Quality Aspects of Herbal Drugs

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***Abstract*— The safety and efficacy of the herbal medicine is based on their quality. As there is growing demand of herbal medicines, there is a need to assure their quality. Near about 80% of the population is depending on the herbal drugs for the prevention, cure, and treatment of disease, therefore to maintain the quality of herbal drugs is vital element. So the different chemical, phytochemical tests, analytical techniques are used for determining the quality aspects of the herbal materials in the herbal pharmaceuticals. The present review is focused on the various quality control tests for herbal drugs such as organoleptic evaluation, chemical evaluation, foreign matter, stability determination, analytical evaluation, etc. we have also discussed the benefits of quality control of herbal medicines. This will assist in maintaining the quality standards of the herbal drugs, which is the challenging task and need of the moment in the quality assurance and pharmaceutical research.**

***Index Terms*— Herbal drugs, quality control, evaluation, standardization.**

I. INTRODUCTION

Herbal medicines are those with active ingredients obtained from plant sources such as leaves, roots, flowers, barks, rhizomes, stems, etc. These are used worldwide for the prevention and treatment of many chronic and chromic conditions such as cardiovascular diseases, depression, immunity system diseases, inflammation, prostate problems, kidney diseases, etc. Over the last few decades, the development and production of chemically synthesized drugs have increased. However, most of the population still relies on herbal medicines. The safety and efficacy of herbal drugs is based on their quality and therefore it is necessary to maintain their quality [1]. Quality is the main concern to humans in all aspects of life and when it comes to the 'quality of pharmaceuticals' it is of extreme important as they are used for the betterment of the people. They have to undergo various quality control tests and evaluation parameters before being marketed. Unfortunately there are no strict norms for herbal medicines as compared to the synthetic drugs. This leads to decreasing quality of the herbal drugs by intentional and unintentional adulteration, spurious drugs, substitution drugs, and many other ways that are responsible for lowering quality of herbal medicines. So it is essential to control the 'Quality standards' of the herbal drugs and products for the well- being of human kind [2].

II.BENEFITS OF QUALITY CONTROL OF HERBAL MEDICINES

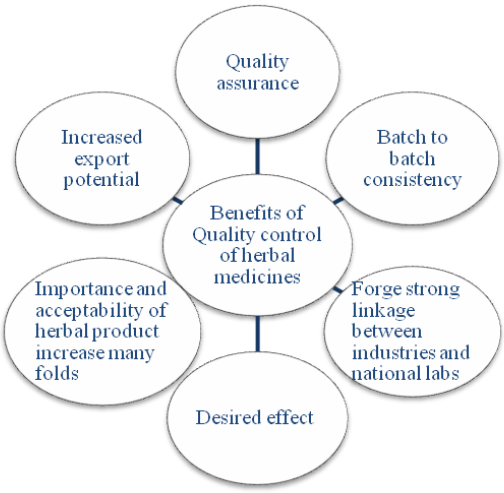

Fig 1: Benefits of quality control of herbal medicines.

III. QUALITY CONTROL PROCEDURES FOR HERBAL DRUGS

A. Organoleptic evaluation

Morphological study includes morphological and organoleptic evaluation. phological evolution involves evaluation of the drug by size, shape, colour, odour taste special features. This type of evaluation varies from one morphological part to another; ur and taste remain same parameters for all parts. It comprises detailed biological macroscopic and microscopic illustration of the physical characteristics

of all plant that can be used to make sure both identity and purity [3]. Organoleptic evaluation of herbal product plays a vital role in judging the censoring acceptability or non-acceptance of herbal items in the market. Physical parameters involve color, odor, appearance, clarity, viscosity, moisture content, pH, etc. [4]. Color of herbal medicine may be white, off white, yellow, brown, buff,etc. Odour of the drug may be distinct that is characteristic or indistinct. Odour may aromatic particularly for volatile oil containing drug, e.g. Mentha leaf. If the drug is deteriorated odour becomes less distinct. Odour may be spicy, e.g. Cinnamon. If may be balsami, e.g. Balsams or Camphor like or camphoraceous. Taste may be sour (acidic) salty (saline) sweet, bitter, alkaline, metallic, pungent acrid or mucilaginous, e.g. Ginger has pungent taste. Liquorice has sweet, Linseed have mucilagenous taste.

