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REVEIW ARTICLE

STANDARDIZATION OF DRUGS IN AYURVEDA – A SHORT REVIEW

***Dr. Prasanna Bollipogu**

Assistant Professor, Dravyaguna Department, Dr. N.R.S. Govt. Ayurvedic College, Vijayawada, India

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ABSTRACT

Standardization of drugs means confirmation of its identity and determination of its quality and purity. In the current clinical practice, Medicinal plants has became the richest bio-resource of drugs for traditional systems of medicine, modern medicines, nutraceuticals, food supplements, folk medicines, pharmaceutical intermediates and chemical entities for synthetic drugs. In view of the increasing needs of the population, shortage of authentic raw material, present trends of commercialisation and the preparation, marketing of Ayurvedic medicines has led to adulteration. Due to urbanisation and busy life-style even the patient has become more sophisticated and started showing inclination to purchase and to obtain drugs from the manufacturer instead of obtaining it from his own physician. Also substitution of genuine herbs with cheap, spurious drugs resulting in dumping of market with sub-standard and inferior quality drugs. In Ayurvedic drug preparations it is estimated that about 1000 single drugs and around 8000 compound formulations of recognized merit are in vogue. Efficacy of any medicine depends on its genuineness. Ayurvedic treatments are getting disrepute in many instances because of substandard drugs. A multi-dimensional approach is the only possible solution for that by this drug standardization. Hence, standardization of drugs placed a great demand in the field of Ayurveda. In this present review, an attempt has been made to give an overview of certain Standarization methods.

INTRODUCTION

Standardization of drug means confirmation of its identity, quality, safety, efficacy and purity. The word "standardization" should encompass entire field of study from cultivation of medicinal plant to its clinical application. The basic resources of medicines come from nature and they are used as medicaments from ancient time to present day. Each plant is like factory capable of synthesizing unlimited number of highly complex and unusual chemical substances. In order to obtain quality oriented herbal products, care should be taken right from the proper identification of plants, season and area of collection and their extraction and purification process and rationalizing the combination in case of polyherbal drugs. In India, the department of AYUSH Government of India launched a central scheme to develop standard operating procedures for the manufacturing process to develop pharmacopeia standards for Ayurvedic preparations. The subject of herbal drug standardization is now massively wide and deep.

Need of standardization: One of the major problems faced by the Ayurveda physicians is the unavailability of unique quality control parameters. Today physician is totally depending upon mediators for drug collection. Adulteration, substitution, ignorance of dealers creates problem. Our ancient books has been mentioned many methods to standardize drug and also about adulteration. But the traditional approach towards standardization is insufficient for current herbal market.

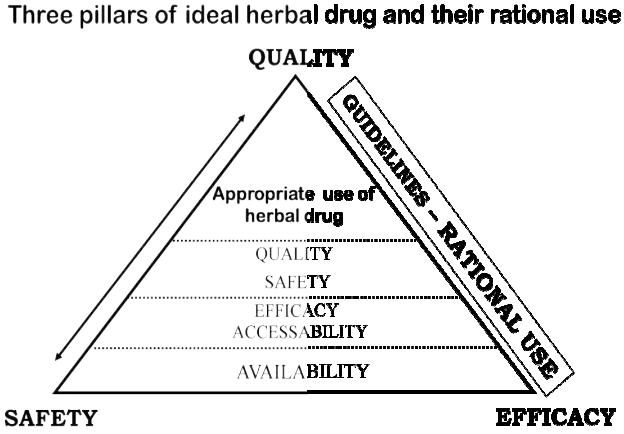


Figure 1.

All these consequences will be nullified only when the rules and regulations are becoming mandatory for the authentication and standardization of raw materials used in the formulation. The major obstacle in the wider acceptability of Ayurveda and its products is the lack of proper standardisation techniques. People are also becoming aware of the potency and side effect. The lack of quality standards has resulted in mild to serious adverse effects ranging from hepato-toxicity to death. These have necessitated development of modern and objective standards for evaluating the safety, quality and efficacy of these medicines. To gain public trust and to bring herbal product into mainstream of today health care system, the

researchers, the manufacturers and the regulatory agencies must apply rigorous scientific methodologies to ensure the quality of the traditional herbal products.

