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Standardization and Validation a Tool for Identification and Generation of Features for Herbal Formulations

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Abstract

Many characteristic varieties of medicinal herbs and their system have been used since time immemorial. Realistic experience and several modern studies have honestly shown that therapy with medicinal flora is more valuable than the use of artificial chemicals. The sector is rich in medicinal flora growing wild or cultivated, forming a large herbal and economic health that must be covered, accelerated for the improvement of the system, the wealth of the country and the health of the people. Natural medicine technology is used to transform botanicals into medicines, for which standardization and remarkable handling are necessary with proper integration of current medical strategies and traditional records. Identification of the pure energy share is an important requirement for quality management and determining the amount of the digging. Standardization of herbal drugs by confirming their identification, quality and purity. Consequently, it is necessary to improve the safety of herbs and develop some quality control along with adherence to WHO guidelines for Ayurvedic medicines.

Keywords: Churna, Herbal Formulation, High Performance Thin Layer Chromatography, Quality Control, Standardization

1.Introduction

1.1 Introduction to herbal preparations

Medicinal plant plays a vital role in worldwide health. Despite the high-quality advances made with the aid of present –day medicinal drug in latest a long time, flora nonetheless make an extensive contribution to health care [1]. Even in historic cultures, tribal human beings methodically collected statistics approximately herbs and advanced nicely described herbal pharmacopoeias. The assembly of the World Health Organization

shall anticipate its obligations for taking account of its regulation, coverage formulation, policies and country wide measures to make certain the use of safety and the effectiveness of conventional medication [2].

The WHO has listed a few terms associated with natural medicines according to its definitions. Natural medicines consist of herbs, herbal substances, herbal preparations and completed natural products. In a few countries, herbal drugs may traditionally include herbal organic or inorganic active substances that are not of plant origin [for example, animal and mineral substances]. Herbs consist of raw plant material consisting of leaves, seeds, stems, vegetation, fruits, timber, bark, roots, rhizomes or different components of the plant, which can be complete, overwhelmed or powdered [3].

Natural materials encompass, fresh juices, gums, constant oils, essential oils, resins and dry powders of herbs [4]. Herbal preparations are the basic for completed herbal products and can encompass comminuted or powdered herbal substances, or extracts, tinctures and fatty oils of natural material sherbs [3]. Finished natural products includes herbal preparations made from one or more herbs. However, completed products or mixture herbal products to which chemically defined active substances have been added, along with synthetic compounds and / orisolated parts from natural substances, are not considered to be herbal [3,1]. Each plant is like manufacturing unit able to synthesizing infinite variety of exceptionally complicated and uncommon chemical materials whose systems ought to in any other case escape the mind for all time. There are as a minimum one hundred twenty exclusive chemical materials originated from flora which might be considered as essential tablets currently in use inside the global, whilst numerous other pills are simple artificial changes of the natural products [5].

From the information in Atharva-Veda, early texts of Ayurveda which include Charaka Samhita and Sushruta Samhita had been advanced. Even though the former focuses on the reasons of sicknesses and the charter of a person, the later emphasizes on Ayurvedic surgical procedure and the information of its strategies. The records of Ayurveda can be traced again to the period among the pre-Vedic durations (4000 B. C.-1500 B. C.). Consistent with Ayurvedavatarana (the descent of Ayurveda), Lord Brahma, the Hindu God of advent exceeded on his “knowledge of existence” to Daksha Prajapati and Ashwins, eventually to Indra. This knowledge is then transferred to specific rishis (sages), in which these disciples of Ayurveda wrote exclusive treatises primarily based on their interpretations. Here, each Bhardwaj and Dhanvantari received the understanding from Indra. They later advanced school of drugs and college of surgical operation respectively [6].

Because the prehistoric length, natural medicines have existed global-huge with long recorded history. They were used in historic Chinese, Greek, Egyptian and Indian medicinal drug for diverse therapies purposes; while the local American and African use herbs in their recuperation rituals as part of their lifestyle. The Indian Ayurvedic machine has included herbals as certainly one of its most effective recuperation components, which might be

recorded inside the literature inclusive of Vedas and Samhitas.

