A Brief Review on the Standardization of Herbal Medicines

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Abstract
Medicinal plants are an important source of drug production. Medicinal plants and herbal medicines account for a large percentage of the pharmaceutical market. Since the side effects of synthetics are well known, most synthetics are derived from plants. But herbal remedies suffer from the lack of standard parameters. The main limitation is the lack of standardization of raw materials, processing methods and end products, production measurements and the lack of quality control criteria.

Key words: **Standardization, Quality Control, Medicinal Plants, Herbal Medicines**

Introduction

The first sources of drugs come from nature and have been used medicinally since ancient times. People around the world have a unique knowledge of the natural resources they rely on, including amazing botanical expertise. Traditional medicine provides 85% of the world's population with their health needs. Maintaining the safety, quality and efficiency of the facilities and their products is necessary to prevent serious health problems.[1]

Indian health care has a lot of medicine and Ayurveda continues to be a force to be reckoned with modern medicine, especially for the treatment of various chronic diseases.

WHO defines traditional medicine as including diverse health practises, approaches, knowledge and beliefs incorporating plant, animal and/or mineral based medicines, spiritual therapies, manual techniques and exercises applied singularly or in combination to maintain well being as well as to treat, diagnose or prevent illness. WHO has provided some terms related to herbal drugs, according to their definitions.[2]

Need OF Standardization

The new drug system is based on positive test data, toxicological studies and human clinical trials. But pharmaceutical standards for raw materials / finished products are not available. cGMP is not fully defined for the herbal industry, and at least minimum standards for pharmaceutical products are not regulated or regulated. The World Health Organization has established specific guidelines for evaluating the safety, efficacy and quality of herbal medicines. It is not easy to prepare herbal remedies because there are many factors that influence the biological effectiveness and the healing effect. To obtain a high-quality herbal product, proper care must be taken to identify the plants, time, place of collection, extraction and purification, and to determine the combination in the case of multiple medicinal drugs.[3]

Standardization and quality control of herbal crude drug process

According to WHO (1996a and b, 1992), the classification quality control of medicinal plants is a process that include the physical-chemical evaluation of surface coating properties such as selecting and managing raw materials, safety, evaluating the efficacy and stability of the final product, Documenting safety and risk

based one experience, reporting product information to customers and promote the product. It usually focuses on the following indicators:
1.Macro- and micro-examination: to identify the correct varieties and search for counterfeits
2.Foreign organic matter: The removal of materials other than the source plant to obtain the substance in its pure form.
3. Ash values: These are criteria for determining the identity and purity of the material - total ash, fly ash, water-soluble ash and acid-ash- no, etc. Error in estimation of true weight Minimize medicinal substances. Low moisture content indicates better stability the product degradation.
4. Extractable values: These are the index weights of the extractable chemical compounds of the raw material in the environment of various metals
5. Raw Fiber: This helps to determine the components of the wood and is radiological for determining cleanliness.
6. Chromatographic testing: including the identification of raw materials based on the use of key chemical compounds as indicators
7. Quantitative chemical assessment: to estimate the amount of the main classes of compounds.[4]

Method of Standardization

Physical Evaluation - Each monograph contains botanical, macroscopic and microscopic descriptions of the physical characteristics of each plant that can be used to establish identity and purity. Each description accompanied by detailed photos and illustrations that provide visual documentation of the carefully defined property.

Microscopic Evaluation - Complete and accurate identification of plant material requires thorough physical examination. Microscopic analysis of plants is important to confirm the identity of the material and to test for impurities.

Chemical evaluation- This includes the detection, isolation, identification and purification of chemical components. Chemical analysis of the substance is done to evaluate the potency of the plant substance in relation to its active principle Chemical tests may also include a colour reaction test to determine the identity of the substance and the adulterant**.**

Biological evaluation -The pharmacological activity of certain drugs has been used to evaluate and compare those drugs. Analysing live animals and their intact or isolated organs can reveal the potency of a drug or preparation. These analyses are known as bioassays or bioassays

Purity Determination -monograph has standards for purity and other quality indicators mentioned above.

Analytical methods - should adhere to a standard monograph. Analytical methods are necessary to determine identity, quality and relative strength. A number of analysis methods are available. However, it is difficult to know which one is the right one to use, but among the analytical tools known in the monograph standard, chromatography is important.

