Review Article

Concise report on Standardization of herbal drugs and its products

Shuchi Mehta[1], Ashish Garg[2], Sweta Garg[2], Manish Kumar[3], Ajay Shukla[3*]

[1]*Department of Pharmacognosy, Guru Ramdas Khalsa Institute of Science & Technology Pharmacy, Jabalpur, India*

[2]*Department of Chemistry and Pharmacy, Rani Durgavati University, Jabalpur, India*

[3]*Department of Pharmaceutical Science, Mohanlal Sukhadia University, Udaipur Rajasthan, India*

Received: 2 July 2018 Revised: 28 July 2018 Accepted: 14 August 2018

Abstract

Utilization of herbal drugs as medicine is the ancients' form of health care and it is used in all cultures all over history. The primeval persons learned by trial and error basis to identified valuable plants. In modern times, more demand increasing towards herbal products because herbal products having low toxicity as compare to other medicine and there is increasing awareness and general acceptability of herbal drugs in today's medical practice. It is however a known fact that over 80% of the world population used herbal medicines and product for healthy living. As well as demand of herbal products increases the need of herbal quality assurance for customer satisfaction also increases. For the prevention of drug adulteration and developed abuse herbal products, WHO have been released guidelines to all herbal industries. The identification of this highly active moiety is an important requirement for Quality control and dose determination of plant related dugs. Standardization of herbal drugs means confirmation or validation of its purity, quality and identity. It is mandatory for every herbal industry. It must need for collection, handling, processing and production of herbal medicine as well as employ such parameters in ensuring the safety and compulsory need for the global herbal market. In this review covers all guidelines which are required for development of herbal products at global scale. This review covers all quality control parameters.

Keywords: Herbal drugs, standardization, quality control

Introduction

The term "herbal drugs" word means by sources plant or part of plants that are used for the treatment of various diseases, in terms of phyto-pharmaceuticals. Firstly it collectcoll or harvesting, drying, storage and then isolated and used (EMEA et al., 1998). The use of herbal drugs as medicine in the earliest form of healthcare known to delicacy and it is used in all cultures throughout history. Ancient humans well known their dependence on nature for a good healthy life and since that time humankind depended on the variety of plant resources for food, shelter, clothing and medicine to cure immensurable of diseases. The first written records explaining the use of plant in the healing of Mesopotamian clay tablet writing and Egyptian papyrus. Led by nature, taste and experience, primeval men and women cured illness by using plant parts, animal parts and minerals that were not a part of usual diet. Primeval persons learned by trial and error basis to identified beneficial plants with helpful effects from those that were inactive or toxic, and also which processing methods or mixtures had to be used to meet steady and ideal results. Even in a ancient cultures ethnic, ancestral or tribal people collect information related to herbal plant and developed which is defined herbal phrmacopeais (Kunle et al., 2012).

The standardization of herbal drugs includes

1. Firstly Authentication of herbal drugs which includes collection, parts of the plant collected botanical identification by botanist.

2. Removal of all Foreign matter (herbs collected should be free from soil, insect parts or animal excreta, etc.)

3. Determination of organoleptic evaluation of herbal drugs as (sensory characters – taste, appearance, odor, feel of the drug, etc.)

4. Tissues of diagnostic significance present in the drug powder.

Address for Corresponding Author:
Mr. Ajay Kumar Shukla
Department of Pharmaceutical Science, Mohanlal Sukhadia University, Udaipur, Rajasthan, India
Email: ashukla1007@gmail.com

DOI: https://doi.org/10.31024/apj.2018.3.3.3

5. Determination of ash values and extractive values.

6. Determination of volatile matter

7. Determination of moisture content determination

8. Chromatographic and spectroscopic evaluation. TLC, HPTLC, HPLC methods will provide qualitative and semi quantitative information about the main active constituents present in the crude drug as chemical markers in the TLC fingerprint evaluation of herbals (FEH). The quality of the drug can also be assessed on the basis of the chromatographic fingerprint.