Standardization can be of two types as follows:

1. True standardization: It represents a definite phytochemical or group of constituents known to have activity.

2. Pseudo standardization: Ayurvedic classics like Charaka Samhita and Sushruta Samhita etc. also contain descriptions of metals and minerals apart from the medicinal plants, their processing techniques and their utilization in therapeutics.
Herbo mineral and metallic preparations occupied a significant seat in Ayurvedic pharmacopoeia and have routinely been used in practice in different parts of India for many centuries. Such preparations are held to be safe, efficacious even in minute doses, when manufactured and used following specified classical guidelines, not to lead to any significant untoward effects. Ayurveda using the parameters of those times, which may appear quite crude in comparison to the modern age scientific parameters. It doesn't mean that ancient wisdom was unscientific. It's merely an ignorance caused due to the communication gap between ancient and modern parameters. We live an era when sophisticated and advanced technologies are easily available to us. Ayurvedic drug manufacturers should make use of these technologies in the further development of the existing formulations. But to cope up with the demand of Ayurvedic medicines standardizations of such herbal, herbo-mineral and mineral formulations is a dire necessity. Thus, in the broader sense standardization involves such unique techniques by which we can adjust the drug preparation to a define content of a constituent or a group of substances with known therapeutic activity by adding excipients or by mixing polyherbal drugs.

METHODOLOGY

Methodology is divided in to following for the better indulgent:

1. Process standardization
2. Rasausadhis standardization
3. Overview on herbal drug standardization
4. Polyherbal standardization
5. DNA fingerprinting technique
6. Techniques in extraction of herbals
7. Phytosomes/ pharmacosomes: A novel drug delivery system for herbal drugs
8. Instrumental techniques for herbal drug standardization and identification
9. Herbal nanomedicines standardization
10. Global status of the regulatory guidelines for herbal medicines
11. Recent advancement in the methodology for the standardization of herbal medicines.

They should emphasize their own protocol standards to develop reproducible, safe, economical and effective Ayurvedic medicines by:

1. Standardization of the raw material
2. Development of in-process quality control technique
3. Standardization of the finished product
4. Safety studies in animals
5. Effective dose studies and clinical trials
6. Pharmaco-kinetic explanations

W.H.O. Guidelines: It is accepted worldwide that the standardization of herbal drug is wide and deep. According to WHO, the herbal drug standardization is the process involved in the physicochemical evaluation of crude drugs that covers various aspects like selection and handling of crude drug material; safety, efficacy and stability assessment of finished products; documentation of safety and risk of the product formulation to consumer and product promotion.

Pharmacopeial Guidelines: Quality control of crude drugs material, plant preparations and finished products.

- Stability assessment and shelf life.
- Safety assessment; documentation of safety based on experience or toxicological studies.
- Assessment of efficacy by pharmacological information's and biological activity evaluations.

WHO Guidelines Monograph Titles: In the modern herbal Ayurvedic monographs the standardization parameters are discussed in a comprehensive way. According to the modern Ayurvedic monograph the quality control protocols include the following:

- Descriptive / Botanical evaluation: Reference to the identity of the drug – by phytomorphological, microscopical, organoleptic evaluation, foreign matter etc.
- Physicochemical evaluation: Reference to the physicochemical character of the drug – by TLC, Ash, Extractable matter, Water content and volatile matter, Volatile oils.
- Pharmacological: Reference to the pharmacological parameters by bitterness value, Haemolytic activity, Astringency, Sterling index, Foaming index.
- Toxicological: Pesticide residue, Metals.
- Microbial contamination: Total viable count, Pathogens, Aflatoxins
- Radioactive contamination.

