeutic effects.

Address for correspondence

M.Purushothaman *

Professor and Director

Vasavi Institute of Pharmaceutical Sciences, Kadapa-516247, Andhra Pradesh, India

E-mail:*vedpurushoth@gmail.com*

***Mobile:** +91-9440754715*

Pharmacological properties of an herbal formulation depend on phytochemial constituents present therein. Development of authentic analytical methods, which can reliably profile the phytochemical composition, including quantitative analyses of market/bioactive compounds and other major constituents, is a major challenge to scientists[5-8]. For the purpose of research work on standardization of herbal formulations, a profound knowledge of the important herbs found in India and widely used in Ayurveda formulation is of utmost importance[9-14]. Even when the chemical composition of a plant extract is known, the pharmacologically active moiety may not be. Environment, climate and growth conditions influence the composition, as does the specific part of the plant and its maturity. Monographs detailing standardization of active ingredients would improve the marketplace. Even if an herbal product is standardized to, for example, 4% of a

constituent, the remaining 96% of ingredients is not standardized and may affect the product's solubility, bioavailability, stability, efficacy and toxicity. Just as controlled trials are necessary to establish safety and efficacy, manufacturing standards are required to ensure product quality[15,16]. Now a days newer and advanced methods are available for the standardization of herbal drugs like fluorescence quenching, the combination of chromatographic and spectrophotometric methods, biological assays, use of biomarkers in fingerprinting etc. Bioassay can play an important role in the standardization of herbal drugs and can also become an important quality control method as well as for proper stability testing of the product. India can emerge as the major country and play the lead role in the production of standardized, therapeutically effective Ayurvedic formulation. India needs to explore the medicinally important plants. This can be achieved only if the herbal products are evaluated and analyzed using sophisticated modern techniques of standardization such as UV- visible, TLC, HPLC, HPTLC, GC-MS, spectrofluorimetric and other methods[17-22].

Standardization of herbal drugs:

Standardization of herbal formulations is essential in order to assess of quality drugs, based on the concentration of their active principles, physical, chemical, phyto-chemical, standardization, and In-vitro, In-vivo parameters. The quality assessment of herbal formulations is of paramount importance in order to justify their acceptability in modern system of medicine. One of the major problems faced by the herbal industry is the unavailability of rigid quality control profiles for herbal materials and their formulations. In India, the department of Ayush, Government of India, launched a central scheme to develop a standard operating procedures for the manufacturing process to develop pharmacopeial standards for ayurvedic preparations. The subject of herbal drug standardization is massively wide and deep. There is so much to know and so many seemingly contradictory theories on the subject of herbal medicines and their relationship with human physiology and mental function. India needs to explore the medicinally important plants. This can be achieved only if the herbal products are evaluated and analyzed using sophisticated modern techniques of standardization[23-29]. World Health Organization (WHO) encourages, recommends and promotes traditional/herbal remedies in natural health care programmes because these drugs are easily available at low cost, safe and people have faith in them. The WHO assembly in number of resolutions has emphasized the need to ensure quality control of medicinal plant products by using modern techniques and applying suitable standards[30-32]. Standardization of raw materials includes the following steps:-

Authentication- Each and every step has to be authenticated, area of the collection, parts of the plant collection, the regional situation, as phytomorphology botanical identity, microscopic and histological analysis(characteristic features of cell walls, cell contents, starch grains, calcium oxalate crystals, hairs, fibers, vessels etc.) Several studies of the histological parameters are list of palisade ratio, vein islet number, vein termination, stomatal number, stomatal index, trichomes, stomata, quantitative microscopy, taxonomic identity, foreign matter. Loss on drying, swelling index, foaming index, ash values and extractive values, Chromatographic and spectroscopic evaluation, Determination of heavy metals, pesticide residues, Microbial contamination, Radioactive contamination. The parameter stability of herbal formulations that includes pharmacognostic parameters, physico-chemical parameters, phyto-chemical parameters, microbiological assay, chromatographic analysis.