Quantitative analysis-The most accurate method of quantitative analysis is bychromatogram. The main purpose of the methods is to provide a valid method of measurement. Most of these are related to drug use and symptomatology .[5]

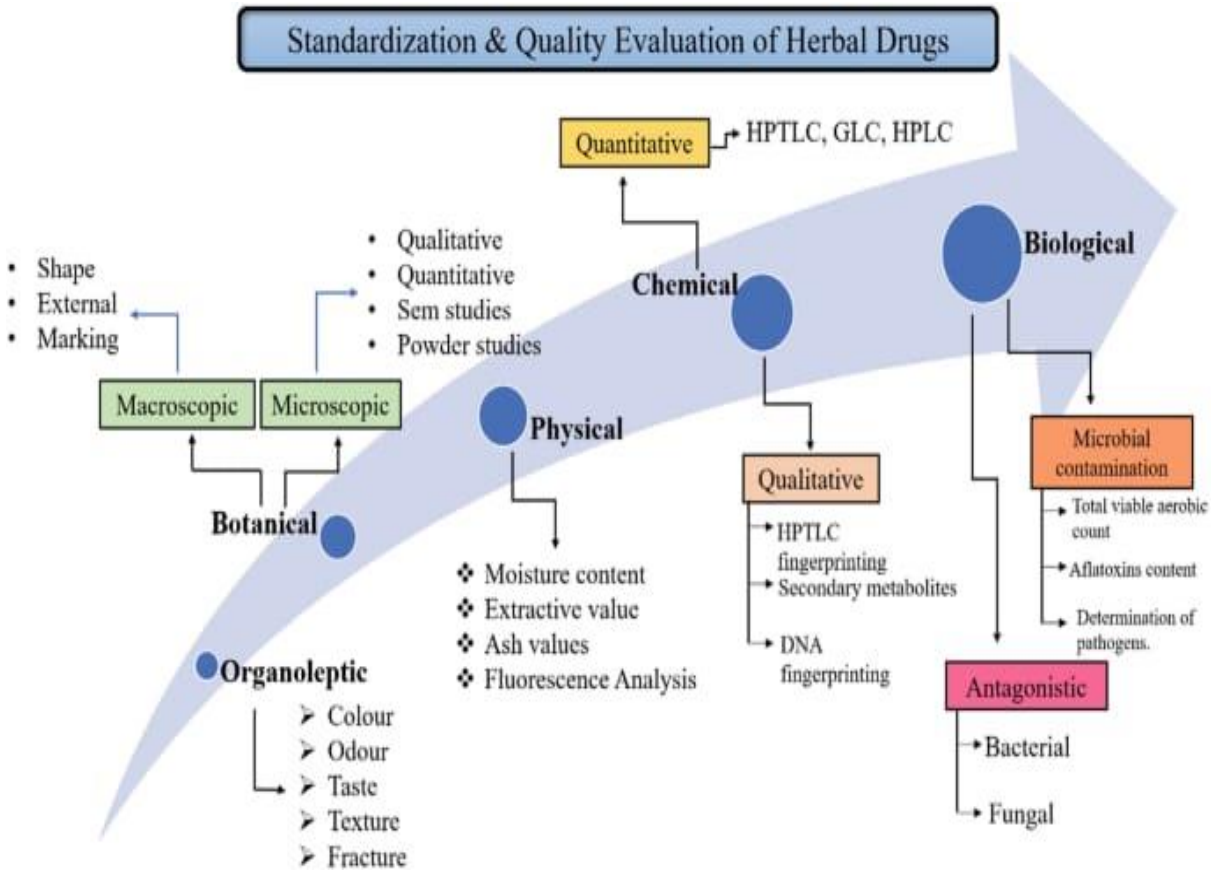

Fig no.1 standardization and quality evaluation

Factor affecting the quality control of herbal drug

Microscopic Evaluation – Quality control of herbal drugs has traditionally been based on the appearance and today microscopic evaluation is indispensable in the initial identification of herbs, as well as, in identifying small fragments of crude or powdered herbs, and detection of foreign matter and adulterants. A primary visual evaluation, which needs more than a simple magnifying lens, can be used to ensure that the plant is of the required species, and that the right part of the plant is being used. At other times, microscopic analysis is needed to determine the correct species and/or that the correct part of the species is present. For instance, pollen morphology may be used in the case of flowers to identify the species, and the presence of certain microscopic structures such as leaf stomata can be used to identify the plant part used. Although this may seem obvious, it is of prime importance, especially when different parts of the same plant are to be used for different treatments. Nettle (Urticaurens) is a classic example where the aerial parts are used to treat rheumatism, while the roots are used for mild prostatic hyperplasia.[6]

