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Who Guidelines on Quality Control and Standardization of Herbal Medicines

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ABSTRACT:
Herbal medicines are being used as medicines from ancient period. The increased use of herbal medicines, and concerns over their safety and effectiveness have clearly raised the need of standardization of these herbal medicines. WHO has set up guidelines for quality control and standardization of these medicines, which are used as a standard by the majority of countries. This WHO guidelines present general consideration on potentially dangerous contaminations and residues in herbal drugs and include guiding principles of assessing quality of herbal drugs in terms of major contaminations and residues. It also recommends analytical methodologies for qualitative and quantitative determination of such contaminations and residues. Within overall context of quality assurance these guidelines intended to give general specialized guidance to Member state in assessing quality relating to safety of herbal materials and products classified as drugs with respects to major and common contaminations and residues. Standardization of the medicinal plants will insure laterally that the plants are conserved for their medicinal and nutritional value. Standardization confirms the safety of the medicinal plant but effectiveness has to be judged clinically or in the laboratory. Significance of toxicological examination has increased manifolds as impurity can occurs at various stages, from collection, warehouse, analysis or processing to extraction of active principles. These parameters should be recorded for years together; their database should be generated, recorded and assayed statistically to see the difference in quality and quantity of the chemical compounds.

KEYWORDS: Herbal medicines, WHO guidelines, quality control, standardization.

I. INTRODUCTION:

Quality Control: The high demand of the herbal medicines worldwide and herbal products makes the global market for their use globally along with it, the safety and quality of the medicinal plants and finished herbal products are a major concern for the health authorities, pharmaceuticals, and the public.

The registration and regulation of the herbal medicines varies from country to country. The regulation of the herbal medicines is categorized either as prescription or OTC medicines.

At the 9th, 10th and 11th meetings of the national centres participating in the WHO Drug Monitoring Programme, the International Conference of Drug Regulatory Authorities (ICDRA), requested the WHO to develop and constantly update the technical guidelines on the quality, safety and efficacy of herbal medicines.[1]

At the WHO informal meeting on the methodologies for the quality control of finished herbal products was held in Ottawa, Canada, 20-21 July in 2001. The participants in the meeting also reviewed the production process of the herbal medicines, right from the starting raw materials to the distribution and supply of the finished herbal products.

The discussions and recommendations from these meetings led to the development of these general guidelines addressing the important issues of safety, quality and efficacy of herbal medicines with special reference to the contaminants and residues.

The World Health Organization (WHO) has published guidelines on quality control of herbal medicines in order to ensure their safety, efficacy, and quality. These guidelines aim to provide a framework for manufacturers, regulators, and consumers to evaluate the quality of herbal medicines.

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The guidelines cover various aspects of quality control, including:

Identity: The guidelines recommend that herbal medicines be properly identified using scientific methods such as microscopy, chromatography, and spectrophotometry.

Purity: The guidelines specify that herbal medicines should be free from contaminants such as heavy metals, pesticides, and microbial pathogens.

Potency: The guidelines recommend that the potency of herbal medicines be determined by quantifying the active ingredients using appropriate analytical methods.

Stability: The guidelines suggest that stability testing should be conducted to determine the shelf-life of herbal medicines.

Safety: The guidelines highlight the importance of ensuring the safety of herbal medicines by conducting toxicological studies and clinical trials.

In addition to these aspects, the guidelines also cover issues related to manufacturing practices, quality assurance, and regulatory requirements. It is important to note that the guidelines are not legally binding, but rather serve as recommendations to guide the development and implementation of national regulations and standards for herbal medicines.