9. Determination of heavy metals – e.g. cadmium, lead, arsenic, etc.

10. Determination of pesticide residue – according to WHO and FAO (Food and Agricultural Organization) set limits of pesticides, which are usually present in the herbal sources. These pesticides are mixed with the herbs through the time of cultivation. Mostly pesticides like DDT, BHC, toxaphene, aldrin source serious side-effects in human beings if the crude drugs are mixed with these agents.

11. Microbial contamination – generally medicinal plants having bacteria and molds are coming from soil and atmosphere. Determination of the limits of E. coli and molds clearly throws light towards the harvesting and production practices. These substance known as afflatoxins will produce serious side-effects if taken along with the crude drugs (Patil et al., 2011).

Identification and standardization of herbal active compounds

The identification of purely herbal active moiety is a significant requirement for Quality control and dose purpose of plant related dugs. A traditional herbal plant can be checked as an artificial laboratory as it produces and contains chemical substances. Those substances, responsible for biological activity of the herbal plant, are mostly secondary metabolites. for example, of Alkaloid constituents, are nitrogenous principle organic moiety combine with acid to form crystalline salt and also herbal plants contains flavonoids, Resin, Oleoresins, lactones, saponin and volatile oils. Investigation of phytochemical screening of the medicinally herbs, not done in proper way in India. This would be useful in standardization and dose determination of any herbal drugs (Waldesch et al., 2003; Sharma et al., 2010). Herbal medicinal plant has played an important role in world health. They are dispersed worldwide, but they are mainly rich in tropical countries. It is well-known that about 25% of all modern medicines are indirectly or directly came from herbal plants. The knowledge of herbal plant based drugs developed gradually and was passed on, therefore, laying the basis for many systems of traditional medicine all over the world. In a number of communities herbal medicine is still a central part of their medical system. The World Health Organization (WHO) has a provided of specific Guidelines for the evaluation of the safety, efficacy and Quality of herbal medicinal drugs or herbal medicines. WHO find out that 80% of the world people now use herbal medicine or drugs, except in some countries herbal medicinal drugs may also used by traditional, natural or in form of inorganic active constituents. Those are the not directly obtained from plant. An herbal medicinal drug is a main constituent in usual medicine and a common ingredient in Homeopathic, Ayurvedic, and Naturopathic and in other medicine system. Herbs are regularly measured as safe toxicity, side effects of allopathic drugs, has led to more increased in numeral of herbal drugs manufacturers. For the past few years, herbal drugs have been mostly used by the citizens with no prescription, Leaves, stem, bark, flower, seeds, roots and extract of all these have been used in herbal medicinal drugs over the thousands of their use (Bhutani et al., 2003).

Official standards

The identification, purity and quality of herbal drugs are determined by reference given in a pharmacopoeia. Pharmacopoeia prescribes like Analytical, physical and structural standards for the herbal drugs. A significant identification and examination of crude drugs is important in processes of herbal formulation because of more diversity and changes in their chemical nature or characters. To reduce this problem all pharmacopeias have certain standards. Specific test for specific plant material are given below. Alkaloids content dragendorff test, Fat content Acid value Iodine value, saponification value molish test carbohyadrates Millon tests Amino acid Volatile oil Hemolytic activity Assay for Phosphate/Aluminium/ Camphor /Potassium /Lead/Iron/Gold/Calcium (Nikam et al., 2012; Pandey et al., 2016; Bodhisattwa et al., 2011). The main objective of these guidelines is to contribute to the quality assurance of medicinal plant materials used as the source for herbal medicines, which aims to improve the quality, safety and efficacy of finished herbal products and minimize the risks involved in any pharmaceutical production that cannot be eliminated through testing the final product (WHO 2002).

Diagrammatic presentation of various standardization and evaluation parameters, using for the herbal products quality control as per WHO guidelines given in figure 1.