Foreign matter -- Herbal medicines must be prepared from the part of the plant mentioned and must not contain other parts of the same plant or other plants. It should be completely free of mold or insects, as well as debris and contaminants such as sand and stones, toxic and harmful external substances and chemical residues. Animal matter such as insects and "invisible" micro-organisms can produce toxins and are also contaminants of herbal medicines. Macroscopic examination becomes easy Sachan et al. International Journal of Phytomedicine It is used to determine the presence of foreign matter, although microscopy is necessary in some special cases (for example, starch added to "water" plant material). In addition, when foreign materials contain, for example, chemical residues, TLC is often required to identify impurities [7, 8, 9].

Ash content -To determine the ash content, the incinerated plant material and residual ash are measured as total ash and non-acidic ash. Total ashis the total amount of material remaining after burning and includes

ash from any part of the plant and ash that does not dissolve in acid. The last one is the residue obtained after boiling all the ash with dilute hydrogen peroxide and burning the rest of the inert material. The second method measures the amount of silica present, especially in sandy loam and soil .[7]

Heavy metal - Pollution with toxic metals can be accidental or intentional. Contamination of heavy metals such as mercury, lead, copper, cadmium and arsenic in herbal medicines can be attributed to many reasons, including environmental pollution, and which may affect the health of consumers.is rare [10].The potential intake of a toxic metal can be determined based on its presence in the product and the prescribed or prescribed dose of the product. This can be incorporated into the toxicity perspective by comparing it to the so-called Provisional Tolerable Weekly Values(PTWI) for toxic metals established by the Food and Agriculture Administration. World Health Organization (FAO-WHO) [11]. Instrumental analyses have to be employed when the metals are present in trace quantities, in admixture, or when themselves have to be quantitative. Generally, the main methods commonly used are atomic absorption spectrophotometry (AAS)inductively coupled plasma (ICP) and neutron activation analysis [12]

Microbial contaminants and aflatoxin -Medicinal plants may be associated with a broad variety of microbial contaminants, represented by bacteria, fungi, and viruses. Inevitably, this microbiological background depends on several environmental factors and exerts an important impact on the overall quality of herbal products and preparations. Therefore, the risk assessment of the microbial load of medicinal plants has become an important topic in the development of new hazard analysis and critical control programs (HACCP). Medicines often bring in different types of bacteria and fungi, which are derived from the soil. Improper methods of harvesting, washing, drying, handling and storage can also cause contamination, which may be caused by Escherichia coli or Salmonella spp, although other bacteria and fungi are also part of the natural microflora, many aerobic bacteria dominant. Laboratory methods for the diagnosis of microbial contamination can be found in popular medicine and WHO guidelines [8]. Limit values are also found insources

Radioactive contamination -However, a nuclear accident can cause serious contamination. The WHO, in collaboration with other international organizations, has developed guidelines for general exposure to radionuclides from nuclear accidents. These publications confirm that health risks from radiation contamination from radionuclides are generally not a major concern, but risks from major nuclear accidents such as Chernobyl and Fukushima. How dangerous it is depend on the specific radionuclide, the level of contamination and how much of the contamination was consumed. Considering the amount of herbal medicine that people consume,it is unlikely that they will cause health problems. Therefore, no limits have been set for radiation contamination [6].

Validation -The validation of herbal products is a major public health concern both in developed and resource-poor countries, where faker selling adulterated herbal medicines are common. In this regard,there is no control by the government agencies, despite the existence of certain guidelines in some individual countries and those outlined by the WHO. If the herbal products are marketed astherapeutic agents, and irrespective of whether the products really have any positive effects to cure and reduce the severity of the disease, it is necessary to ensure scientific validation and periodic monitoring of the quality and efficacy by drug control administrators. It is feasible that the introduction of scientific validation would control the production of impure or adulterated herbal products and would eventually ensure their rational use.This can also lead to industry regulations so that only doctors and health workers can dispense drugs.The method used is to use available compounds that perform similarly in the specified chromatographic systems, and to calculate the retention values and/or retention times relative to these compounds as standards Chemical quality control is designed to identify and isolate active substances. TLC and HPLC are the main analytical

methods that are widely used. In cases where active ingredients are unknown or very difficult, the quality of plant extracts can be assessed with "fingerprint" chromatograms [10]

