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Standardization of Unani Medicines-Parameters and Exigency: A Review

Mohd Rafi Thoker[a*], Mir Yousuf Ali[b], Zaibunnissa Begum[b], Syed Khalid Murtaza[a]

[a] *Department of Saidla and Ilmul Advia Govt. Unani Medical College Kashmir, India*

[b] *Department of Ilmul Advia, Govt. Nizamia Tibbi College, Charminar, Hyderabad, India*

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ABSTRACT

The use of unani medicines is one of the oldest forms of healthcare known to humanity and has been used in all cultures throughout history. Unani medicines derived from plants are being increasingly utilized to treat a wide variety of clinical diseases .Our dependence on medicinal plants has in no way been minimized by the use of modern system of synthetic drugs. Demand for medicinal plant is increasing in both developing and developed countries due to growing recognition of natural products, being non-narcotic, having no or minimal side-effects, easily available at affordable cost and sometimes the only source of health care available to the poor. A marked growth in the worldwide phytotherapeutic market has occurred over the last 25 years and has thus attracted the interest of most large pharmaceutical companies to manufacture herbal preparations. However in this techno-sawy era, various challenges are encountered with herbal medicines including unani medicines like assessment of safety and efficacy of quality control, safety monitoring, regulatory status, etc. The exigency of standardization of Unani medicine has arisen to combat these challenges. Thus standardization of Unani medicines (both single and compound) has become rudimentary. Standardization of a drug means confirmation of its identity, quality and purity throughout all phases of its cycle i.e. its preparation, shelf life, storage and uses by various parameters. WHO has given various parameters for the process of standardization and evaluation of herbal drugs? These include organoleptic, botanical, physical, chemical and biological. These parameters provide requirements for the development of Unani medicine for its identification, purity, safety and efficacy and are crucial for preparation of accurate and potent formulation to follow GMP and GLP standards as per various regulatory authorities varying in different countries across the globe.

INTRODUCTION

Unani system of Medicine is one of the oldest systems of medicine which originated from Greece. It was Hippocrates (460-377 BC) the physician and philosopher from Greece who freed Medicine from the realm of superstitions and magic, and gave it the status of Science.

The theoretical framework of Unani Medicine is based on the teachings of Hippocrates. With the passage of time a number of other scholars enriched the system considerably. Galen (131-210 AD) stands out as the one who stabilized its foundation on which Arab physicians like Rhazes (850-925 AD) and Avicenna (980-1037 AD) constructed an imposing edifice. From the time of its origin, it went through various ups and downs passing through different civilizations. Unani Medicine got enriched by imbibing what was best in the contemporary systems of traditional medicine in Egypt, Syria, Iraq, Persia, India, China and other Middle East and Far East countries (Heptulla *et al.,* 1991). In olden times, physicians used to treat patients on individual basis, and prepare drug according to the

* Corresponding Author: Mohd Rafi Thoker
E-mail Address: drrafithoker73@gmail.com
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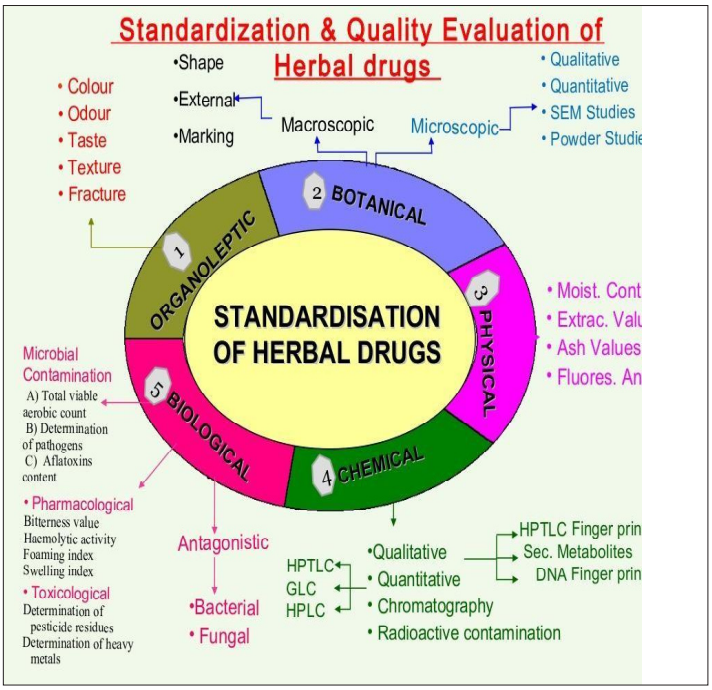
requirement of the patient. But the scenario has changed now; herbal medicines are being manufactured on the large scale in Pharmaceutical units, where manufactures come across many problems such as the availability of good quality raw material, authentication of raw material, availability of standards, proper standardization methodology of single drugs and formulation, quality control parameters. Thus standardization of unani medicine has become compulsory to combat these challenges (Padh *et al*., 2001).