Due to the provision of chemical analysis techniques in the early nineteenth century, scientists began to extract and regulate active compounds from the herbals, resulting in transition from raw herbs to artificial prescribed drugs. that is whilst using herbal drugs commenced to say no. Artificial prescribed drugs, but, are discovered out to be exceedingly greater highly-priced and produce severs unwanted facet-outcomes in spite of their strong pharmacological movement. as a result, human beings these days are moving back to natural drugs, that are originated from the nature and claim to be more secure [7].

Herbal arrangements are the idea for finished natural products and may include comminuted or powdered natural materials, or extracts, tinctures and fatty oils of natural materials. They are produced by extraction, fractionation, purification, concentration, or other physical or biological methods. Natural product is used very usually in one-of-a-kind fitness practices or healing procedures of conventional medicines like Chinese medication, Ayurveda, Unani, Naturopathy, Osteopathy and Homeopathy [8].

World Health Organization (WHO) stresses the importance of the qualitative and quantitative techniques for characterizing the samples, quantification of the biomarkers or chemical markers and the fingerprint profiles. If a precept energetic aspect is understood, it is maximum logical to quantitate this compound. In which active ingredients contributing to therapeutic efficacy is acknowledged botanical preparations need to be standardized to those compounds. Wherein the lively elements are not yet recognized a marker substance which must be specific for the botanical might be selected for analytical cause [9].

Natural drug technology is used for converting botanical substances into drugs, in which standardization and notable manipulate with right integration of current medical strategies and traditional records is essential. With a purpose to display constant composition of natural arrangements, adequate analytical strategies the want to be completed which consist of photometric evaluation, High Performance Liquid Chromatography [HPLC], High Performance Thin Layer Chromatography [HPTLC], and Gas Chromatography – Mass Spectrometry [8].

2. Material and Methods

2.1 Why validation / standardization

The process of standardization is carried out to specify the content, quality and therapeutic effect of each herbal medicine. In this era of global competition, the standardization of herbal medicines, such raw material should be authentic. The raw material should confirm to the standard physio-chemical standards, size, shape and storage conditions. The principal purpose for standardizing herbal extracts is to gain the best possible manage in double blind clinical studies. Standardization has advantages, it produces a constantly powerful product with guaranteed components. When you consider the exceptional of maximum commercial herbs, standardization will at the least make certain that they incorporate something and that the right herb is used. Many herbalists' appearance to the brighter facet of standardized natural products than to the quantum intake of greater people, inclusive

of doctors and pharmacists, who are conversant in the consistency and percentage of energetic elements.

The worldwide perspective, there is a shift towards the use of medicine from natural origin, as the dangers and the shortcoming of modern medicine are getting more apparent. It is the cardinal responsibility of the regulatory authorities to ensure that consumers get the medication, which guarantees purity, safety, potency and efficacy [10].

Standardization of herbal medicines is not an easy mission many factors affect bio efficacy and reproducible therapeutic effect. Care should be taken proper to obtain herbal products quality oriented. In the case of polyherbal drugs special consideration should be given to the treatment of the plant, the season and the time of collection and their extraction and purification process and rationalizing the combination. The physical, chemical and pharmacological parameters should be checked after all the routines for a better diagnostic efficacy, and before selecting the final product, it is necessary to validate the batch and the entire manufacturing process [11].

2.2 Steps for Validation / Standardization

A. Macroscopic Measures
B. Microscopic Measures
C. Powdered Microscopic Measures
D. Foreign Matter Measures
E. Chromatographic Measures
F. Genomic Level Measures
G. Proteomics Level Measures
H. Bio efficacious Measures
I. NMR Measures

<insert figure 1 here>.