WHO GUIGLINES FOR QUALITY STANDARD HERBAL FORMULATION

Extraction should be standardized based onactive principles or important compounds andchromatographic fingerprint (TLC, HPTLC, HPLC and GC). [11]

The standardization of medicinal raw materials includes the following aspects:

- Authentication (part of collection, plant parts collected, local authority, botanical identity such asphytomorphology, microscopic and histological analysis, taxonomic identity, etc.)
- Foreign materials (must be free of soil, insect parts, or animal waste, etc.) found in medicinepowder.
- Moisture
- Volatile substances
- Determination of heavy metals
- e.g. Cadmium, lead, arsenic, etc

Analytical Specification of Herbal Formulation Followed as per Requirement of the Medicines

Analytical Specifications of Herbal Formulations Followed as per Requirement and Form of the Medicine: Description, Colour, Odour, Total – ash, Acid – insoluble ash, Water and Alcohol-soluble extractive, Viscosity, Refractive index, Specific gravity at 250 C·Alcohol content Test form ethanol, Total acidity, Non reducing and reducing sugar, PH, Total sugar content, Loss on drying at 105 ºC, Particlesize (80-100 mesh for Churna; 40- 60 mesh for Kvathachurna), Weight variation, Disintegration time -Not more than 15 min, Identification TLC/HPTLC/GLC, Assay,Test for heavy/Toxic metals: Lead, Cadmium, Mercury ,Arsenic, Microbial contamination: Total bacterial count ,Total fungal count, Test for specific Pathogen: E. coli ,Salmonella spp. S.aureus, Pseudomonas aeruginosa ,Pesticide residue: Organochlorine pesticides ,Organophosphorus pesticides, Pyrethroids, Test forAflatoxins,[13]

Organoleptic or macroscopic evaluation: Organic evaluation of drugs by means of organs of sense(skin, eye, tongue, nose, and ear) or microscopic evaluation which include evaluation of drugs by colour, odour, taste,size, shape, and special feature, like touch , texture, etc. itis the technique of qualitative evaluation based on the study of morphological and sensory profile of wholedrugs.[15]The fractured surfaces in cinchona, quillia, and cascara barks and quassia wood are important characteristics .Aromatic odour of umbelliferous fruits and sweet taste of liquorices are the examples of this type of evaluation where odour of drugs depends upon the type and quality of odorous principles (volatile oils) present.[16]

Microscopic evaluation: It involves detailed examination of the drugs and it can beused to identify the organized drugs by their knownhistological characters. It is mostly used for qualitativeevaluation of organized crude drugs in entire and powerforms with help of microscopic. Using microscope detectingvarious cellular tissues, trichomes, stomata, starchgranules, calcium oxalate crystals and aleuronic grains aresome of important parameters which play important role identification of certain crude drug [16]

Final Product:Prepared drug should possess standard nature ofcharacteristics. The manufacturing procedure and formula,including the amount of recipients, should be described indetail.[17]A finished product specification should be definedto ensure consistent quality of the product. The finishedproduct should comply with general requirements forparticular dosage forms. The processes involves wide arrayof scientific investigations, which include physical, chemicalland biological evaluation employing various

analyticalmethods and tools. The specific objectives of such studies to ensure plant quality differ from the methods used. [18]

Labelling

The quality of consumer information about the product is important to the final herbal product. Information and warnings on the label help to reduce the risk of improper use and side effects. The primary source of plant product information is the product label. The contents of the label and its regulations prescribed under the Drugs and Substances Act 1945 [19] must be followed.

Advantages

1. Low production costs
2. They may have fewer side effects
3. It is useful in chronic conditions
4. General availability

Disadvantages of herbal medicines

1. Lack of dosage instructions
2. The danger of poisoning in relation to wild plants
3. It interacts with other drugs.
4. Good for many situation