Morphological or Organoleptic evaluation

It includes the evaluation of herbal medicinal drugs by size, shape color, odor, taste and particular characteristics like

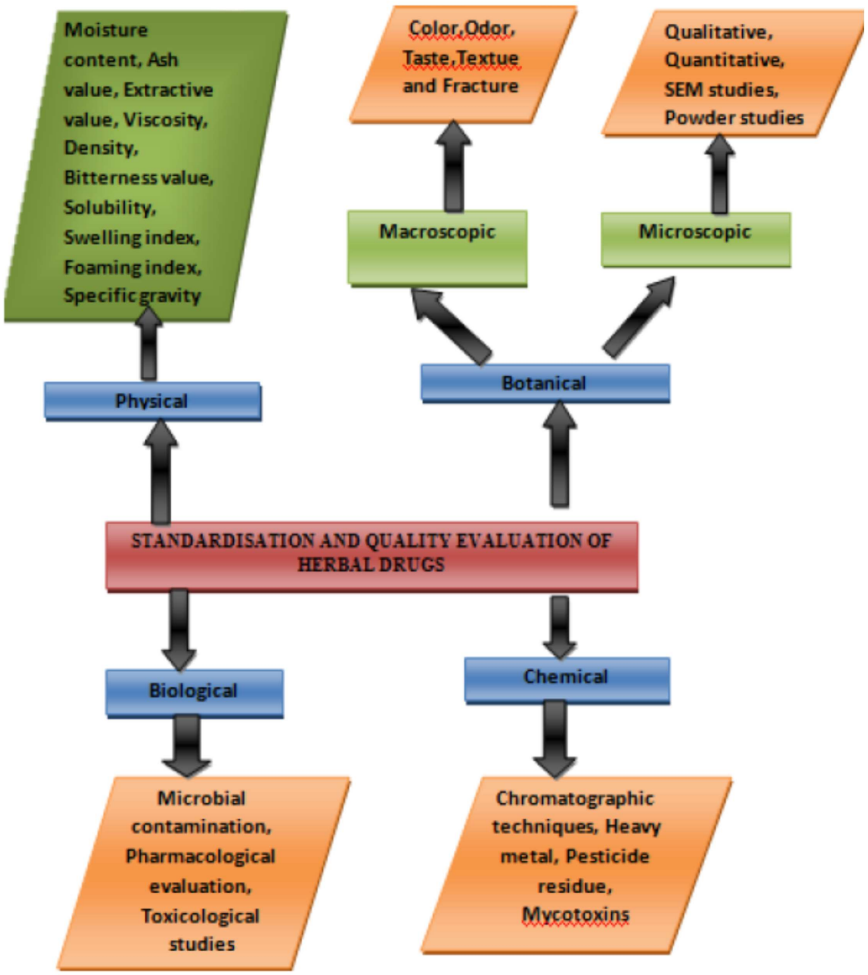

Figure 1. Standardization and quality evaluation of herbal drugs methods

touch, texture etc using sense of organs. This is a method of qualitative evaluation related to the study of morphological and sensory report of whole herbal drugs.eg. Fractured surfaces in cascara, cinchona, and quillia bark and quassia wood are essential individuality. Umbelliferous fruits have aromatic odour and liquorice have sweet taste are the example of this type of evaluation (Kokate et al., 2010; Ansari et al., 2011; Pandey et al., 2013).

Microscopic evaluation

It is used to recognize the organized herbal drugs on the basis of their known histological characters. It is frequently used for qualitative analysis of organized crude drugs in total and powder form with the help of microscope. The inner pseudoparenchyma cells are found round or oval shape. They contain mainly protein and fixed oil. Crude drugs are microscopically identified by taking thin TS (Transverse section), LS (Longitudinal Section) in a bark, wood and leaf of plant. The different parameters included in microscopy are given bellow.

I. Stomata II. Trichomes III. Leaf Content IV. Quantitative Microscopy

Some Microscopic Identification tests are given below (Pandey et al., 2013; WHO et al., 1988; Shukla et al., 2013).