2.2.1 Macroscopic Measures

Medicinal plant materials are categorized by into sensory, macroscopic and microscopic properties. An investigation to determine them characterization is the first step to creation the identity and degree of purity of such materials and should be done before any further tests are underway. Organic evaluation of drugs using sensory organs (skin, eye, tongue, nose, ear) or macroscopic evaluation, which includes evaluation of drugs by color, smell, taste, shape, and special features such as touch, texture, etc. it is a qualitative evaluation technique based on study of the morphological and sensory profile of whole drugs.

However, judgment must be exercised when with regard to aroma and taste due to variability person – to – person assessment or the same way man at different time. Macroscopic identity medicinal plant material is based on shape, size, color, surface properties, texture, refraction properties and appearance of the cut surface. However, as these properties are assessed subjectively and substitutes or fake can they closely resemble the real material. It often it is necessary to document the findings by microscopy and / or physiochemical analysis[8].

2.2.2 Microscopic Measures

Microscopic examination of medicinal plants materials is necessary for identification broken or powdered materials; can sample they must be treated with chemical agents. An examination with a microscope alone cannot always however, provide full identification when used in conjunction with other analytical methods can they often provide invaluable supporting evidence.

Microscopy includes comparative microscopic inspection of powdered herbal drug. Further progress in microscopic technology have increased the accuracy and capabilities of microscopy as a means of plant raw material identification due to the implication of light and scanning electron microscopes (SEM) in the standardization of herbal medicines [12].

2.2.3 Powdered Microscopic Measures

Microscopic examination of medicinal plants material is necessary for identification powdered materials, can sample they must be treated with chemical agents. An examination with a microscope alone cannot always however, provide full identification when used in conjunction with other analytical methods can they often provide invaluable supporting evidence. Quality control of herbal drugs has traditionally been based on appearance and today microscopic evaluation is indispensable in initial identification of herbs, as well as in the identification of small fragments of raw or powdered herbs and foreign detection matter and adulterers [13].

2.2.4 Foreign Matter Measures

Herbal drugs should be made from the said part of the plant and lack other parts of the same plant or other plants. They should be completely free of mold or insects, including excrement and visible contaminants such as sand and rocks, poisonous and harmful foreign substances and chemical residues. Animal matters like such as insects and "invisible" microbial contaminants that can they produce toxins, they are also potential contaminants herbal medicines. Macroscopic examination can easily be used to determine the presence of foreign substances, although microscopy is necessary in certain special cases.

2.2.5 Chromatographic Measures

2.2.5.1 Thin Layer Chromatography Method (TLC)

TLC is the most common, versatile method of choice for herb analysis and instrumental chromatography methods such as GC and HPLC were also used. Nowadays, TLC is still commonly used for analysis of herbal medicines from different pharmacopoeias such as Indian Herbal Pharmacopoeia, Ayurvedic Pharmacopoeia, American Herbal Pharmacopoeia (AHP), Chinese Drug Monographs and Analysis, Pharmacopoeia of People's Republic of China, etc. rather TLC is used as a simply an initial screening method with semi – quantitative evaluation along with other chromatographic techniques because there is relatively less change in simple TLC separation herbal medicine than in instrumental chromatography. Thin layer chromatography is a technique in which a solute undergoes distribution between two phases, stationary phase acting through adsorption and mobile phase liquid form. The adsorbent is relatively thin, uniform a layer of dry, finely powdered material applied to the glass, plastic or metal sheet or plate. Glass plates are the most commonly used. Separation can be achieved based on partitioning or a combination of partitioning and adsorption, depending on the support, its preparation and use other solvent. Identification can be influenced by spotting obtained an identical RF – value and approximately the same size, respectively with the unknown and the reference sample chromatographed on the same plate. Visual comparison the size and intensity of the spots

usually serve for semi – quantitative estimation. TLC had multiple benefits detection possibilities in the analysis of herbal medicines. In addition, TLC is relatively simple and can be used analysis of multiple samples. More than 30 spots per plate samples can be studied simultaneously at one time. In thin layer chromatography (TLC) are very important steps for qualitative and quantitative analysis. That is, use thin layer chromatography for herb analysis drugs are still popular [10].