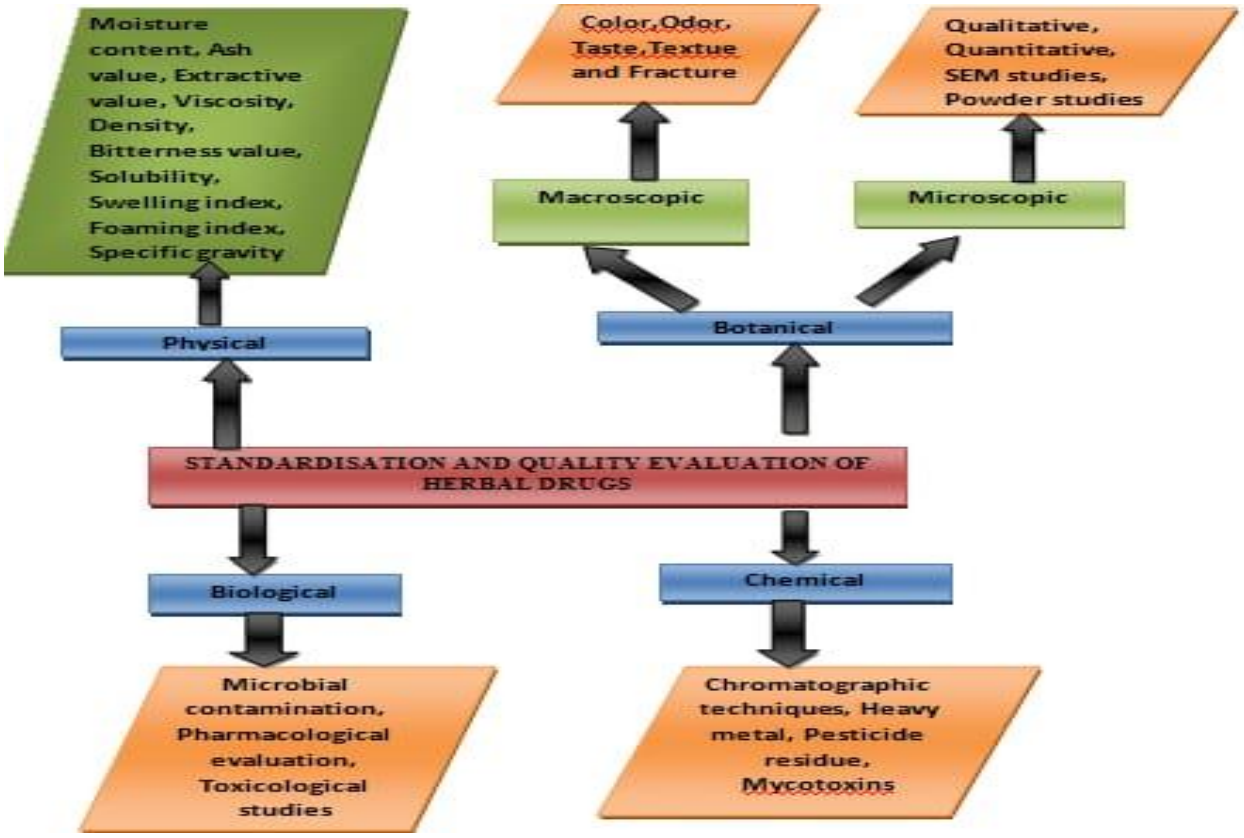

Fig no.2 herbal medicine

DNA FINGERPRINTING TECHNIQUE

DNA analysis is an important tool in determining herbal remedies. This method is useful for identifying the original drug that cannot be distinguished from a substitute or adulterated drug. It has been reported that the DNA genome fingerprint is the same regardless of the plant part used, although the phytochemical content varies with the plant part used, the cultivar and the environment. This concept of fingerprinting has been increasingly used in recent decades to determine the ancestry of plants, animals and other microorganisms. Genotyping of plant species and strains is useful because most plants, even of the same genus and species, show considerable variation between strains. Another reason for using DNA fingerprinting in commercial herbal medicines is the availability of intact genomic DNA from plant samples after processing. Contaminants can be detected even in stored samples,which enables drug authentication68. Another useful application of DNA fingerprinting is the availability of intact genomic DNA of commercial herbal medicines, which helps to detect adulterants even in treated samples. It produces normal proteins and acts as a replacement for defective proteins. In addition, these symptoms help in the treatment of various diseases and help to distinguish the original plant from the fake medicine. Cannabis sativa and Arabidopsis thaliana L. Heyne has been separated from his various cheats by using ISSR signals. [20]

Authentication and Reproducibility of Herbal Ingredient

Theproblems associated with illegal herbal products represent serious public health problems that arise when their herbal products are not authenticated. Herbal compounds should be carefully identified by macroscopic and microscopic comparisons with real materials and detailed descriptions of real plants.[21]

1. The difference between different species: the difference in structure n most of which is governed by the gene and connected to the earth. of origin

2. Environmental factors: The quality of plant material is affected by environmental factors such as weather, altitude and other growing conditions

3. Harvesting time: For some plants, it is necessary to determine the optimal time for harvesting as the concentration of compounds in the plant is known to vary during the growing cycle, even when growing up.