Pharmacognostic evaluation: It includes color, odor, taste, texture, size, shape, microscopical characters, and histological parameters.

Physico-chemical parameters: It includes foreign matter, total ash, acid-insoluble ash, swelling and foaming index, assay, successive extractive values, moisture content, viscosity, PH,
Disintegration time, friability, hardness, flow capacity, flocculation, sedimentation, alcohol content.

Chemical parameters: It includes limit tests, chemical tests etc.

Chromatographic and spectroscopic analysis: It includes TLC, HPLC, HPTLC, GC, UV, IR, FT-IR, AAS, LC-MS, GC-MS, fluorimetry etc.

Microbiological parameters: It includes the full content of viable, total mould count, total coliforms count. Limiters can be used as a quantitative tool or semi-quantitative to determine and control the amount of impurities, such as reagents used in the extraction of various herbs, impurities ships directly from the manufacturing and solvents etc[17-22].

WHO GUIDELINES FOR QUALITY STANDARDIZED HERBAL FORMULATIONS

1) Quality control of crude drugs material, plant preparations and finished products.

2) Stability assessment and shelf life.

3) Safety assessment; documentation of safety based on experience or toxicological studies.

4) Assessment of efficacy by ethnomedical informations and biological activity evaluations[30-32]. The bioactive extract should be standardized on the basis of active principles or major compounds along

with the chromatographic fingerprints (TLC, HPTLC, HPLC, and GC).

1. Quality Control of Herbal Drugs: Quality control for efficacy and safety of herbal products is of paramount importance. Quality can be defined as the status of a drug that is determined by identity, purity, content, and other chemical, physical, or biological properties, or by the manufacturing processes. Quality control is a term that refers to processes involved in maintaining the quality and validity of a manufactured product. The term "herbal drugs" denotes plants or plant parts that have been converted into phytopharmaceuticals by means of simple processes involving harvesting, drying, and storage. Hence they are capable of variation. This variability is also caused by differences in growth, geographical location, and time of harvesting. A practical addition to the definition is also to include other crude products derived from plants, which no longer show any organic structure, such as essential oils, fatty oils, resins, and gums. Derived or isolated compounds (e.g. strychnine from *strychnous nux-vomica*) or mixtures of compounds (e.g. abrin from *Abrus precatorius*).

In general, quality control is based on three important pharmacopeial definitions

- Identity- it should have one herb
- Purity – it should not have any contaminant other than herb
- Content or assay-the active constituents should be within the defined limits.

2. Stability Assessment and Shelf Life: The past decade has seen a significant increase in the use of herbal medicines. As a result of WHO's promotion of traditional medicine, countries have been seeking the assistance of the organization in identifying safe and effective herbal medicines for use in national health care systems. Prolonged and apparently uneventful use of a substance usually offers testimony of its safety. In a few instances, however, investigation of the potential toxicity of naturally occurring substances widely used as ingredients in these preparations has revealed previously unsuspected potential for systematic toxicity, carcinogenicity and teratogenicity. Regulatory authorities need to be quickly and reliably informed of these findings. They should also have the authority to respond promptly to such alerts, either by withdrawing or varying the licences of registered products containing suspect substances, or by rescheduling the substances to limit their use to medical prescription.

Assesement of quality: All procedures should be in accordance with good manufacturing practices.

Crude plant material: The botanical definition, including genus, species and authority, description, part of the plant, active and characteristics constituents should be specified and, if possible content limits should be defined. Foreign matter, impurities and microbial content should be defined or limited. Voucher specimens, representing each lot of plant material processed, should be authenticated by a qualified botanist and should be stored for at least a 10-year period. A lot number should be assigned and this should appear on the product label.