Objectives of the quality control of herbal medicines:

The following points should be considered together, and relating to the Quality Assurance of the herbal medicines regarding safety, for example:

- Quality control methods for medicinal plant materials.[2]
- Good agricultural and collection practices (GACP) for medicinal plants.[3]
- International pharmacopoeia, 4th ed. [4],[5]
- Good manufacturing practices (GMP): main principles for pharmaceutical products.[6]
- GMP: Supplementary guidelines for the manufacturing of herbal medicinal products.[7]
- Guide to good storage practices for the pharmaceuticals.[8]
- Good trade and distribution practices (GTDP) for pharmaceutical starting materials.[9]
- General guidelines for methodologies on research and evaluation of traditional medicines.[10]
- WHO monographs on selected medicinal plants. [12],[13]

Standardization: Standardization is the process of evaluation of the quality and purity of the crude drugs by means of various parameters such as morphological, physical, chemical, microscopical, and biological observations.[14]

The standardization of herbal drugs begins from the collection of herbal drugs to its packaging and use as a medicine.

The difficulties and barriers in the standardization of the herbal drugs takes place due to:

- Variability in the chemical composition of the soil and changes in the climate influencing the range of Phyto-constituents present in the herbal medicines.[15]
- Increase in the deforestation is leading to increase in the number of endangered species of medicinal plants. And this leads to the addition of substitutes and adulterants in the place of herbal medicines, which results in compromise with the safety and decrease in the efficacy of the medicines.

The World Health Organization (WHO) has published guidelines for the standardization of herbal medicines. These guidelines are aimed at promoting the safe and effective use of herbal medicines and ensuring their quality, efficacy, and safety.

The guidelines recommend that manufacturers of herbal medicines follow good manufacturing practices (GMP) to ensure the consistent quality of their products. They also suggest the use of validated analytical methods to determine the identity, purity, potency, and quality of herbal medicines.

Additionally, the guidelines emphasize the importance of conducting preclinical and clinical studies to evaluate the safety and efficacy of herbal medicines. The studies should be conducted using scientifically rigorous methods and should follow ethical principles.

The WHO also recommends that national regulatory authorities establish a regulatory framework for the registration and licensing of herbal medicines. This framework should ensure that herbal medicines are safe, effective, and of consistent quality.

Overall, the WHO guidelines on the standardization of herbal medicines provide a comprehensive approach to promoting the safe and effective use of herbal medicines. By following these guidelines, manufacturers can produce high-quality herbal medicines that meet the needs of

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consumers, and regulators can ensure that these medicines are safe and effective.

Some important terms:

- **Herbal medicines:** These include herbs, herbal preparations, herbal materials, and finished herbal products.[10]
- **Herbs:** The herbs include crude plant material such as the leaves, fruit, flower, seeds, wood, bark, roots, rhizomes, or other parts of plant which may be entire, fragmented or powdered.[10]
- **Herbal materials:** These are the plant or parts of medicinal plants in the crude state. They include herbs, fresh juices, gums, fixed oils, essential oils, resins, and dry powders of herbs.[10]
- **Herbal preparations:** They may include powdered or comminuted herbal materials, or extracts, tinctures, and fatty oils, expressed juices and processed exudates of herbal materials. They are produced with the aid of extraction, distillation, expression, fractionation, purification, concentration, fermentation, or other biological process.[10]
- **Finished herbal products:** Medicinal products which contains active substances exclusively herbal drugs or herbal drug preparations. They may also contain excipients in addition to the active ingredients.[10]
- **Medicinal plants:** A wild growing or cultivated plant, which has some medicinal properties and can be used for its medicinal/therapeutic purposes.[7]

Contaminants and residues in the herbal medicines:

In general, the following terms and their explanations as they relate to contaminants and residues in herbal drugs have been espoused verbatim or where necessary acclimated from thedelineations for pesticide residues in foods, developed by the Codex Alimentarius Commission and the Food and Agriculture Organisation (FAO/WHO) Meeting on Pesticide Residues. therefore, when Member States consider the terms applicable to their individual requirements, these documents should be consulted. The reason for this suggestion is that in future the FAO/WHO Joint Meetings on Pesticide Residues(JMPR) will presumably continue as the group commanded to estimate the safety of pesticides and the FAO/WHO Joint Expert Committee on Food Additives(JECFA) for contaminants in herbal drugs and in foods.