B. Chemical evaluation

Chemical evaluation of herbal drugs includes various chemical tests. These tests include qualitative chemical tests, quantitative chemical tests and chemical assays. Chemicals tests are carried out by using different chemical reagents for identification of nature and quantity of chemical constituents [5].

a. Qualitative chemical tests

These are identification tests for various phytochemical constituents like alkaloids, glycosides, tannins, etc. These chemical tests provide information about nature of active principle. Examples encompassBorntrager test for antraquinone glycoside of 'O' type, Vitali Morin test for tropane alkaloid, Molisch's test for carbohydrates, spot test for identification of fixed oils. These tests are also used to identify antioxidant activity of herbal formulations [6].

b. Quantitative Chemical Tests

Quantitative chemical tests give the amount of active constituent present in the crude drug. Examples include Saponification values for lipids, ester value for volatile oils and acid number for resins.

c. Chemical Assays

Chemical assays give an approximate value of total phyto-chemical constituents present in a crude drug. Examples include total alkaloid in Belladonna leaf, total alkaloid in Ipecacuanha, total resinous principle in Jalap and total vitamins in Cod liver oil.

C. Determination of Ash Values

The ash of the drug organized material is composed of non- volatile inorganic components which under control incineration results in ash emergence. This consists of inorganic material and this value varies within wide limits.

Different types of ash values are used for evaluation of herbal drugs like total ash, water soluble ash and acid insoluble ash. Total Ash value is useful for detection of anycontamination caused by silica, chalk powder, lime or any other earthy matter. Acid insoluble ash is used to detect excessive earthy materials, which has different amount of calcium oxalate crystals in the cells. Water soluble ash is used to evaluate the presence of water exhausted material in herbal drugs. The percentage composition of ash is calculated by the furnace method.

2g of the sample is weighed into a preheated and weighed porcelain crucible.The crucible is inserted into a furnace and regulated to a temperature of 630°C and heated for 3 hours.The set-up is then allowed to cool to room temperature and weighed again. Percentage composition of ash is then calculated [7].

Ash value is determined by using formula[8]

$$Total\ Ash = \frac{Weight\ of\ the\ ash}{Weight\ of\ the\ original\ sample} \times 100\ \%$$

$$Water\ soluble\ Ash = Total\ weight\ of\ ash - Weight\ of\ water\ insoluble\ substance$$

$$Acid\ insoluble\ ash = \frac{100 \times (W2 - W1)}{W}$$

Where, W1- weight in gm of the empty dish

W2- weight in gm of the dish with acid insoluble ash

W = weight in gm of the sample

Significance: Ash value is used to determine the quality, purity and identity of the drug.

D. Determination of foreign matter

Herbal materials should be completely free from visual signs of polluted by moulds or insects, and

other animal contamination, involving animal dirt. No abnormal odor, discoloration slime or signs of complication should be determined. It is hardly possible to derive marked plant materials that are completely free from some form of innocent foreign matter. However, no poisonous, dangerous or otherwise noxious foreign matter or residue should be allowed [9]. Definition:

Foreign matter is substance containing of any or all of the following [9]:

- Parts of the herbal material or materials else those named with the control identified for the herbal material concerned.
- Any plants part or product of a plant other than that named in the identification and narration of the herbal material concerned.
- Mineral mixtures not adhesive to the herbal materials, such as soil, stones, sand and dirt.

Procedure-

- Weigh a sample of herbal drug. Take the quantity specified in the test.
- Spread this sample in a thin layer. Sort the foreign matter into groups either by visual inspection, using a magnifying lens (6× or 10×) or by using a suitable sieve, according to the requirements for the specific herbal drugs.
- Pass the remainder of the sample through a Number 250 sieve, dust is regarded as mineral admixture.
- Weigh the portions of this sorted foreign matter to within 0.05 gm.
- Calculate the content of each group in grams per 100 gmof air-dried herbal drug sample[9].