2. Standardization and its Parameter

Standardization of a drug means confirmation of its identity, quality and purity throughout all phases of its cycle i.e. its preparation, shelf life, storage and uses by various parameter (Jacobsen *et al.,* 2010). According to WHO, standardization and quality control of herbals is the process involved in the physicochemical evaluation of crude drug covering aspects, such as selection and handling of crude material, safety, efficacy and stability assessment of finished product, documentation of safety and risk based on experience, provision of product information to consumer and product promotions.



The various parameters for evaluation and standardization of Unani medicines are as follows:-

1. Morphological or Organoleptic Evaluation
2. Microscopic or Botanical Evaluation
3. Physical Evaluation
4. Chemical Evaluation
5. Biological Evaluation

2.1. Organoleptic Evaluation

A sensory or organoleptic character describes colour, odour, taste, texture and fracture. In this methods of description, general condition of the drug size, shape outer surface inner surface are referred. For example brown colours of cinnamon (darcheni), fractured surface in cinchona are important characteristics. Aromatic odour of umbellifrous fruits like apium graveolans (karafas), sweet taste of liquorices (mulethi), ovoid tears of gum acacia (samagi arabi) and disc shaped structure of nux vomica (kuchla) are also examples of this method of evaluation (Udomvarapan *et al.,* 2005).

2.2 Microscopical Evaluation

This method involves microscopical examination of various parts of the drug. This method involves more detailed examination of drug and it can be used to identify organized drugs by their known histological characters. Before examining the drug through microscope the material is suitably prepared by powdering, cutting thin sections of the drug or preparing a macerate. The various parameters involved are quantitative microscopic procedures like palisade ratio, stomata, stomatal number, stomatal index, vein islet number, vein termination number, trichomes, calcium oxalate crystals and quantitative microscopic like lycopodium spore method. For example for Digitalis purpurea these values are as (Salam *et al.,* 2006).

Stomata l index 1.3-3.5

Vein islet number 2.5-3.0

Palisade ratios 3.7-4.2

Stomata number 25-50

Multicellular glandular trichomes

2.3. Physical Evaluation

Physical standards are to be determined for drugs, wherever possible. These are rarely constant for crude drugs, but may help in evaluation, specifically with reference to forgein organic matter, moister content, optical rotation, refractive index ,melting point, ash values, extractive values, volatile oil content, viscosity and solubility in different solvents (Inoma et al., 2017). Drugs should be free from moulds insects, animal, faecal matter and other contamination such as earth stones and extraneous matters. The maximum limit for the foreign matter is defined in the monograph of crude drug. The limit is mentioned for natural drugs of vegetable origin in their respective monograph. Checking moisture content helps reduce errors in the estimation of the actual weight of drug material. Low moisture suggests better stability against degradation of product. Every drug has limited for moister content e.g aloe has moister content not more than 10w/w and ergot has not more than 8w/w.

Certain drugs are found to have the property of rotating the plane of polarized light in the pure state and are described optically active. Honey has optical rotation of +3° to -15° while Eucalyptus oil has optical rotation of 0° to +10°. Refractive index is constant for a liquid and depending upon its purity it is considered as one of the criteria of standardization. For example refractive index for clove oil is 1.527 to 1.535. Melting point is considered one of the parameter for judging the purity of crude drugs. Pure drugs have very sharp and constant melting points .For example bee wax has a melting point between 34-44° C. Ash value is the residue reaming after the incineration of a drug which simply represents inorganic salts, naturally occurring in drug or adhering to it or deliberately added to it, as a form of adulteration. Ash values are determined as total ash, acid insoluble ash, water soluble ash and sulphated ash. These values are useful for detecting low grade products, exhausted products, excess of sand and earthy matter with drug, calcium oxalate crystals, etc. Extractive values obtained by exhausting crude drugs are indicative of approximate measures of their chemical constituents. These values are useful for the evaluation especially when the constituents of a drug cannot be readily estimated by any other means. These values also help in identification of adulterants. These can be water soluble, alcohol soluble or ether soluble.