Contamination: The unwanted preface of impurities of a chemical or microbiological nature, or of foreign matter, into or onto a starting material, intermediate product or finished herbal product during production, sampling, packaging or repackaging, Storage or transport.[6]

Cross-contamination: The contamination taking place of any starting material, intermediate product or finished product with any other starting material, intermediate product or finished product.

Foreign matter: Materials which contains any one or all of the following:

- Parts of any specific medicinal plant material or materials other than those which are named with the specified limits for the concerned plant material;
- Any whole or part of or product of organism, other than that which is named in the description of the concerned plant material;
- The mineral admixtures such as stones, dust, soil, sand, glass, metal or plastics or any other extraneous materials. These may be loosened or adhering to those plant materials.[2]

Acceptable daily intake (ADI) of a chemical: A day-to-day input, which, during an entire life span, appears to be without perceptible threat to the health of the consumer, on the base of all the known data at the time of the evaluation of the chemical by the Joint FAO/ WHO meeting on Pesticide Residues. It's expressed in milligrams of the chemical per kilogram of body weight.[16]

Acceptable residual level (ARL): The ARL is given in the milligram (mg) of pesticide per kg of the medicinal plant material and it can be calculated from the maximum acceptable daily intake (ADI) of the taken pesticide on humans, as recommended by the FAO and WHO, and the Mean daily intake (MDI) of the medicinal plant material.[16]

Acute reference dose (ARD): ARD is the quantity of pesticide to which a person is exposed, generally, at one day's regimen of herbal drugs and which results in acute personal effects on the human body. ARD estimations include a safety factor to assure that the senior, babies, children,

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and those whose systems are under stress because of illness, are defended.[16]

Extraneous Maximum residue limits (EMRL): Apesticide residue or a impurity arising from environmental sources(including former farming uses) other than the use of a pesticide or impurity substance directly or laterally on the herbal drug. The attention is expressed in milligrams of pesticide residue or impurity per kilogram of the herbal drug.[16]

Maximum residual limit (MRL): The MRL is the maximum attention of a pesticide residue (expressed as mg/ kg) recommended by the Codex Alimentarius Commission to be fairly permitted(in food commodities and animal feeds). MRLs are grounded on good farming practices(GAP) data established for foods, and foods deduced from commodities that misbehave with the separate MRLs are intended to be toxicologically respectable.[16]

Permitted daily exposure: The term "permitted day-to-day exposure"(PDE) is defined, in the ICH guidelines, as a pharmaceutically adequate input of residual solvents to avoid confusion of differing ADIs for the same substance.[17]

Pesticides: For the purpose of these guidelines, pesticides are defined as any substance intended for precluding, destroying, attracting, repelling, or controlling any pest including unwanted species of shops or animals during product, storehouse, transport, distribution, and processing. The term includes substances intended for use as a plant-growth controller, defoliant, desiccant, fruit thinning agent, or sprouting inhibitor and substances applied to crops either before or after crop to cover the commodity from deterioration during storehouse and transport. The term typically excludes fertilizers and plant nutrients.[16]

Pesticides residue: Pesticide residues are any specified substance in food, farming commodities or animal feed responding from the use of a pesticide. The term includes any derivations of a pesticide, similar as conversion products, metabolites, response products and contaminations considered to be of toxicological significance.[16]

Persistent organic pollutants (POPs): Persistent organic pollutants (POPs) are chemical substances that persist in the atmosphere, bioaccumulate through the food web and pose a threat of causing adverse personal effects to human health and the atmosphere. With the substantiation of long- range transport of these substances to regions where they've nothing been used or produced and the consequent hazards they pose to the atmosphere of the whole globe, the international community has, on several occasions, called for critical global action to reduce and exclude releases of these chemicals.

Tolerable intake: Tolerable intake is defined as an estimate of the intake of a substance over a continuance that is considered to be without perceptible health threat.[18]

Residue solvents: These are residues of organic solvents that are used or produced in the manufacture of and processing of herbal medications products. Solvents are classified by the ICH (CPMP/ICH283/95) according to their implicit threat into

- Class 1 (solvents like benzene to be avoided)
- Class 2 (limited toxic potential like hexane and methanol); and
- Class 3 (low toxic potential like ethanol).