History of important events in herbal drug standardization:

- 2007 WHO. Guidelines for assessing quality of herbal medicines with reference to contaminants and residues. Geneva, Switzerland: World Health Organization; 2007.
- 2007 WHO Guidelines on good manufacturing practices (GMP) for herbal medicines. Geneva, Switzerland: World Health Organization; 2007.
- 2009 AYUSH department with collaboration with Quality Council of India (introduced certification scheme for AYUSH drug products.
- 2009 USP. United States Pharmacopeia 32/National Formulary 27. Rockville, MD: The United States Pharmacopeial Convention; 2009.
- 2011 An EU directive passed in 2004 erects "disproportionate" barriers against herbal remedies by requiring them to be "licensed" before they can be sold. It's called the Traditional Herbal Medicinal Products Directive (THMPD), Directive 2004/24/EC.
- 2011 Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues." The document was published in the Federal Register on Tuesday, July 5, 2011.
- 2012 National seminar on Recent Advances and Future Challenges in Ayurveda, Banaras Hindu University, Ganga kaveri publishing house, 2012.

Table 1. Brief overview of the process of standardization

Sl. No.	Standardization of raw herbal drugs	Norms to be followed During Standardization	Standardization
1.	Passport data of raw plant drugs	GSL (Good survey of literature)	Follow define GMP
2.	Correct taxonomic identification and authentication	GAP (Good agricultural practice)	Toxicity evaluation
3.	Study on the medicinal part: root, stem, bark, etc.	GCP (Good clinical practice)	Chemical profiling
4.	Collection details: location, stage and development, time storage etc.	GHP (Good harvesting /handling practice)	Pharmacodynamics
5.	Organoleptic evaluation of raw drug	GLP (Good laboratory practice)	Pharmacokinetics
6.	Microscopic and molecular examination	GMP (Good manufacturing practice)	Posology
7.	Chemical composition	GMT (Good marketing technique)	Stability
8.	Biological activity of whole plant	-	Presentation & Packing
9.	Shelf life of raw drugs	-	Therapeutic merits

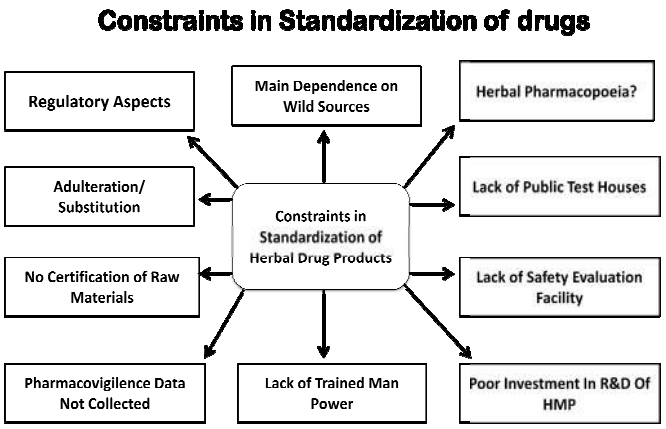


Figure 2.

***Causes and Effects in Standardization of Ayurvedic Drugs*:** The term Ayurvedic drugs, comprises of, herbal mineral animal resources substances broadly the standardisation of Ayurvedic drugs – based upon

1. Collection of the herbs in proper season and time, 2. Part of the herb or plant that is used and 3. The processing of that herb into powder, or extract or any other forms, 4. To be mixed in what order, with what ingredient etc were very clearly and thoroughly described.

Invariably, when everything is written in textbook and if it is not followed by some unauthorized and unqualified manufacturers, how can anyone blame the Ayurvedic drugs and its science along with its philosophy? Today all are trying to judge the standards with procedures fixed for another system of medicines – which is not correct. Formulation and preparation of medicines is based on the aetiology of the disease and the formulations were designed accordingly. Fundamentally there is a vast difference viz in the aetiologies of the different systems of medicines in Ayurvedic and Allopathic. Why only Ayurvedic drug is targeted? No other traditional system is commented in the parallel manner. May be, this is a widely accepted medicine and has a wide application. Can anyone test the allopathic medicines with Ayurvedic science and its standards? Or scientific techniques?

Hence the slogan should be revised and replaced as "maintenance of standards" and quality control of Ayurvedic drugs which can be achieved if the attempt is in the right direction. There is a factor called Idiosyncrasy- procedural and experimental errors to give an accurate method in evaluation. Modern and authorized scientists can come forward with an exclusive analytical and evaluative methods for Ayurvedic drugs preferably with innovative genuine methods rather than trying to compare with methods that are not suitable to Ayurvedic drugs. The standardisation methods of Ayurvedic drugs should be relevant and also evaluative.