1. Starch test: Hemicellulose T.S. of Crude drug + 1 Drop of Iodine Solution Blue color

2. Mucilage test: Ruthenium Red Pink color

3. Lignin test: Lignin T.S. of crude drug + 1 drop of phloroglucinol + 1 drop of HCL Pink color

Chemical evaluation of herbal drugs

The most of herbal drug contain definite chemical constituents to which their pharmacological and Biological activity depended. Qualitative chemical test used to recognize drug quality and purity. The identification, isolation and purification of active herbal chemical constituents is depends chemical methods of evaluation. Preliminary phytochemical examination is also a part of chemical evaluation. Some Qualitative chemical test for chemical evaluation herbal crude drug includes borntrager test, dragendroff reagent etc. (Sharma et al., 2013; Pandey et al., 2016; Shukla et al., 2013).

Importance parameters of evaluation of herbal medicinal drugs

1. Macro and microscopic assessment: For Identification of right variety and search of adulterants.
2. Foreign organic matter assessment: This involves removal of matter other than source plant to get the drug in pure form
3. Determination of ash value: helpful in determining the quality and purity of crude drugs, especially in powder form. The objective of ashing vegetable drugs is to remove all traces of organic matter, which may otherwise interfere in an analytical determination.
4. Determination of moisture content: 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.
5. Determination of extractive values: These are indicative weights of the extractable chemical constituents of crude drug under different solvents environment.
6. Determination of crude fibre: This helps to determine the woody material component, and it is a criterion for judging purity.
7. Determination of qualitative chemical evaluation: This covers identification and characterization of crude drug with respect to phytochemical constituent. It employs different analytical technique to detect and isolate the active constituents. Phytochemical screening techniques involve botanical identification, extraction with suitable solvents, purification, and characterization of the active constituents of pharmaceutical importance.
8. Determination of chromatographic examination: Include identification of crude drug based on the use of major chemical constituents as markers

Determination of Foreign Matter

Herbal medicinal drugs should be prepared from the authenticated part of the plant. They should be totally free from insects or moulds, including visible and excreta contaminant such as stones, sand, harmful and poisonous foreign matter and chemical moieties. Animal objects such as insects and invisible microbial contaminants, which produce toxins, as well as the possible contaminants of herbal medicines. Macroscopic evaluation can easily used to determine the occurrence of foreign matter, although microscopy is essential in certain special cases for example starch intentionally added to “dilute” the herbal plant material (WHO et al., 2003).

% of foreign Organic Matter = N × W × 94,100 × 100/S ×M × P

Where; n = No. of chart particles in 25 field.

S = No. of spores in the same area of 25 fields.

W = Weight in mg of lycopodium taken.

M= weight in mg of the sample

P= number of characteristics particles per mg of the pureforeign matter. 94,000= number of spores per mg of lycopodium (WHO et al., 2004).

Determination of Total Ash Value

Used for determination of quality and purity of a crude herbal drug, using ash of herbal drug because they contains inorganic radicals like phosphates, carbonates and silicates of sodium, Potassium, Magnesium and calcium. Sometimes, inorganic variables like calcium oxalate, silica, carbonate content of the crude drug like affects 'Total ash value'. Such variables are then removed by treating through acid (as they are soluble in hydrochloric acid) and them acid insoluble ash value is determined e. g. Rhubarb, Liquorice etc. The residue after incineration is the total ash content of the crude herbal drug, which simply represents inorganic salts, naturally found in drug or adhering to it or deliberately added to it, in the form of adulteration of herbal drugs.

Two types of total Ash value mainly:

1. Water soluble Ash value 2. Acid-insoluble Ash value.

Determination of Extractive Values

The herbal extracts obtained by exhausting crude drugs are indicative of approximate measure of their chemical constituents. The varieties of solvent are used for determination of extractives. These are classified as fallows.

1. Water soluble extractives values. 2. Alcohol Soluble extractives values. 3. Ether Soluble extractives values.

Determination of heavy Metals

In general, quantitative and limit tests correctly determine the concentration of heavy metals in the form of impurities and contaminants. The heavy metals like Arsenic, mercury, lead, thalium, and cadmium have been exposed to be contaminants of few herbal ingredients. A simple determination of heavy metals, using pharmacopeias methods and it is based on color reaction with special reagents such as diethyldithiocarbonate or thioacetamide and amount is determined by comparison with a standards. The methods usually used for analysis are inductive coupled plasma (ICP), Netron activation analysis (NAA), Atomic Absorption Spectrophotometry (AAS) etc (Watson et al., 1999; WHO et al., 2007).