Volatile oil content has a pharmaceutical significance in aromatic drugs. These drugs are standardized on the basis of their volatile oil content. For example volatile oil content of fennel is not less than 1.4(%w/w) and that of cardamom seeds is not less than 4.0(%w/w). Viscosity of a liquid is constant at given temperature and is an index of its composition and is used as means of standardization of liquid drugs. Liquid paraffin has viscosity not less than 64 centistokes at 37.8°. Solubility of a drug is also affected by adulteration. Castor oil is soluble in only in three volumes of 90% alcohol, while the adulterated form may show good solubility in alcohol.

2.4 Chromatography

The different chromatographic and instrumental methods of analysis are also physical methods of evaluation. The method was first devised by Tswett and latter introduced by Consden, Gorden and Martin in 1944. Chromatography represents a group of methods for separating molecular mixture that depend on the differential affinities of solute between two immiscible phases. One of the phases is a fixed bed of large surface area which is called a stationary phase while the other is a fluid or gas which moves through or over surface is been coated as thin layer on an inert support material. The mobile phase may be a pure liquid solutions or it may be a gas or mixture of gases. There are different types of chromatography like Thin Layer Chromatography (TLC), High Performance Thin Layer Chromatography (HPTLC), Gas Liquid Chromatography (GLC), High Performance Liquid Chromatography (HPLC), Column Chromatography, Gel Permeation Chromatography and Affinity Chromatography (Poole et al., 2012).

2.5. Spectrophotometric Evaluation

Spectrophotometry is a method to measure how much a chemical substance absorbs light by measuring the intensity of light as a beam of light passes through sample solution. The basic principle is that each compound absorbs or transmits light over a certain range of wavelength. This method was first devised by Arnold Beckman in 1940. From the time of its discovery various types of spectrophotometry are in use like ultra violet and visible spectroscopy, infra-red spectroscopy, fluorescence analysis, nuclear magnetic resonance spectroscopy, x-ray diffractions, and radioimmunoassay (Sieh *et al.,* 1982).

2.6 Chemical Evaluation

Most of drugs have definite chemical constituents to which their biological or pharmacological activity is attributed. Qualitative chemical test are used to identify certain drug or to test their purity. The isolation, purification, identification of active constituents is based on chemical methods of evaluation. Qualitative chemical test such as acid value, saponification value etc. Some of these are useful in evaluation of resins (acid value, sulphated ash), balsams (acid value, saponification value and bester values), volatile oils (acetyl and ester values) and gums (methoxy determination and volatile acidity) (Patwekar, *et al.,* 2016).

Preliminary phytochemical screening is a part of chemical evaluation. These qualitative chemical tests are useful in identification of chemical constituents and detection of adulteration (Kumari *et al.,* 2016).

Tests	Reagents used	Colour formed
Tests for alkaloids		
Mayer's tests	Potassium mercuric iodide solution	Creamy precipitate
Wagner's tests	Iodine potassium solution	Brown precipitate
Hager's tests	Saturated solution of picric acid	Yellow colour
Dragendarff's tests	Potassium bismuth iodide solution	Raddish brown precipitate

2.Tests for Proteins and free amino acids		
Millon's tests	Millon reagents	White precipitate
Ninhydrine tests	Ninhydrin solution	Violet colour
Folin	Folin phenol reagent	Blue color
Pauly	Sulphanilic acid, sodium nitrite and sodium carbonate	Cherry red color
3.Tests for carbohydrates and Glycosides		
Fehling's test	Fehling's solution	Brick red ppt formed
Benedict's test	Benedict's reagent	Colored ppt formed
Molisch's tests	Alcoholic a-naphthol+sulphuric acid	Purple to violet colour rings
Barfoed's tests	Barfoed reagents	Red colour(monosaccharide) after 10 min.colour form(disaccharide)
4.Test for fixed oils and fats		
Filter paper test	Filter papers	Oil stains on filter paper indicates presence of fixed oils.
Test for Phenols		
Liebermann's test		Red colored obtained which on dilution with NaOH turned blue
Test for Tanins		
a.	5% of Ferric cholorid solution	A deep blue-black colour is formed
b.	diluteNH4OH and potassium ferricyanide solution.	The solution turns red in colour

2.7. Biological Evaluation

When the estimation of potency of crude drug or its preparation is done by means of its effect on living organisms like bacteria fungal growth or animal tissue or entire animal, it is known as bioassay or biological evaluation. This method is generally utilized when standardization is not adequately done by chemical or physical methods and also for conformity of therapeutic activity of raw drug and finished product (Clark *et al.,* 1993).