E. Determination of bitter value

Bitter substances can be determined chemically. The bitterness value of herbs is described byWHO which compare the threshold Bitter Concentration (TBC) of dilute solution quininehydrochloride. The bitterness value is seen in unit's equivalent to the bitterness of a solution containing 1 g of quinine hydrochloride in 2000 ml. Thus, the bitterness value of the solution (1 gm of quinine hydrochloride in 2000 ml of drinking water) is set at 2×105 units. The method is similar to reported in the European Pharmacopoeia. The following process, based on WHO:

1. Pure drinking water is used for extracting the Upper parts of the herb, for mouth-wash after each tasting, and for dissolution of the quinine.
2. People will avoid from food, drinks and medicaments an hour before the test.
3. Since sensitivity to bitterness varies high between persons and at different times in the same people, each peoples in the test tasted both the herbal drug extract and the quinine solution within a immediately of time.
4. All Subjectsfirst required tasting the drinking water to be used in the test and a solution of 0.059 mg of quinine hydrochloride in 10 mL of that H2O. Only those who sensed no bitterness in the water, but sensed bitterness in the quinine solution shouldinclude in the test.
5. The tasting each series of dilutions of the extract or quinine solution must begin with the lowest concentration in order to maintain sufficient sensitivity of the taste buds.
6. All the solutions and the drinking water for mouth washing should be at 20-25°C.
7. The procedure –
8. Preparation of standard quinine solution- Exactly 0.1 g of quinine hydrochloride is dissolved in sufficient drinking-water to produce 100 mL. Subsequently, 5 mL of this solution is diluted to 500 ml with safe drinking-water to give the stock standard solution of quinine hydrochloride labeled SQ, and contained 0.01 mg of the quinine standard/ml.

Table 1: Preparation of standard solution

Tube no	1	2	3	4	5	6	7	8	9
QS(mL)	4.2	4.4	4.6	4.8	5.0	5.2	5.4	5.6	5.8
Water(mL)	5.8	5.6	5.4	5.2	5.0	4.8	4.6	4.4	4.2

- *Preparation and dilutions of herbal extract (test) stock solution*- Exactly 1 gm of the herb was extracted with Tap water to produce 1000 mL of aqueous drug solution. Subsequently, 5 mL of the extract is diluted to 500 ml with drinking water.

Tube no	1	2	3	4	5	6	7	8	9	10
SE(mL)	1	2	3	4	5	6	7	8	9	10
Water(mL)	9	8	7	6	5	4	3	2	1	0

Table 2: Preparation and dilution of herbal extract stock solution

- *Procedure for the test*- First, of the all participant rinse his or her mouth with drinking-water, and then taste 10 mL of the most dilute solution by Spiral it in the mouth for 30Sec, noting whether

or not the solution tasted bitter. He or she clasps the solution in the mouth for another 30Sec and record whether or not there is a loss of bitterness. Subsequently, the solution is spit out, and the mouth rinsed with Tap water. The participants wait for 10 min before the next higher concentration is tasted. The procedure above is repeated until the dilution with TBC (that is the lowest concentration at which a solution continues to taste bitter after 30 seconds) is attained by the participant. After the first series of tasting (either with the quinine solution or the herbal extract), the mouth is rinsed thoroughly with drinking-water until no bitter sensation remained. A waiting time of 10 minutes must pass before carrying out the second series of tasting. Bitterness value (units/g) is calculated from Formula.

- Bitterness value (units/g) = (2000 x C)/ (A x B)

  Where A = the concentration of the herbal stock solution (SH) in (mg/ml),

  B = the volume of SH (in ml) in the tube with the threshold bitter concentration, and

  C = the quantity of quinine hydrochloride (in mg) in the tube with the threshold bitter concentration [10].