4. A part of the plant is used: Active ingredients differ between parts of the plant, and it is unusual to confuse plant ingredients with parts of the plant that are not used. Additionally, plant resources that have been mined and thus depleted are sometimes used as cheats to increase the weight of a group of plant resources

5. Post-harvest factors: storage conditions and processing treatments greatly affect the quality of plant structure.

WHO GUIDELINES FOR QUALITY STANDARD HERBAL FORMULATION

1. Quality control of health raw materials, herbal preparations and finished products

2 Stability and durability assessment

3. Safety assessment. Safety documents based on experience or toxicological studies.

4. Evaluating the effectiveness of public information and evaluating biological activities. Extractionbased on active principles or important compounds should be compared with chromatographic fingerprints (TLC, HPTLC, HPLC and GC)

.In general, all medicines, whether synthetic or herbal, must meet basic requirementsto be safe and effective.[22] [23] Equipment for simple operations including harvesting, drying and storage.[24]

1.Quality Control of Herbal Medicines

Quality control is a term that refers to the processes involved in maintaining the quality and status of a manufactured product. In general, there are three main parts of medicine

a. Identity or originality - must have a plant

b. Purity - must not be contaminated other than the plantidentification

Identify can be achieved by macroscopic and microscopic examination. In addition, identity tests include simple chemical tests such as color or precipitation and chromatographic tests. Thesechemical and chromatographic tests help to provide batch to batch comparability and the chromatogram may beused as a 'fingerprint' for the herbal ingredient by demonstrating the profile of some common plant constituentsuch as flavonoids, alkaloids and terpenes. To prove identity and purity, criteria such as type of preparationsensory properties, physical constants, adulteration, contaminants, moisture, ash content, and solvent residueshave to be checked. Voucher specimens are reliable reference sources. Outbreaks of diseases among plants mayresult in changes to the physical appearance of the plant and lead to incorrect identification[27]26Purity is closelylinked with safe use of drugs and deals with factors such as ash values, contaminants (e.g. foreign matter in the form of other herbs), and heavy metals. However, due to the application of improved analytical methods,modern purity evaluation also includes microbial contamination, aflatoxins, radioactivity, and pesticide residuesAnalytical methods such as photometric analysis, Thin layer chromatography (TLC), High performance liquidchromatography (HPLC), High performance thin layer chromatography (HPTLC), and Gas chromatography(GC) can be employed in order to establish the constant composition of herbal preparations. Depending onwhether the active principles of the preparation are known or unknown, different concepts such asnormalization versus standardization" have to be applied in order to establish relevant criteria for uniformity.Content or assay is the most difficult area of quality control to perform, since in most herbal drugs the activeconstituents are unknown. Sometimes markers can be used. In all other cases, where no active constituents ormarker can be defined for the herbal drug, the percentage extractable matter with a solvent may be used as form of assay, an approach often seen in pharmacopeia[27, 28]A special form of assay is the determination ofessential oils by steam distillation. When the active compounds (for example, sennosides in senna) and indicators (for example, alkydamids in echinacea) are known, there are many new methods for chemical analysis such as ultraviolet / spectroscopy visible (UV / VIS), TLC, HPLC, HPTLC, GC, Mass spectrometry or a combination ofGC and MS (GC/MS) can be used[29]

2.Evaluation of stability and durability

The long-term use and unstable nature of a substance is an indication of its safety. However, in many cases, studies on the toxicity of natural substances widely used as food in these products have revealed a previously unknown risk of systemic toxicity, cancer, andDrRajesh Kumar .al / Journal International Science and Pharmaceutical Research has shown. IJPSR) ISSN Immediately notify law enforcement of these findings.