Plant preparations: The manufacturing procedure should be described in detail. If other substances are added during manufacture in order to adjust the plant preparation to a certain level of active or characteristics constituents or for any other purpose, the added substances should be mentioned in the manufacturing procedures. A method for identification and, where possible, assay of the plant preparation should be added. If identification of an active principle is not possible, it should be sufficient to identify a characteristic substance or mixture of substances to ensure consistent quality of the preparation.

Finished product: The manufacturing procedure and formula, including the amount of excipients, should be described in detail. A finished product specification should be defined to ensure consistent quality of the product. The finished product should comply with general requirements for particular dosage forms.

Stability: The physical and chemical stability of the product in the container in which it is to be marketed should be tested under defined storage conditions and the shelf-life should be established.

Safety assessment: Herbal medicines are generally regarded as safe based on their long-standing use in various cultures. However, there are case reports of serious adverse events after administration of herbal products. In a lot of cases, the toxicity has been traced to contaminants and adulteration. However, some of the plants used in herbal medicines can also be highly toxic. As a whole, herbal medicines can have a risk of adverse effects and drug-drug and drug-food interactions if not properly assessed. Assessment of the safety of herbal products, therefore, is the first priority in herbal research. These are various approaches to the evaluation of safety of herbal medicines. The toxic effects of herbal preparation may be attributed mainly to the following: Inherent toxicity of plant constituents and ingredients and Manufacturing malpractice and contamination. Evaluation of the toxic effects of plant constituents of herbal formulation requires detailed phyto-chemical and pharmacological studies. It is, however, safe to assume that, based on human experiences in various cultures, the use of toxic plant ingredients has already been largely eliminated and recent re-

ports of toxicity could largely ne due to misidentification and overdosing of certain constituents. Substitution and misidentification of herbal substances, documented or regulatory approaches, development of monitoring and surveillance systems, assessment of toxicity, risk assessment approach. The evaluation of new herbal products consists of six steps, which define the following: Characteristics of new substances, history and pattern of use, any adverse reaction, biological action, toxicity and carcinogenicity, and clinical trial data.

The presence of impurities is either an intended addition, or accidental contamination via processing. The substitution of plants arises because of similar plants/ wrong identification, or the use of cheaper alternatives.

Assessment of toxicity: Toxicity investigation will also be required because the analysis alone is unlikely to reveal the contributions to toxicity itself. In assessing toxicity of an herbal medicine, the dose chosen is very important. Toxicity assessment involves one or more of the following techniques- In vivo techniques, in vitro techniques, cell line techniques, micro- array and other modern technique Standardization techniques to adequately model toxicity.

Assessment of efficacy: Herbal medicines are inherently different from conventional pharmacological treatments, but presently there is no way to assess their efficacy other than by currently used conventional clinical trial methodologies, in which efficacy is conventionally assessed by clinical, laboratory, or diagnostic outcomes: Clinical outcomes include parameters such as improved morbidity, reduced pain or discomfort, improved appetite and weight gain, reduction of blood pressure, reduction of tumor size or extent, and improved quality of life. Laboratory /other diagnostic outcomes include parameters such as reduction of blood glucose, improvement of hemoglobin status, reduction of opacity as measured by radiological or imaging techniques, and improvement in electrocardiogram (ECG) findings.

CONCLUSION:

It is concluded that now a days, many of the medicinal plants available in the mar-ket have ambiguous identification along with adulteration and contamination. The physicochemical evaluation of the powder drug reveals the standard parameters for the quality and purity of herbal drug and also gives information regarding the authenticity of crude drug. Therefore a consensus is being arrived at to incorporate the qualitative finger-printing together with other physicochemical properties of quality protocols for herbal medicines is an ongoing process and this shortcoming could be overcome shortly. Literature on herbal medicines, lack of scientific data in support of the medicinal activity claimed and their safety and efficacy assumed. Hence there is a need to incorporate certain parameters of the pharmacological evaluation of moderns on modern lines.

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