GUIDELINES FOR ASSESSING SAFETY OF HERBAL MEDICINES WITH REFERENCE TO CONTAMINANTS AND RESIDUE:

Determination of Arsenic and toxic metals: In general, quantitative tests and limit tests directly determine the concentrations of poisonous metals in the form of contaminations and impurities. The ultimate is ineluctably present in the samples being tested i.e., herbal drugs and their herbal products.[19]

In general, if the heavy metals burden of the herbal material is unknown, it's suggested that it be determined qualitatively and quantitatively on several batches rather collected over several times. These data should be used to establish acceptance limits that should be checked by applicable limit tests.[20]

Determination of radioactive contaminants:

Methods of measurement: Following a severe nuclear accident, the atmosphere may be polluted with airborne radioactive materials. These may deposit on the plants. Their activity concentration and the type of radioactive impurity can Leaves of medicinal plants. Their activity concentration and the type of radioactive impurity can be measured by the radiation monitoring laboratories of utmost

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of the WHO Member States. The activity concentration of radioisotopes in herbs should be assessed by The competent national radio hygiene laboratories taking into account the applicable International Atomic Energy Agency(IAEA), FAO and WHO. Since radionuclides from accidental discharges vary with the type of installation involved, a generalized methodology of measure isn't yet available. still, should similar impurity be a concern, suspect samples can be analysed by a competent laboratory. Details of laboratory methodologies are available from theIAEA.[20]

Determination of aflatoxins: Determination of aflatoxins should take place after using a suitable clean-up process, during which great care should be taken not to come exposed or to expose the working or general atmosphere to these dangerous and poisonous substances. therefore, Member States should acclimatize their good practices for national pharmaceutical control laboratories and GMP consequently. Only products that have a history of aflatoxin impurity need to be tested. There are specific sampling problems especially of aflatoxins due to the way in which impurity spreads, as described for some food commodities, similar as nuts and corn. This may need to be taken into consideration when sampling, for illustration in terms of sample selection and sample size, and when the analysis is made. Tests for aflatoxins are designed to determine the possible presence of aflatoxins B, B, G and G, which are largely poisonous impurities in any material of plant origin. Country numbers are based on information provided by national health authorities.[21]

Determination of microbiological contaminants:
Microbial contamination limits in herbal materials, preparation and finished products:
Differential limits are set according to the intended use of herbal material and the drugs themselves. Some instances are given here.[19]

Raw medicinal plant and herbal materials intended for further processing:
For impurity of raw medicinal plant, and herbal materials intended for farther processing (including added decontamination by a physical or chemical process) the limits, accommodated from the provisional guidelines established by an international consulting group [19], are given for unprocessed herbal material harvested under adequate aseptic conditions:

- Mould propagules, maximum 10^5 per gram
- Escherichia coli, maximum 10^4 per gram
- Shigella, absence per gram or ml.

Herbal materials that have been pre-treated:
For herbal materials that have been pre-treated (e.g., with boiling water as used for herbal teas and infusions) or that are used as topical dosage forms, the limits are:

- Escherichia coli, maximum 10^2 per gram
- Aerobic bacteria, maximum 10^7 per gram
- Other enterobacteria, maximum 10^4 per gram
- Clostridia, absence per 1 gram
- Yeasts and moulds, maximum 10^4 per gram
- Shigella, absence per 1 gram.
- Salmonellae, absence per 1 gram

Other herbal materials for internal use:
For other herbal materials for internal use, the limits are:

- Yeasts and moulds, maximum 10^3 per gram
- Aerobic bacteria, maximum 10^5 per gram
- Clostridia, absence per 1 gram
- Shigella, absence per 1 gram.
- Escherichia coli, maximum 10 per gram
- Other enterobacteria, maximum 10^3 per gram
- Salmonellae, absence per 1 gram

Herbal medicines to which boiling water is added before use:
For herbal medicines to which boiling water is added before use, the limits are:

- Yeasts and moulds, maximum 10^4 per gram
- Aerobic bacteria, maximum 10^7 per gram
- Other enterobacteria, maximum 10^3 per gram
- Salmonellae, absence per 1 gram
- Escherichia coli, maximum 10 per gram
- Clostridia, absence per 1 gram
- Shigella, absence per 1 gram.