Determination of Radioactive contamination

The microbial growth in herbal medicinal drugs is usually avoided by irradiation. Dangerous contamination may be

the result of a nuclear accident. The WHO, in close support with several other international organizations, has developed guiding principle in the event of a wide spread contamination by radio nuclides resulting from major nuclear accidents. The nuclear accident in chernobyl and Fukushima may be severe and depend on the specific radionuclide, the stage of contamination and the quantity of the contaminant taken. Examples of such radionuclides include extended lived and short lived fission products, actinides and activation products (28, AOAC et al., 2005; De Smet PAGM et al., 1992).

Determination of pesticides residue

Determination of pesticides residues are any particular substance in food, agriculture commodities or animal feed resulting from the use of pesticides. Herbal medicinal drugs are prone to hold pesticide residue, which gather from agricultural practices, such as Spraying, behavior of soil during cultivation and addition of fumigants during storage. The Pesticides mainly contain chlorine in the molecules, which can be determined by analysis of chlorine; insecticides containing phosphate can be identify by measuring total organic phosphorus. The varieties of methods are used to measure pesticides by GC, MS, OR GCMS. Some simple methods are also published by the WHO and Europian pharmacopeia has in general limits for pesticides residue in herbal medicine (Bjaj et al., 2012).

Determination of specific optical rotation (Shukla et al., 2013)

Determination of Specific rotation formula -D25= 100 × φlc

Where: φ = corrected observed rotation in drug at-25°

D = d line of sodium light

l = length of the polarimeter tube in done.

c = concentration of substance in percent w/v.

Methods of Standardisation of Ayurvedic medicines

1) Raw material standardization

2) In process standardization

3) Finished product standardization

1. Raw material identification and standardization

Under this process following parameters considered carefully. Area of the collection, parts of the plant, the regional situation, botanical identity, microscopic and histological analysis, taxonomic identity, Foreign matter, Loss on drying, swelling index, foaming index, ash values, extractive values, Chromatographic, spectroscopic evaluation, Determination of heavy metals, pesticide residues, Microbial and Radioactive contamination proper way.

2. In during process standardization

In during process standardization is the key method for the development of quality herbal products. So the standard operating process should be pursuing strictly, if other substances are added in through manufacture in order to adjust the herbal formulations. A method for qualitative, quantitative and where possible, the assay of the plant preparation should be added. If identification of a bioactive principle is not possible, it should be sufficient to recognize a characteristic substance or mixture of herbal medicinal substances to ensure consistent quality of the product.

3. Finishing product

Prepared finished product should have standard nature of characteristics. All information associated to product formula, including the exact amount of recipients, should be described in specify. A finished herbal product specification should be defined to ensure and validated consistent quality of the product. The finished herbal product should fulfill with general requirements for particular dosage forms and quantity. The processes involves wide array of scientific screening like as physical, chemical and biological evaluation employing various analytical methods and tools. The specific object of such investigation in validate herbal quality are as varied as the processes used. Analytical Specifications of Herbal products followed as per requirement according to official monograph (WHO) and form of the medicine. Following mentioned different products specifications are (WHO et al., 1998; Calixto et al., 2000):

- Examination of Colour, Odour
- Determination of total – ash
- Determination of acid – insoluble ash
- Determination of water & Alcohol-soluble extractive
- Determination of viscosity
- Determination of refractive index
- Determination of specific gravity at 250 C.
- Determination of alcohol content Test for methanol.
- Determination of total acidity.
- Determination of no. reducing and reducing sugar
- Determination of PH
- Determination of total sugar content
- Determination of loss on drying at 105 ºC
- Determination of particle size (80-100 mesh for Churna; 40- 60 mesh for Kvathachurna)