Methods of standardization: Methods of standardization should take into consideration all aspects that contribute to the quality of the herbal drugs, namely correct identity of the sample, Genobiotic, Organoleptic evaluation, Pharmacognostic evaluation, quantitative evaluation, Chemobiotic, phytochemical evaluation, Test for the presence of Xenobiotics, Microbial load testing, Toxicity testing, and Biological activity.

Different techniques involved in standardization of crude drugs

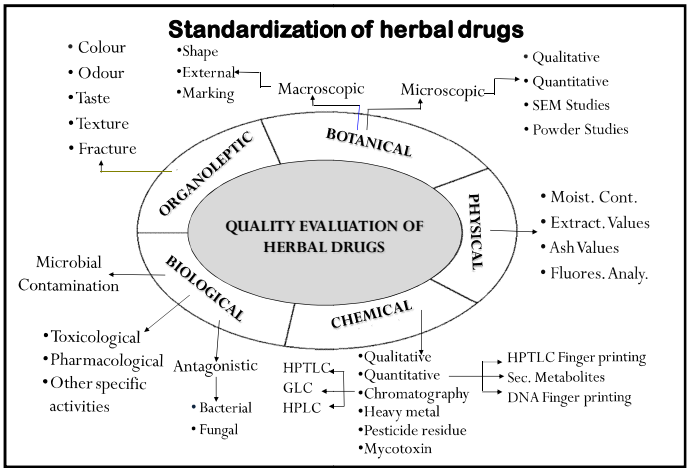
- Macroscopic methods
- Microscopic methods
- Physical methods
- Chemical methods
- Biological methods

Some Ancient / Classical Methods for Standardisation:

1. Authentication
   a) Each and every step has to be authenticated.
   b) Stage of collection.
   c) Parts of the plant collected.
   d) Regional status.

Macroscopical Evaluation: The macroscopic evaluation of crude drugs refers to the evaluation of a drug by colour, odour, taste, size, shape, along with some special features like touch and texture, etc. The Macroscopic evaluation is also called Morhological or Organoleptic Evaluation. The morphological evaluation- The parameters used for this type of evaluation include the following:

Colour: Size: Odour: Taste:



Quantitative Microscopy: It involves following different parameters like:

1. Leaf constant: Palisade ratio, Vein islet number and Vein termination, Trichomes.

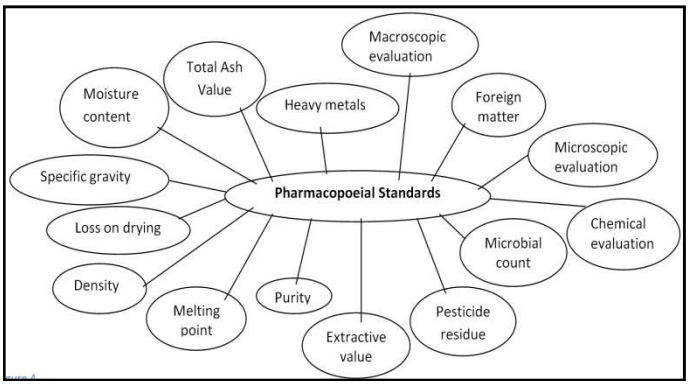
2. Stomatal No., and Stomatal Index.
3. Viscocity, Melting point, Solubility.
4. Quantitative microscopy.
5. Density, Optical rotation
6. Foreign matter, Specific gravity.
7. Organoleptic evaluation.
8. Ash values and extractive values.
9. Moisture content, Refractive Index.
10.Chromatographic and spectroscopic evaluation.
11. Heavy metal determination.
12. Pesticide residue.
13. Microbial contamination.
14. Radioactive contamination.

Standardisation of Finished Products: Although the raw materials used in the formulation were standardised, it becomes mandatory to check the quality of the final product. Following parameters are to be adopted in order to standardise an Ayurvedic formulation as per Ayurvedic Pharmacopoeia of India

***Organoleptic*:** Physical characteristics like viscosity, particle size, specific gravity, specific rotation, refractive index, etc..,

Chemical characteristics that include chemical tests for identification and bio-assay procedures.
Biological activity (Efficacy and toxicity)
Microbiological examination.
Storage, Packing and Labelling.