Quality assessment

All procedures should be in accordance with good manufacturing practices

Crude plant material

Botanical description of plant material, including genus, species and reference, description, plant part, active components and properties, should be indicated and, if possible, limitations should be defined internal. Foreign substances, impurities and micro-organism content should be identified or minimized

3. Safety assessment

Herbal medicines are considered safe based on long-term use in various cultures. However, there are reports of serious side effects after consuming herbal products. In most cases, poisoning has been attributed to impurity and adultery. However, some plants used in herbal medicinecan be very poisonous.Evaluation of the toxic effects of plant constituents of herbal formulation requires detailed phyto-chemical andpharmacological studies. It is, however, safe to assume that, based on human experiences in various cultures, theuse of toxic plant ingredients has already been largely eliminated and recent reports of toxicity could largely nedue to misidentification and overdosing of certain constituents[30]. Adulteration of botanical preparations isanother important issue. Due to over exploitation of certain plants, habitat loss and fragmentation of the forest,many medicinal plants have reached to the level of the endangered or rare species. These and many other factors(like cost of raw material) cause problem for availability of genuine drug, which encourages the adulteration ofplant by substitution with inferior commercial varieties, artificially manufactured substances, exhausted drugs orcheaper plant or by another vegetative part[31]. Many reports show that many herbal products contain drugs and heavy metals. A drug cheat can be used. Agricultural chemicals are used to protect the plant from chemicals. In addition to the mechanism of action, the pharmacokinetics and drug interactions of many herbs are still in their infancy. At the same time, the increasing number of reports of serious illnesses or diseases caused by herbal medicines increases the need for national legislation and registration of herbal medicines and the establishment of safety monitoringDoctors should never prescribe or recommend herbal remedies without proven efficacy and as a well-studied remedy[32,33]

Standardization Of Bhasmas

Bhasma is made of metals like zinc, lead, gold, silver, tin, copper, mixed metals and alloys including precious stones, corals and mica and other minerals and other minerals and others in the proper sense and post-property. purification and proper cleansing with fruit juice or plant mineral[34]. Bhasma is highly recommended for the treatment of various chronic diseases and is consumed with milk, butter, honey or ghee to eliminate the harmful effects of metals and increase their bioavailability in the body.[35]The Indian Ayurvedic Formulary lists more than one method for preparing bhasmas of certain metals The Law on Drugs and Drugs lists several traditional texts that a vaidya can refer to prepare the Bhasma[36]. A standardization of process and the end product both is called for Pharmacopoeial standards have been published by the Government of India for a large number of single drugs of plant origin and the work on classical composite formulations is being carried in several human laboratories. The CCRAS has developed a technique called phase spot test for identification and quality assessment of bhasmas[37]In recent years sophisticated test equipments and techniques of data analysis have been put to fruitful use for the physicochemical characterization of the bhasmasThese studies also explored intensively. the different Bhasma preparation methods of the same metal, chemical nature and crystalline structure of the intermediates and the final products. These have involved Atomic Absorption Spectrophotometry (AAS), flame photometryInductively Coupled Plasma Atomic Emission Spectrometry (ICP- AES), X-ray diffraction (XRD) analysis and pHmetry, etc. AAS uses the property of atoms to absorb specific wavelengths of electromagnetic radiation. The amount of light absorbed can provide a quantitative estimate of the absorbed element. ICP-AES use plasma (eg inductively coupled plasma) to produce excited atoms. These atoms emit electromagnetic radiation a certain wavelength characteristic of an element. By measuring the intensity of this emission, the concentration of the element in the sample can be determined.

Conclusion

Plant products have been developed and are being developed around the world as home remedies, in over-the-counter medicines and as raw materials for the pharmaceutical industry, and they are important indications for the treatment of world. Therefore it is necessary to create internationally recognized guidelines for quality evaluation. Certain herbs have gained popularity over the years, but the public, doctors and the media still have little understanding of the safety and effectiveness of herbal remedies. Evidence is emerging for the dangers of consuming too much of some of these plants. As with many things, media credibility, unknown science, and grandiose claims are subject. With the global acceptance of herbal products as medicine for the treatment of various ailments and diseases, the need for standardization of medicinal plants has now become very urgent. The use of modern analytical tools to test various quality parameters for an effective pharmaceutical product cannot be overstated.Ensuring the safety and effectiveness of herbal medicinerequires monitoring the quality of products from collection through processing to final product packaging. It is recommended that various public agencies follow the international approach to plant quality by adopting the WHO guidelines and develop spaces using the various quality parametersmentioned above. This will strengthen the regulatory process and reduce quality violations.

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