- Determination of weight variation
- Determination of disintegration time -Not more than 15 min
- Identification test of TLC/HPTLC/GLC
- Determination of Assay
- Determination of heavy/Toxic metals: Lead, Cadmium, Mercury, Arsenic
- Determination of microbial contamination: Total bacterial count, Total fungal count
- Determination of specific Pathogen: E. coli, Salmonella spp. *S. aureus, Pseudomonas aeruginosa*
- Determination of pesticide residue: Organochlorine pesticides, Organophosphorus pesticides, Pyrethroids
- Determination of aflatoxins (B1, B2, G1, G2)

Advanced techniques and standardization of herbal drugs and its products

Quality control of herbal preparation is a tedious and difficult job. Hence in standardization process of herbal medicinal drugs and its prepared formulations are now days analyzing by using hyphenated techniques based. Various advanced these technologies are HPLC, HPLC-MS, GC-MS and FTIR etc. These modern and fingerprint analysis techniques is the most effective tool for quality control of herbal medicines because of its accuracy and more reliability. By these techniques that determines the correct concentrations of potent bioactive chemical constituents and a set of distinctive chemical substances in herbal drugs. Knowing the relative concentrations is a means of assuring the best quality of herbal products have or not. It can serve as an important tool for identification, authentication and quality control of herbal drugs (Usha et al., 2010).

Future prospective

Standardization of herbal drugs means confirmation or validation of its purity, quality and identity. It is mandatory for every herbal industry, follow as guidelines of WHO and maintain the quality of products. Its need starts from collection, handling, processing and production of herbal medicine as well as employ such parameters in ensuring the safety and compulsory need for the global herbal market. The global herbal market increasing suddenly and India cuoild play key role. Hence it is mandatory to follow all the factors or rule which affecting the quality of herbal products, international level or export quality. These factors which are responsible for quality of herbal drugs or products should maintain and improve the bioactive potency of products. Who want to lead in market globally. Others consideration keep maintain as related to quality of herbal drugs may need more complete information on aspects of herbal products. As the variety of seeds, condition of cultivation and harvesting represent an important aspect in producing a reproducible quality of herbal medicinal products. Quality of herbal products are depends on physical, chemical, biological factors, hence assessment of these factors should be done, validate and documented. This plays a very important role in the identification and purity of drug. All these parameters are mandatory for the development, validation and export quality of herbal drugs.

Conclusion

Ayurveda is one of the most famous oldest therapeutic systems that has nourished and flourished from earliest ages till date. India can come into sight as the major country and playing the lead role in improvement of standardized, therapeutically effective ayurvedic formulation and development. India may explore to investigate the medicinally importance of herbal plants. This can be happen, only if the herbal formulated products are proper way evaluated and analyzed by using sophisticated hyphenated modern techniques like as UV spectroscopy, TLC, HPLC, HPTLC, GC-MS, LC-MS spectrofluorimetric and other methods. The determination of general peaks in a set of chromatographic fingerprints gives useful qualitative and quantitative analytical information on the distinctive components of herbal medicines investigated. Consequently chromatographic fingerprint analysis provides potentially useful quality control tool for standardization of herbal medicines.

Conflicts of interest: None

References

Ansari SH. 2011. Essentials of Pharmacognosy, Birla Publications Pvt Ltd.

AOAC. 2005. Official Methods of Analysis of AOAC International, 18th edn. AOAC International, Gaithersburg, MD,

Bajaj J, Dave V, Sharma S, Shukla A, Chakole RD. 2012. Pharmacognostical and Phytochemical Studies on Achyranthes Aspera. World Journal of Pharmacy and Pharmaceutical Sciences, 1(4):1316-1331.

Bhutani KK. 2003. Herbal Medicines an Enigma and Challenge to Science and Directions for New Initiatives. Indian Journal of Natural Products, 19 (1):3-8.

Bodhisattwa M, Nagori BP, Rambir Singh. 2011. Recent Trends in Herbal Drugs: A Review. International Journal

of Drug Research and Technology, 1(1):17-25.