In this metod requirements are suitable animal models for testing and controle and methodology for experiment and assessment of results. Various activities which are done in method are hepatoprotective activity, hypoglycemic activity, anti-fertility testing, antispermatogenetic activity, anti-inflammatory activity, neuropharmacological activities, anti-ulcer activity, etc. The other parameter included in biological evaluation are:-

Pharmacological evaluation which includes bitterness values, haemolytic activity, astringency, swelling index, foeming index.

Toxicological evaluation which comprises of detection of pesticide residue and presence of heavy metals lie cadmium and lead.

Microbial contamination like total viable count, determination of pathogens like E .coli, S. aureus, etc. and, aflatoxins by TLC using standard aflatoxins.

3. Exigency (Need) of Standardization

Like other traditional system of medicines standardization of unani medicine has become compulsory as their demand is increasing day by day in both national and international market. After post General agreement on tariffs and trade (GATT) era there is big surge in herbal based medicines and so the unani medicines to find out their potential for treatment and cure of diseases and ailments which can or cannot be cured by well-established allopathic formulations (Lambert *et al.,* 1997).

Thus exigency of standardization of unani medicines has arisen because of following reasons:-

3.1. Identity of Drug

Identification of a drug is of paramount importance in unani medicines for both single and compound formulations. The botanical definition, including genus, species and authority, description, part of the plant, active and characteristics constituents should be specified. Voucher specimens, representing each lot of plant material processed, should be authenticated by a qualified botanist and should be stored for authentication.

3.2. Purity of Drug

Herbal ingredients of high quality should be free from insects, animal matter and excreta. It is usually not possible to remove completely all contaminants; hence specifications and standards are set in order to limit the percentage of such unwanted plant contaminants. Aerobic bacteria and fungi are normally present in plant material and may increase due to

faulty growing, harvesting, storage or processing. It is essential that limits be set for microbial contamination on the bases of different methods of standardization. Some pesticide residue like DDT or other chlorinated hydrocarbons are also impurities of unani medicine. Toxic metals like Lead, cadmium, mercury, thallium and arsenic have been shown to be contaminants. Thus Limit tests are necessary for acceptable levels of pesticide and toxic metal contaminants.

3.3. Safety of Drug

Assessment of the safety of herbal products is the first priority in herbal research because herbal medicines are generally regarded as safe based on their long-standing use in various cultures. However, some of the plants used in herbal medicines can also be highly toxic. The toxic effects of herbal preparation may be attributed mainly to the 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 reports of toxicity could largely be due to misidentification and overdosing of certain constituents.

3.4. Efficacy of Drug

Unani 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, etc and laboratory outcomes include parameters such as reduction of blood glucose, improvement of hemoglobin status, etc. Standardization, however, may sometimes be incompatible with the existing legislative framework and caution is needed regarding the ethical implications of such studies

3.6 Toxicity of Drug

Assessment of toxicity of unani medicine has become essential because other analysis alone is unlikely to reveal the contributions to toxicity itself. In assessing toxicity of a herbal medicine, the dose chosen is very important. Various methods and techniques of standardization like In vivo techniques, in vitro techniques, cell line techniques, and micro- array are adapted to get acquainted with their toxicities.

3.6. Validation of the Drug

Selling adulterated herbal medicines is common both in developed and developing countries. . The validation of herbal products is a major public health concern in this regard. Despite the existence of certain guidelines in some individual countries and those outlined by the WHO there is not yet complete control by the government agencies. Thus it is necessary to ensure scientific validation and periodic monitoring for the herbal products which are marketed as therapeutic agents and whether the products really have any positive effects to cure and reduce the severity of the disease. It is feasible that the introduction of scientific validation by standardization would control the production of impure or adulterated herbal products and would eventually ensure their rational use.

3.7. To follow GMP (Good Manufacturing Practice) and GLP (Good Laboratory Practice) Standards given by WHO

Standardization is also mandatory to comply with the guidelines laid by WHO for quality standardized herbal formulations. These guidelines are as per (Yadav *et al.,* 2008).

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 ethno medical information and biological activity evaluations.

4. Conclusion

Standardization of crude drugs is a code of conduct and an essential need of the time. Substitution and adulteration have now become a very common practice, which makes global crude drug market unsafe for crude drug depending world population. The quality of herbal medicines (unani

Medicine) is the sum of all factors which contribute directly and indirectly to the safety, effectiveness, and acceptability of the product. Thus while developing a herbal drug formulation it is must to have all the related knowledge of its standardization in respect of its various parameters for that particular drug so that correct substance in correct amount for desired therapeutic effects can be manufactured by following monographs of different pharmacopeias.

Conflict of Interest

The authors declared no conflict of interest

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