Other herbal medicines:
For other herbal medicines, the limits are:

- Yeasts and moulds, maximum 10^3 per gram
- Aerobic bacteria, maximum 10^5 per gram
- Other enterobacteria, maximum 10^3 per gram
- Clostridia, absence per 1 gram
- Escherichia coli, absence per 1 gram.[19]

MATERIALS AND METHODS FOR STANDARDIZATION OF HERBAL MEDICINES:
BOTANICAL PARAMATERS: [22]

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- **Sensory evaluation**: Visual observation and macroscopy, colour, odour, taste, fracture are the observations made for the identification of the crude drug.
- **Foreign matter**: It should to be determined if the foreign matter is inorganic like; stones, soil, etc or organic like moulds, insects, animal excreta, etc. Foreign matter are considered as:

- Materials which are not collected from the original plant source like the organic foreign matters.
- Parts of the organ or the whole organs from which the drug is derived other than the parts named in the definition and description.

Methods for determination of the foreign organic matter:

- Manual method
- Lycopodium spore method

Microscopy: The identification of histological characters (under low and high power). Study of the individual characteristics in all respect of quantitative and qualitative measurements. Observing and identifying the characteristics in more slides to confirm the particular organised crude drug. And then comparing these characteristics with the characteristics of same powdered form of crude drug which is mentioned in the reference books.

PHYSICOCHEMICAL PARAMETERS:

Chromatographic fingerprinting: [23]

Separation, identification, contamination spotting and assay of herbal medicine in the formulation or in the extract are carried out by following methods- HPTLC, HPLC/ Densitometric chromatography, GLC, TLC.

Significance- The herbal medicine shows variability in its chemical ingredients according to various locations weather. To avoid any erroneous identification chromatographic fingerprint remains the assessment of choice.

Ash values: [24]

The types of ash determined are Total ash, Acid insoluble and water soluble. Ash value is used to determine the quality and purity of the medicine and to establish its identity. Ash contains inorganic radicals lie phosphates, carbonates, and silicates of sodium, potassium, magnesium, calcium, etc. These are present in definite quantity in a particular crude medicine, hence quantitative determination in terms of various ash values helps in their standardization. Ash value is used to determine foreign inorganic matter present as contamination.

Total ash value:

The methodology of total ash is designed to determine the quantity of material that remains after ignition. Ash is classified as physiological ash which is derived from the plant tissue itself and non- physiological ash which is the residue after ignition of extraneous matter (e.g., sand and soil). It's carried out at low temperatures perhaps because alkali chlorides, which are volatile at low temperatures, may be lost. The total ash consists of carbonates, phosphates, silicates, and silica.

Acid insoluble ash:

Occasionally, inorganic variables like calcium oxalate, silica, and carbonate content of the crude medicine affects 'Total cash value'. Such variables are removed by treating with acid (as they're soluble in hydrochloric acid) and acid insoluble ash value is determined. Acid insoluble Ash, Water soluble ash and sulphated ash are also estimated.

Extractive values: [25]

It's useful for evaluation of a crude medicine. It gives an idea about the nature of the chemical components pre-transferred in a crude medicine. Useful for estimation of components extracted with the solvent used for extraction. Employed for material for which yet no suitable chemical or biological assay exists. It can be done by following methodologies Cold maceration, hot extraction, and ethanol.

Moisture content and volatile matter:

The moisture content of the medicine should be minimized in order to prevent decomposition of crude medicine either due to chemical change or microbial impurity. The moisture content is determined by heatinga drug at 105˚c in an oven to a constantweight.