Calixto JB. 2000. Efficacy, Safety, Quality Control, Marketing and Regulatory Guidelines for Herbal Medicines (Phytotherapeutic Agents). Bthraez Imliaend Ijcoiunranl Auls Oef Omf Hedericbaall Adnrudg Bsiological Research, 33:179-18.

De Smet PAGM, Keller K, Hansel R, Chandler RF. 1992. Aristolochia species In: Adverse Effects of Herbal Drugs, Springer-Verlag, Heidelberg.

EMEA. 1998. Quality of Herbal Medicinal Products. Guidelines. European Agency for the Evaluation of Medicinal Products (EMEA), London.

Kokate CK, Gokhale SB, Purohit AP. 2010. pharmacognosy, Nirali prakashan, Pune.

Kunle F, Oluyemisi, Egharevba, O Henry, Ahmadu, O Peter. 2012. Standardization of herbal medicines- A review. International Journal of Biodiversity and Conservation, 4 (3):101-112.

Kunle OF, Egharevba HO, Ahmadu PO. 2012. Standardization of herbal medicines-A review. International Journal of Biodiversity and Conservation, 4(3)101-112.

Nikam PH, Kareparamban, Jadhav A, Vilasrao K. 2012. Future Trend in Standardization of Herbal Drugs. Journal of Applied Pharmaceutical Sci. 02 (06):38-44.

Pandey P, Garg A, Shukla A. 2016. Preliminary phytochemical and physicochemical Investigation and thin layer chromatography of *Butea monosperma* flower extract. Journal of Medical Pharmaceutical and Allied Sciences, 1-10.

Pandey P, Sharma P, Gupta R, Garg A, Shukla A, Nema N, Pasi A. 2013. Formulation and Evaluation of Herbal Effervescent Granules Incorporated With Martynia Annua Extract. Journal of Drug Discovery and Therapeutics 1 (5):54-57.

Patil S, Zafar S, Bapat US, Bhoir M. 2011. Standardization and Stability Study of Jawarish-eBisbasa, a Unani Formulation, Biological Forum. An International Journal, 2011; 3(2):14-17.

Quality Control Methods for Medicinal Plant Materials (WHO). 2002. Geneva, A.T.T.B.S. Publishers and Distributor Delhi.

Sharma P**,** Pandey P, Gupta R, Roshan S, Jain AP, Shukla A. 2013. Development of Quality Control Parameters for Henna Powder. International Journal of Pharmaceutical Sciences Review and Research 21(1):293-295.

Sharma PP. 2010. How to Practice Gmps Vandana, Publications, 6th edition.

Shukla A, Gupta R, Sharma P, Jain AP. 2013. Comparative Study of Microwave Assisted With Conventional Extraction of Calcium Sennosides from Senna Leaf. Research Journal of Pharmaceutical, Biological and Chemical Sciences, 4(3):103-108.

Usha K, Salim K, Mirza KJ, Mauji R, Abdin MZ. 2010. SCAR markers: A potential tool for authentification of herbal drugs. Fitoterapia, 81: 969-976.

Waldesch FG, Konigswinter BS, Remagen HB. 2003. Herbal medicinal products- Scientific and Regulatory Basis for Development Quality Assurance and Marketing Authorization. Published by Medpharmstuttagart and CRC press, Washington DC, 37-52.

Watson DG. 1999. Pharmaceutical Analysis. Churchill Livingstone, Edinburgh.

WHO. 1988. Quality Control Methods for Medicinal Plant Materials. World Health.

WHO. 1998. Quality Control Methods for Medicinal Plant Materials, World Health Organization, Geneva.

WHO. 2003. Guidelines on Good Agricultural and Collection Practices (GACP). World Health Organization, Geneva.

WHO. 2004. Guidelines on Good Agricultural and Collection Practices (GACP) for Medicinal Plants. World Health Organization, Geneva.

WHO. 2007. Guidelines for assessing quality of herbal medicines with reference to contaminants and residues. World Health Organization.

Williamson E, Okpako DT, Evans FJ. 1996. Pharmacological Methods in Phytotherapy Research, Preparation and Pharmacological Evaluation of Plant Material.John Wiley and Sons, Chichester.