2.2.5.2 High Performance Liquid Chromatography (HPLC)

High Performance Liquid Chromatography is among the modern one's daily applications highly used in separation and isolation natural pharmaceutical active compounds including alkaloids and glycosides, whose role in modern conventional medicine is indisputable. It is the most convenient method [14]. Information so created has potential applications in identifying genuine drug, in eliminating counterfeiters, and in maintenance the quality and consistency of the medicine. HPLC fingerprinting includes recording of chromatograms, retention time of individual peaks and absorption spectra (recorded by a photodiode array detector) with different mobile phases. This is very important in pharmaceutical industry today, because new product (Natural Synthetic) must be placed on the market as soon as possible. Having such a powerful cleaning technique at your disposal allow less time to be spent on synthesis conditions [15,16,17].

2.2.5.3 Common Methodology for the HPTLC method of Analysis

Analytical method for estimating the quality of herbal drug. These are moving rapidly towards integration and a comprehensive way to address the complex nature of herbs medicines. High performance thin layer chromatography (HPTLC) is one of the complicated instrumental techniques for qualitative and quantitative analysis of herbs and herbal medicines. When founded as a new analytical procedure, always begins with a broad literature survey, i.e., primary information on physiochemical sample characteristics and nature of sample (structure, polarity, volatility, stability and solubility). It involves considerable trial and error. General the steps involved in the HPTLC method are as follows:

A. Basic steps:

- Stationary phase selection
- Mobile phase selection and optimization
- Sample preparation and application
- Chromatogram development (separation)
- Detection

B. Implements of HPTLC

- Ability to analyze raw samples containing multi – component substances.
- The separation process is particularly easy to follow with colored compounds.
- Several samples can be separated in parallel to each other on the same board, resulting in high performance, time saving and fast analysis with low cost.
- The choice of solvents for HPTLC development is wide because the mobile phases are completely evaporated before that detection step.

- Two – dimensional separations are easy to perform.
- Stability during chromatography should be tested using two - dimensional development.
- Specific and sensitive color reagents can be used detection of separate spots (anti – dandruff agent/ kidde agent).
- HPTLC can be combined and subsequently used for the different assessment methods they allow identifying compounds that have different light – absorption characteristics or different color.
- Contact detection allows radioactively labelled compounds be monitored and microbial activity in places be to judge [10].

2.2.5.4. Gas Chromatography and Mass Spectrometry (GC – MS)

Many biologically active chemical compounds are volatile there by making gas chromatography an important quality tool herbal medicine review. It has high sensitivity detection of all volatile and thermostable chemical compounds. GC devices can be directly interfaced with fast scanning mass spectrometer of various types. GC and GC – MS are unanimously accepted methods for the analysis of volatiles components of herbal medicines, due to their sensitivity, stability and high efficiency. In particular, word division on MS provides reliable information for qualitative analysis of the complex components [18,19].

2.2.5.5 Liquid Chromatography – Mass Spectroscopy (LC – MS)

LC – MS has become the method of choice in many phases drug development. Recent advances include electrospray, thermo-spray and ionization techniques which offer the unique advantages of high detection sensitivity and specificity, liquid secondary ion mass spectroscopy, later laser mass spectroscopy with 600 MHz offers accurate determination molecular weight proteins, peptides. The patten of isotopes can be detected by this technique [15].

2.2.5.6 Gas Chromatography – Flame Ionization Detector (GC – FID)

A number of detectors are used in gas chromatography. The most common are flame ionization detectors (FIDs) and thermal conductivity detector (TCD). Coupling capillary column gas chromatographs with a Fourier Transform Infrared Spectrometer provides an effective means of separation and identification constituents of various mixtures [20]. Both are sensitive to a wide range of components and both work over a wide range of concentrations. While TCDs are essentially universal and can be used to detect any component other than the carrier gas (if their thermal conductivities are differing from the carrier gas at the detector temperature), FIDs are primarily sensitive to hydrocarbons and there are more sensitive to them than TCD. However, the FID cannot detect water. Both detectors are also quite robust. Since TCD is non-destructive, so it can be operated in series before the FID (destructive). Providing complementary detection of the same analytes [21].