E.g. – Aloe should have moisturecontent not more than 10% w/w Moisturecontent can be determined by followingmethods- Gravimetric, Volumetric, and instrumental.Gravimetric method-Loss on Drying,Volumetric-Azeotropic Toluene distillationmethod,Instrumental- GC, NMR etc.

Volatile oil content:

Volatile oils are the liquid components of the plant cells, immiscible with water, volatile at ordinary temperature and can be steam distilled at

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ordinary pressure. numerous herbal medicines contain volatile oil which is used as flavoring agent. For the medicines containing volatile constituents, toluene distillation methodology/ steam distillation methodology is used to determine the volatile oil contents.

PHARMACOLOGICAL PARAMATERS: [26]

Bitterness value:

Medicinal plants having strong bitter taste are therapeutically used as appetizing agents. The bitterness is determined by comparing the threshold bitter concentration of an extract material with that of quinine hydrochloride. The bitterness value is expressed as unit's coequal to the bitterness of a solution containing 1gm of quinine hydrochloride in 2000 ml.

Method for determination-0.1gm of quinine hydrochloride is dissolved in 100ml drinking water and the stock solution is prepared. Then it is diluted and tested and compared with drug.

Bitterness value in unit per gm = 2000×C÷A×B

Where, A = concentration of stock solution, B = volume of test solution in tube with threshold bitter concentration C = quantity of quinine hydrochloride in the tube with threshold bitter concentration.

Haemolytic property:

Numerous medicinal plant materials, of the families Caryophyllaceae, Araliaceae, Sapindaceae, Primulaceae, and Dioscoreaceae contain saponins. The most characteristic property of saponins is their capability to effect haemolysis; when added to a suspension of blood, saponins produce changes in erythrocyte membranes, causing haemoglobin to diffuse into the surrounding medium. The haemolytic activity of plant materials, or a medication containing saponins, is determined by comparison with that of a reference material, saponin R, which has a haemolytic activity of 1000 units per gm.

Determination- Calculate the haemolytic activity of the medicinal plant material using the following formula: 1000 ×a/b

Where, 1000 = the defined haemolytic activity of saponin R in relation to ox blood, a = quantity of saponin R that produces total haemolysis (gm), b = quantity of plant material that produces total haemolysis (gm).

Astringent property:

It's determined by quantity of tannins present in the medicine Tannins (or tanning substances) are substances able of turning animal hides into leather by binding proteins to form water-insoluble substances that are resistant to proteolytic enzymes. This process, when applied to living tissue, is known as an" astringent" action and is the reason for the therapeutic use of tannins. Chemically, tannins are complex substances; generally occur as emulsions of polyphenols that are difficult to separate and solidify.

Determination of Tannins [27]: Calculate thequantity of tannins as a percentage using thefollowing formula: Where, w = the weight ofthe plant material in grams, T1=Weight ofmaterial extracted in water, T2=Weight ofmaterial not bound to hide powder, T0=Weight of hide powder material solublein water that bind to standard frieberg Hidepowder. [T1-(T2-T0)] ×500/w.

Swelling Index:

The swelling index is the volume in ml taken up by the swelling of 1 g of plant material under specified conditions. Its determination is based on the addition of water or a swelling agent as specified in the test procedure for each individual plant material (either whole, cut or pulverized). It gives an idea about the gum content of the medicine; hence it's useful in the evaluation of crude medicines containing gum.

Foaming index:

Numerous medicinal plant materials contain saponins that can create persistent foam/lather when an aqueous decoction is shaken. The foaming capability of an aqueous decoction of factory accoutrements and their extracts is measured in terms of a foaming index.

Calculate the foaming index using the following formula 1000/a. Where a = the volume in ml of the decoction used for preparing the dilution in the tube where foaming to a height of 1 cm is observed. Saponins give persistent foam when shaken with water. Hence, plant material/extract containing saponins is evaluated by measuring the foaming ability in terms of foaming index.