F. Determination of Swelling index-

Many herbal drugs are of specific for the therapeutic or pharmaceutical utility because of their swelling properties especially gums and drugs which contain significant amount of constituents like mucilage, pectin or hemicelluloses. The swelling index is defined as "the volume in mL taken up by the swelling of 1 gm of herbal material under specified conditions." It is determined by adding of water or a swelling agent as specified in the test procedure for each individual herbal material (whole, cut or powdered). The herbal material must be shaken by using a measuring cylinder with glass stopper repeatedly for 1 hour and then allowed the measuring cylinder to stand for a required period of time. The volume of the mixture (in mL) is noted. The mixing of whole herbal material with the swelling agent is easy, but cut or powdered materials requires vigorous shaking at specified time interval to assure equal distribution of the material in the swelling agent.

Procedure [11]:

- Transfer 1gm of herbal drug to a 25 mL stoppered measuring cylinder.
- Fill the measuring cylinder up to 20 mL mark with water.
- Stir gently occasionally during 24 hour and allow to stand for 3 hours.
- Measure the volume occupied by the swollen drug.

G. Determination of Foaming index

Foaming index is a measurement of foaming ability of an aqueous decoction of herbal material and their extract.

Procedure-

- Add 1gm of drug in 100 mL of boiled water. Heat for 30 minutes. Cool and filter into a 100 mL volumetric flask and make up the volume by adding water.
- Pour this solution into 10 different stoppered test tubes with different volumes that is 1 mL to 10 mL. Adjust the volume to 10 mL with water. Shake well for 15 seconds and allow standing for 15 minutes.
- Measure the height of foam.

If height of the foam in every test tube < 1cm then foaming index will be <100.

If height of the foam in every test tube >1cm then foaming index will be >1000. In such a case, 10 mL of the first decoction of herbal drug is needs to be measured by transferring it to 100 mL volumetric flask (V2) and make up the volume upto 100 mL then follow the same procedure.

Foaming index is calculated by using the formula

Foaming index = 1000/a in case of V1

Foaming index = 1000 × 10/a in case of V2

Where, a= Volume (mL) of decoction used for preparing the dilution in the tube where exactly 1 cm or more foam is observed [11], [12].

H. Determination of microorganism

The microbial contamination in herbal drug and products could be due to microorganisms coming from stems, seeds, leaves, roots, rhizomes and flowers from which herbal extracts are prepared [13].

- *Total viable aerobic count (TVC)*

Total viable aerobic count can be done by using these methods: Membrane filtration method, Plate count or serial dilution. Aerobic bacteria and fungi like yeasts and moulds are determined by TVC.

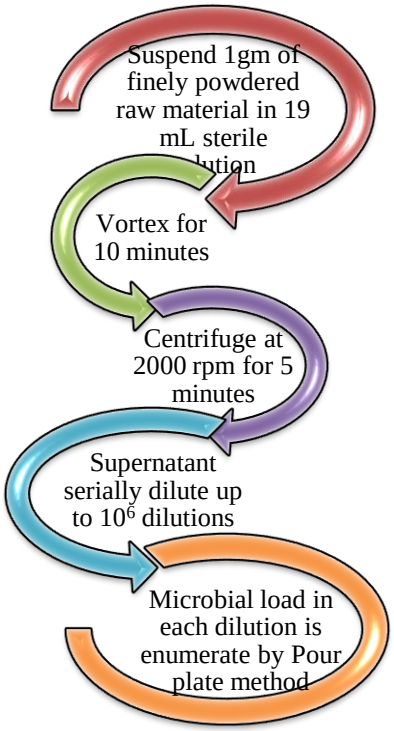

Fig. 2: Flow chart for processing of herbal raw material for enumeration of microbial count.

a. Membrane filtration method

Membrane filter with a pore size of not greater than 0.45 µm is used. The filters with proven effectiveness at retaining bacteria are used such as cellulose nitrate filters are used for oily, aqueous and weakly alcoholic solutions whereas cellulose acetate filters are used for strongly alcoholic solutions. The diameter of membrane filter should be 50 mm. In this technique membrane filter and filtration apparatus are sterilized, solution is introduced, filtered, and examined under aseptic conditions. Then divided into two halves and transferred to culture medium and incubated. After the incubation period it is observed for microbial growth [9].