2.2.5.7 Supercritical Fluid Chromatography (SFC)

Supercritical liquid chromatography is a hybrid of gas and liquid chromatography that combines some of the best features each. SFC allows separation and group destination

compounds with which neither gas nor liquid chromatography. SFC has been applied to a wide range material including natural products, drug, food and pesticides [22]. These compounds are either non-volatile or thermally labile so that GC procedures are unusable or contain no function group to allow detection by spectroscopic or electrochemical technique used in LC [23].

2.2.6 Genomic Level Measures

2.2.6.1 The role of the genetic marker in herbal medicine technology

DNA analysis has proven to be an important tool in standardization of herbal medicines. This technique is useful for identification of phytochemically indistinguishable true drug from a substituted or falsified drug. It has been reported that DNA the fingerprint genome remains the same regardless of the plant part the phytochemical content will vary by part of the plant used, physiology and environment [24]. Another useful application of DNA fingerprinting is availability of intact genomic DNA specificity commercially herbal drugs that help in distinguishing adulterers and in processed samples [25].

It has been well documented that geographical conditions they affect the active components of the medicinal plant and thus their activity profiles. Many researchers have studied geographic variation at the genetic level. Estimates of genetic diversity are also important in designing crop improvement programs germplasm management and evolving conservation strategies. RAPD – based molecular markers have been found to be useful in differentiating different accessions of neem collected from different geographical regions [26]. Another is germplasm analysis to study genetic diversity an important area in which much effort has been invested. Fingerprinting crops such as rice, wheat, chickpea, pea, pearl millet etc. is widely practiced [26,27].

2.2.6.2 Genetic Markers for DNA Fingerprinting

A genetic marker is a gene or DNA sequence with a known location on the chromosome and associated with a specific a gene or trait. It can be described as a variation that can occur due to mutation or change in genomic loci that may be observed. A genetic marker can be a short DNA sequence, such as sequence surrounding a single base pair change (single nucleotide polymorphism SNP), or long, like minisatellites. Som commonly used types of genetic markers are:

- RFLP (Restriction Fragment Length Polymorphism)
- AFLP (Amplified Fragment Length Polymorphism)
- RAPD (Random Amplification of Polymorphism DNA)
- VNTR (Variable Number Tandem Repeat)
- SNP (Single Nucleotide Polymorphism)
- STR (Short Tandem Repeat)
- SFP (Single Feature Polymorphism)
- Micro-Satellite Polymorphism

They can be further categorized as dominant or codominant. Dominant markers allow the analysis of many loci in one time, e.g., RAPD. A primer amplifying a dominant marker could to amplify at many loci in a single DNA sample using a single PCR reaction. Co – dominant markers analyze one locus at a time, and a primer amplifying a codominant marker would yield the target product[28].

2.2.7 Electrophoretic method for herbal drugs:

Capillary electrophoresis was introduced in the early 1980s as a powerful analytical and separation method technique and was developed almost explosively. It enables an efficient way of documenting sample purity/ complexity and handle virtually any type of charged sample components from of simple inorganic ions on DNA. There was therefore an obvious increase in electrophoretic method in particular capillary electrophoresis, used in the analysis of herbal medicines in recent decades. More or less explosive the development of capillary electrophoresis since its introduction has been largely related to the development of liquid chromatography. Most of the techniques used are capillary zone electrophoresis (CZE), capillary gel electrophoresis (CGE) and capillary isoelectric focusing (CIEF). Capillary electrophoresis is promising for separation and analysis of active ingredients in herbal medicines because it only needs a small amount of standard and can be analyzed samples quickly with good separation capability. It is also a good chemical fingerprinting tool herbal medicines because it has similar technical properties to liquid chromatography. Several recently studies dealing with herbal medicines and two types of medicinal compounds, i.e., alkaloids, have been reported and flavonoids, have been extensively studied [29]. In general, CE is a versatile and powerful separation tool with high separation efficiency and selectivity in the analysis of mixtures of low molecular weight components. However, quickly developments in capillary electrophoresis cause improvements in resolution and rather than reproducibility and absolute accuracy. On a successful approach to improving reproducibility both mobility and integrated data are based on internal standards [9].