TOXICOLOGICAL PARAMETERS: [28]

Arsenic and heavy metals:

Impurity of medicinal plant materials with arsenic and heavy metals can be attributed to numerous causes including environmental pollution and traces of pesticides. There are different methodologies to identify the quantity and concentration of heavy metals in herbal medicines. Limit test for arsenic and Limit test for cadmium

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and lead are many of them. The contents of lead and cadmium may be determined by inverse voltammetry or by atomic emission spectrophotometry.Determination- The following maximum amounts in dried plant materials, which are based on the ADI values, are proposed: ▫ lead, 10 mg/kg; ▫ cadmium, 0.3 mg/kg. Stain produced on HgBr2 paper in comparison to standard stain.

Pesticide residues:

Examples of pesticide remnants- Chlorinated hydrocarbons and related pesticides BHC, DDT, Chlorinated phenoxy alkanoic acid herbicides, 4-D;5- T, Organophosphorus pesticides malathion, methyl parathion, parathion, Carbamate insecticides carbaryl (carbaril), Dithiocarbamate fungicides ferbam, maneb, nabam, thiram, zineb, Inorganic pesticides calcium arsenate, lead arsenate, eclectic ethylene dibromide, ethylene oxide, methyl bromide, Pesticides of plant origin tobacco leaf and nicotine; pyrethrum flower, pyrethrum extract and pyrethroids; derris root and rotenoids. Includes total organic chloride and total organic phosphorous.Determination of pesticides- Pesticides should not be more than 1%, an ARL (in mg of pesticide per kg of plant material) can be calculated on the basis of the maximum acceptable daily intake of the pesticide for humans (ADI), as, recommended by WHO, and the mean daily intake (MDI) of the medicinal plant material.

ARL=ADI×E×60/MDI×100 where ADI = maximum acceptable daily intake of pesticide (mg/kg of body weight); E = extractionfactor, which determines the transition rateof the pesticide from the plant material intothe dosage form; MDI = mean daily intakeof medicinal plant product.

Microbial contamination: Impurity either at source or during processing is possible. Maximum possible limits of each organism are given in various manuals. WHO limit for number of micro-organisms per gram of material:

Table 1: Microbial Contamination.

Type of microorganism	Finished product	Raw material
E. coli	10^6	10^2
Salmonella	-	-
Total aerobic bacteria	10^5	-
Enterobacteria	10^3	-

Aflatoxins:

Aflatoxins are naturally occurring mycotoxins produced largely by Aspergillus flavus and Aspergillusparasiticus. The presence of aflatoxins can be determined by chromatographic methodologies using standard aflatoxins B1, B2, G1, G2 emulsions. Determination- IP methodology NMT 2 µg/ kg of aflatoxins B1 & Total aflatoxins 4 µg/ kg USP methodology NMT 5ppb of aflatoxins B1 & Total aflatoxins 20ppb.

Radioactive contamination:

The range of radionuclides that may be released into the atmosphere as the result of a nuclear accident might include long- lived and short-lived fission products, actinides, and activation products. Microbial growth in herbals is commonly avoided by irradiation. This process may sterilize the plant material but the radioactivity hazard should be taken into account. The nature and the intensity of radio-nuclides released may differ markedly and depend on the source (reactor, processing plant, fuel fabrication plant, isotope production unit, etc.). The radioactivity of the plant samples should be checked consequently to the guidelines of International Atomic Energy Agency(IAEA) in Vienna, Australia.

II. CONCLUSION:

The WHO guidelines are followed all over the world but the need of the hour is to modernize these principles with use of newer methodologies of analysis. The herbal medicine assessment in Ayurveda is about the whole medicine rather than concentrating on the active principles or phytoconstituents, therefore finer methodologies of quality control and standardization should be developed. As Ayurvedic medicines are also

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included in the Drugs and Cosmetics Act, 1940 the drugs have to be safe and effective at the same time. This brings about the need for finer quality control and standardization of herbal medicines. We can clearly avoid the external contamination due to the pesticides by organic farming, heavy metal impurity by performing soil analysis and other tests, radioactive impurity isn't truly common in India but it can be prevented by using healthier ways of prevention.

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