b. Serial dilution method

Prepare a series of 12 tubes each containing 9 to 10 mL of 'soybean-casein' digest medium. To each of the- first group of 3 tubes, add 1 mL of the 1:10 dilution of dissolved, homogenized material (containing 0.1 gm or 0.1 mL of specimen); second group of 3 tubes, add 1 mL of a 1:100 dilution of the material; third group of 3 tubes, add 1 mL of a 1:1000 dilution of the material; last 3 tubes, add 1 mL of the diluent. Incubate all these tubes at 30–35 °C for at least 5 days. No microbial growth should appear in the last 3 tubes. If the reading of the results is difficult or uncertain, due to the nature of the herbal drug being examined, then prepare a subculture in a liquid or a solid medium. Evaluate the results after a further incubation period. Determine the most probable number of microorganisms per gram or per ml of the material using Table 3.

Table 3: Determination of total viable aerobic count

Number of tubes with microbial growth			Most probable number of microorganisms per g or mL
100 mg or 0.1 mL per tube	10 mg or 0.01 mL per tube	1 mg or 0.001 mL per tube	
3	3	3	>1100
3	3	2	1100
3	3	1	500
3	3	0	200
3	2	3	290
3	2	2	210
3	2	1	150
3	2	0	90
3	1	3	160
3	1	2	120
3	1	1	70
3	1	0	40
3	0	3	95
3	0	2	60
3	0	1	40
3	0	0	23

If, for the first column, the number of tubes showing microbial growth is 2 or less, the most probable number of microorganisms per g or per mL is < 100.

I. Analytical Methods-

Critical to consent with any monograph grade is the need for accurate analytical method for determines identity, quality and relative strength. There are excess of analytical methods available. However, it is frequently hard to know which is the most accurate to

use, but critical among recognized analytical device in monograph standardization is *chromatography*.

Chromatography is a physical separation that sort out the many constituents (chemical constituents) of herbal drugs between the two phases, one of these is an immobile phase and the other is mobile phase. The group separation of components is established on its affinity for the above mentioned two phases [14]. Chromatography is the science which studies the separation of molecules establish on variance their formation and / or composition. In general, chromatography includes moving mixtures of the substances to be separated, the test preparation over a stationary support. Chromatographic separation can be move out using a variation of supports, immobilized silica on glass plates (thin layer chromatography), very sensitive High Performance Thin Layer Chromatography (HPTLC), volatile gases (gas chromatography), paper (paper chromatography), and liquids which may include hydrophilic, insoluble molecules (liquid chromatography).

a. Thin Layer Chromatography

Thin-layer chromatography is especially valuable especially valuable for evaluate determination of small amounts of impurities. As it is virtual and easy to perform, and the appliances required is cheap, the technique is often used for evaluating herbal material and their preparation.

The following parameters should be inflexible on the basis of published pharmacopoeial monographs or established experimentally as the analysis of each isolated herbal material.

- Class of adsorbent and procedure of activation (if no information on the later can be acquired, heat at 110°C for 30 minutes);
- Procedure of preparation and concentration of the test and reference solution,
- Volume of the solution to be put on the plate;
- Drying conditions (including temperature) and procedure of detecting;

TLC is carried on a glass or plastic plate which is coated with a thin and uniform layer of inert adsorbent such as silica gel or alumina. The plates are activated and the sample solution in a volatile solvent is applied by using micropipette or capillary tube to a spot keeping 1 to 2 cm from the bottom of plate. When spot has dried, the TLC plate is placed in a suitable tank with its lower edge immersed in selected mobile phase. The sample rises by capillary action. At the end of the operation the solvent is allowed to evaporate from the plate and the spots are separated, located and identified by different chemical and physical methods. [15]

b. Gas chromatography-mass spectroscopy (GC-MS)

GC-MS (Gas Chromatography-Mass Spectroscopy) is the scientific technique which is the integration of GC (Gas Chromatography) which separates the different element of the mixtures of the chemical compound since the MS (Mass Spectroscopy) which analyze the elements which are being separated by the GC. In case of the herbal product analysis, the extract can be analyzed for the conspicuous component by the GC-MS technique.