2.2.8 Bio-efficacious Measures

Herbs have been widely used to treat bacterial infections thousands of years ago thanks to multi-component synergy antibacterial activity. Currently, 65 to 80 percent of people in developing countries use botanical medicines as antimicrobials treatment. For example, about 900 years ago it was Traditional Chinese Medicine (TCM) *Coptis chinensis* Franch. He was used to treat acute bacillary dysentery. Products of plant origin have historically decisive in the development of antibacterial substances agents. Berberine extracted from *Coptis chinensis* Franch., *Phellodendri chinensis* C.K. Schneid. and other herbal programs significant effects against intestinal bacterial infection and has been developed as an antibacterial agent. Compared with chemical antimicrobial products, herbs show less medicinal resistance, fewer side effects and also abolition of antibiotics resistance in combination with antibiotics. Antimicrobial drugs derived from microbial or chemical products.

The increasing incidence of dangerous infections caused by resistant bacteria made a survey of new molecules and chemical entities a pressing topic in the medical field global scale. Compared to synthetic chemistry, herbs provide greater structural diversity and offer more opportunities identification of new antimicrobial compounds, which are the most abundant a consistently successful source of drugs. The

herbs are showing excellent antibacterial effect due to their safety, efficacy, antimicrobial synergism and reduced drug resistance based on a multicomponent, multidrug target. A combination of herbs and chemical antimicrobial agents for the treatment of infectious diseases is popular in clinical practiced in China for their synergistic or additive effects. Some herbal extracts or ingredients increase the antibacterial effect activity of antimicrobial substances against sensitive and multi – resistant microorganisms in combination with antibiotics[30].

It is important to note that antioxidants and oxidative stress are very often presented in an overly simplistic way. The various antioxidants that exist are often considered a single functional entity. However, the various endogenous antioxidants that the body produces are generally not inter changeable. They have specific chemical and physiological properties that ensure the protection of all parts of cells and organs or tissues from oxidative damage. Dietary antioxidants also exist in various forms, with polyphenols and carotenoids being the largest group of compounds. Antioxidants which have minimal side effects are much needed. Bioactive components extracted from the root and aerial biomass of medicinal plants contain secondary metabolites (also known as phytochemicals), which represent a diverse group of natural products including alkaloids, phenols, flavonoids, terpenoids, steroids, saponins, tannins, quinones, coumarins and glycosides. Phenolic compounds are the most abundant phytochemical in the plant kingdom which serves as a source of health – promoting properties, such as antimicrobial and antioxidant activities in human's diet [31].

2.2.9 NMR Measures (Nuclear Magnetic Resonance)

In the area of medicinal plant research, plant metabolomes are a valuable resource for evidence – based development new Phyto therapeutics and nutraceuticals. Most commonly used chromatographic techniques for metabolic profiling are nuclear magnetic resonance (NMR) and Mass Spectroscopy (MS). Currently hyphenated techniques such as LC – MS (liquid chromatography – mass spectroscopy) and gas chromatography – mass spectroscopy (GC – MS) were also used for their robustness and higher detection sensitivity. NMR – based studies were performed for its reproducibility plant metabolites grown in different controlled environments or linking one or two activities to the metabolic profile of the extracts. Another application it was in quality control. NMR was therefore the method of choice from the results they are easily reproducible and sample preparation is minimal therefore it is used more often [32].