Pharmacopoeial standards



Physico-chemical parameters

Ash values: Total, Acid insoluble, Water soluble ash values.
Extractive values: Hot water extraction, Cold maceration, Ethanol, Ether and Chloroform.
Volatile matter: Loss on drying.
Volatile oils: by steam distillation.
pH Value

Determination of Crude fibers.
Determination of Moisture content.
Detection of Alkaloids
Detection of Carbohydrates and starch
Detection of Glycosides
Detection of Phytosterols
Detection of Fixed oils and fats
Detection of Saponins
Detection of Phenolic compounds
Detection of Tannins
Detection of Protein and free amino acids
Detection of Gums and mucilage
Detection of Volatile oils

There are basically two techniques used for standardization these are chromatographic fingerprinting and DNA fingerprinting.

Chromatological parameters

TLC (Thin Layer Chromatography), HPTLC (High Performance Thin Layer Chromatography),
HPLC (High-Performance Liquid Chromatography)
Capillary Electrophoresis (CE)
CE Diode Array Detection (CEDAD)
HPLC –Mass Spectroscopy (HPLC–MS)
HPLC –Nuclear Magnetic Resonance Spectroscopy (HPLC–NMR)
Liquid Chromatography- Mass Spectroscopy (LC-MS)
Liquid Chromatography- Nuclear Magnetic Resonance (LC-NMR)
Gas Chromatography (GC-MS)
Supercritical Fluid Chromatography (SFC)

DNA fingerprinting

Genetic Marker

Some commonly used types of genetic markers are
RFLP (or Restriction fragment length polymorphism)
AFLP (or Amplified fragment length polymorphism)
RAPD (or Random amplification of polymorphic DNA)
VNTR (Variable number tandem repeat)
MSP (Micro satellite polymorphism)
SNP (or Single nucleotide polymorphism)
STR (or Short tandem repeat)
SFP (or Single feature polymorphism)

Biological parameters

Bitterness value: unit equivalent bitterness of standard solution of Quinine HCl.
Hemolytic property: by comparison with standard reference solution of saponin
Astringent property: tannins that bind to standard Frieberg Hide powder
Swelling index: in water
Foaming index: foam height produced by 1g material under specified conditions

Toxicological parameters

These include the various identification procedures:
Pesticide residues: including total organic chloride and total organic phosphorus
Heavy metals: like Arsenic, cadmium, mercury and lead
Microbial contaminations: total viable aerobic count of pathogens; viz. *E. Coli*, *Salmonella*, *P. aeruginosa*, *S. aureous* etc.
Aflatoxins: by TLC using standard Aflatoxins (B_1, B_2, G_1 and G_2)
Radioactive contaminations.

Conclusion

Standardization of herbal drugs is essential in order to assess the quality of drugs, based on the concentration of their active principles. The advancement of analytical techniques will serve as a rapid and specific tool in the herbal research,

thereby, allowing the manufacturers to set quality standards and specifications. It is required to have all the crucial knowledge of the particular drug in respect to various parameters while developing an herbal drug formulation.

Drug standardization has not only to establish reasonable analytical methods for analyzing the active constituents, but many other factors should be concerned, so as to seek marketing approval from regulatory authorities or scientific bodies for therapeutic efficacy, safety and shelf- life of herbal drugs. As well as to conduct or sponsor evaluative studies of their toxicity, acceptability, cost and relative value compared with other drugs used in modern medicine. In this field, WHO guidelines are intended to facilitate development in the herbal industry and for the assessment and registration of such products. Although there are a number of standardization techniques available till date but there is still lot to explore on the subject of standardization of the herbal drugs and new approaches are demanded in order to completely explore the standardization of herbal drugs. Hence, it is our prime duty to prove the efficacy and the power of Ayurvedic drugs to the society in the way in which they will be accepted by all. India can emerge as the major country and play the lead role in production of standardized therapeutically effective Ayurvedic formulations. This can be achieved only if the herbal products are evaluated and analyzed using sophisticated modern techniques of standardization.

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