The most intrinsic analysis which is executed by GC-MS is the analysis of the thermo-stable volatile compound and the volatile derivatives. Qualitative and quantitative analysis of the volatile oil determination is executed by the GC-MS technique; it is also possible to choose the multiple elements of the compound and drug biotransformates. LC-MS is chromatography more sensitive than the GC-MS but LC-MS cannot analyze the thermally stable volatile components since it is only able to analyze the thermally unstable non-volatile compound. Identification of compound (qualitative), separation of components, and quantification of other compounds are both volatile and non-volatile in a single analysis. It is feasible to carry out the concurrent analysis of different compounds. Matrix-matched calibration standards are used in the gas chromatography to recompense for the matrix effect in this process and this is one of the easy and lean methods. The GC-MS/MS technique performance is affected by the extract purity which is under analysis and is administered to the system, as the biochemical range of the herbs is broad in range and the nature of the herb is also tangled.

c. High Performance liquid chromatography (HPLC)

HPLC is a technique which has been widely used in the quality evaluation of complex herbal drugs due to its ability to detect the presence of active (chemical or biological) markers both quantitatively and

qualitatively [16]. HPLC is also known as "high pressure liquid chromatography." This technique is a type of column chromatography. The stationary phase (silica based or polymer based) consists of small particle (3-50µm) packing contained in a column with a small bore (2-5mm). One end is attached to a source of pressurized mobile phase(liquid eluent). The three types of high performance liquid chromatography most widely used are partition, ion exchange, and adsorption. HPLC is a popular chromatography method for the analysis of herbal medicines because it is easy to learn and use. It is not limited by the volatility or stability of the sample compound. HPLC can be used to detect all the compounds in the herbal medicines. Therefore, during the last decades, HPLC has received the most considerable application in the analysis of herbal medicines. Reversed-phase (RP) columns are widely used in the analytical separation of herbal medicines[17].

The separation carried out in a separation column between a stationary and a mobile phase. The mobile phase is forced into column by a valve in a sample loop steel and sample is injected into mobile phase. The components of the sample migrate through the column at different rates. The component which has more affinity towards mobile phase moves rapidly. The component which has more affinity towards stationary phase moves slowly. After leaving the column, the individual components are detected by a suitable detector and passed on as a signal to the HPLC software on the computer.At the end of this operation a chromatogram is obtained on HPLC software. The chromatogram allows the identification and quantification of the different substances present in complex herbal medicines.

J. Determination of Stability of herbal products

Stability of herbal product is very complicated. Herbal products undergo changes during harvesting, processing, 0manufacturing and storage. These factors affect the stability and shelf- life of the product. These factors include temperature, moisture, exposure to light, exposure to air (oxygen), and exposure to microorganisms. Various approaches are proposed for the herbal products standardization such as determination of biologically active compound and activity based standardization [18]. Bioactivity and concentration of the active ingredient of the drug can be evaluated at different time intervals to determine the shelf- life and expiry of date of the herbal drug. Activity based standardization of herbal drug depends on the inhibition of activity of a particular enzyme related to the disease. Under defined conditions herbal drug should give fixed IC_{50} value for inhibition of enzyme [19]. (IC50 value for inhibition of enzyme- concentration of the herbal drug required to inhibit 50% of a fixed amount of activity of enzyme)

IV.CONCLUSION

Standardization of herbal drug is the confirmation of its quality, purity, efficacy and identity throughout all phases of its cycle. It is necessary to set appropriate standards for Quality evaluation in herbal drugs in order to reduce the risks for public health. These techniques can be used as quality control parameter for determination of the quality of herbal medicines and pharmaceuticals. The presence of microorganisms, foreign matter and inferior quality of herbal drug can adversely affect the health of consumers, creating a health problem worldwide. Therefore, the safety of consumers of herbal drugs is of the extreme importance.

V.CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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