2.2.9.1 Liquid Chromatography – Nuclear Magnetic Resonance (LC NMR)

LC – NMR improves detection speed and sensitivity and useful in the fields of pharmacokinetics, toxicity studies, drug metabolism and the drug discovery process. Combination chromatographic separation technique with NMR spectroscopy is one of the most effective and time – saving methods separation and structural elucidation of an unknown compound and mixtures, especially for clarifying the structure of light and substances sensitive to oxygen. Online LC – NMR technique allows continuous

registration of time changes as they occur in a chromatographic run, automated data collection a processing in LC – NMR improves speed and sensitivity detection. The recent introduction of pulsed field gradient technique in high – resolution NMR and three – dimensional technique improves application in elucidating structure and molecular weight information. These new hyphenated techniques they are useful in the fields of pharmacokinetics, toxicity studies, pharmaceuticals metabolism and the drug discovery process [23].

3. Methods of Standardization of Ayurvedic Medicines

1) Raw material standardization.
2) In process standardization
3) Finished product standardization

3.1. Raw material standardization

This includes the verification process in which it follows points should be considered. Collection area, parts, plant collection, regional situation, botanical identity, microscopic and histological analysis, taxonomic identity, foreign impurities, loss on drying, swelling index, foaming index, ash values and extractive values, chromatographic and spectroscopic assessment, determination of severe metals, pesticide residues, microbial contamination, radioactive contamination.

3.2. In process standardization

Standard Operating Procedure should have a detailed manufacturing procedure, if other treatment substances are added during production plant preparation. Method of identification and where, if possible, an herbal preparation test should be added. If identification of the active ingredient is not possible, it should be sufficient to identify the characteristic substances or mixture substances to ensure constant product quality.

3.3. Finished product Standardization

The prepared medicine should be of a standard nature property. Manufacturing process and recipe, including the number of beneficiaries, should be described in detail. The finished product specification should be defined ensure consistent product quality. Cash the product should meet the general requirements for dosage forms. The processes involve a wide range of scientific knowledge investigations that include physical, chemical and biological evaluation using different analytical methods and tools. The specific objectives of such investigation in collateral the quality of the herbs varies as do the processes used [10].

4. Quality Control of Herbals (Plant Based Medicines - PBMs)

Quality control is a term that refers to the processes involved preserving the quality and validity of the product tie in general, quality control is based and tree important aspects of the pharmacopoeia-

A. Identity or Authenticity – It should have one herb
B. Cleanliness – It should not contain any impurities other than herb
C. Test or Content – Active components should be inside defined limits.

Identity can be achieved by microscopic examination. In addition to these identity tests that involve simple chemicals tests such as color or precipitation and chromatography tests are also required. These substances and chromatographic tests help to ensure comparability between batches and the chromatogram can be used as a “fingerprint”

of the product which demonstrates the profile of certain common herbs plant chemical components such as flavonoids, alkaloids and terpenes. Show identity and purity such as type preparation, sensory properties, physical constant, adulteration, contaminants, moisture, ash content and solvent residues are checked. An example is reliable references sources for disease outbreaks among natural plants may result in changes in physical appearance herbal plants and lead to incorrect identification, Purity is closely related to the safe use of drugs and deals with the factors such as ash values, impurities and heavy metals. But because of application of improved analytical methods and modern assessment of cleanliness that contains a microbial contaminant, aflatoxins, radioactivity and pesticides. Analytical methods that are photometric analysis, TLC, HPLC, HPTLC and GC. Used to determine the permanent composition of herbs product. Depending on the active resource preparations are known and unknown, different concepts such as "standardization" is important for them to create relevant criteria for consistency. Content and test are very difficult areas of quality control to perform, in the maximum amount of plant products are unknown active folders. Sometimes markers can be used. In other cases where no active components or markers can be defined herbal drugs, percentage of extractable substances with a solvent can be used as form of test, which is often the approach see in the pharmacopoeia.

5. WHO Guidelines

The subject of standardization of herbal drugs is massively wide and deep. Guidelines established by the WHO can be summarized as follows: -

1. Reference to the identity of the drug. Botanical evaluations – sensory characters, foreign organic matter, microscopical, histological evaluation, quantitative measurements etc.
2. Refers to the physio – chemical character of the drug. Physical and chemical identity, chromatographic fingerprints, ash values, extractive values, moisture content, volatile oil and alkaloidal assays, quantitative estimation protocols etc.
3. A reference to the pharmacological parameters, biological activity profiles, bitterness values, hemolytic index, astringency, swelling factor, foaming index etc.
4. Toxicity details – pesticide residues, heavy metals, microbial contamination like total viable count, pathogens like E. coli, salmonella, P. aeruginosa, S. aureus, Enterobacteria etc.
5. Analytical evaluation – Chromatographic - TLC, Paper, HPTLC, HPLC, and Spectroscopic evaluation
6. Microbial contamination.
7. Radioactive contamination [33].

<insert figure 2 here>.

6. Standardization / Validation: A tool for PBMs

Validation of herbal products is a major public health concern in both developed and poor countries, where counterfeiters selling fake herbal medicines are common. In that respect there it is not under the control of

government agencies, although there are some guidelines in some individual countries and those outlined by the WHO. If plant products are marketed as therapeutic agents, regardless of whether the products actually have any positive healing effects and reduce the severity of the disease, it is necessary to ensure scientific verification and periodic monitoring of quality and effectiveness by drug control administrators. It's possible, that the introduction of scientific validation would control the production of impure or adulterated herbs products and possibly ensure their rational use. This could also lead to regulation in the industry so that only qualified doctors and health care providers can prescribe medicines. Several major pharmacopoeias contain monographs listing standards for herbal drugs. The main advantage of an official monograph published in a pharmacopoeia is that standards are defined and available and that the analytical procedures used are fully validated. This is very important as validation can be quite a time-consuming process. By definition, validation is the process of proving that an analytical method is acceptable to it intended purpose for pharmaceutical methods. Guidelines from the United States Pharmacopeia (USPC,1994 to 2001), International Conference on Harmonization (ICH), and US food and Drug Administration (FDA) provide a framework for conducting such validations. Usually, validation studies must include studies of specificity, linearity, accuracy, precision, range, detection and quantitative limits depending on whether the analytical method used is qualitative or quantitative. The availability of standards is also extremely important. For macroscopic and microscopic procedures, this generally means that there must be reliable reference plant samples available. A defined botanical resource (e.g., Voucher specimens) usually solves this problem. Standards for chromatographic procedures are less easy to obtain. Characteristic plant components, either active or markers are rarely commercially available. Sometimes the LC – MS approach can be referred to as a method of characterization. We go a step further, after isolating such it will not be easy to prove its definitive structure. A frequently used method is to use readily available compounds that behave similarly in the chosen chromatography systems and calculate retention values and / or times for these compounds as a standard. Qualitative chemical examination is intended for the detection and isolation of active substances. TLC and HPLC are the main analytical techniques commonly used. In cases where there are no active components known or too complex, the quality of plant extracts can be judged by a "fingerprints" chromatogram [9].

7. Steps involved in monograph preparation

In modern herbal ayurvedic monographs standardization parameters are discussed in a comprehensive way. According to modern ayurvedic monographs preparation, quality control protocols include the following steps: synonyms, publications related to the plant, present components, analytical method.

Descriptive evaluation: Complete description of the drug, Phyto morphological, microscopical, organoleptic assessment and extraneous things etc. [33]

8. Conclusion

A considerable number of methods to verify the authenticity of raw drugs were addressed here. Despite these challenges, it exists the growing need of consumers and health professionals get reliable and up to date safety information and efficacy of medicinal plants. Macroscopic, microscopic, microbiological, physicochemical, phytochemical and chromatographic quality assurance mechanisms are needed for widely used herbal medicines. Ensuring safety and the effectiveness of an herbal medicine requires monitoring the quality of the product, from collection to processing to the final product. It is recommended several government agencies follow a more universal one access to herbal quality, adopt WHO guidelines and also develop monographs using various qualitative parameters. It will strengthen regulatory process and minimize quality degradation.

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Figure 1. Flow chart on validation of the herbal drugs.
Figure 2. Quality control pharmacopoeial standards of herbals.