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Review Article

Herbal Drug Standardization: A Systemic Review

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Abstract

The demand for herbal medicinal products and materials is rising, and maintaining their quality is therefore becoming increasingly important. Numerous physical, chemical, and geographical factors that affect these materials' quality also affect the quality of the herbals. In addition, the quality of herbal materials is becoming increasingly a concern due to adulteration. The quality characteristics of the herbal material the herbal pharmaceuticals are assessed using a variety of chemical and phytochemical tests, analytical techniques, and hyphenated analytical techniques. Formulations made from herbs are now widely accepted as effective treatments for many ailments. the creation of reliable analytical techniques, such as quantitative assessments of marker/bioactive chemicals and other techniques, that can accurately profile the phytochemical makeup. For the manufacture and manufacturing of herbal medications, standardisation is a crucial step in establishing a uniform biological activity, consistent chemical profile, or even just a quality assurance programme. It is crucial to follow WHO-specific recommendations for evaluating the quality, safety, and efficacy of herbal medicines as a condition for worldwide harmonisation. An overview of the numerous methods used for the extraction, characterisation, and standardisation of herbal nanomedicines is presented.

Keywords: herbal drugs, standardization, herbal formulation, quality control

INTRODUCTION:

Plant-derived products are more and more in demand as medicines, nutraceuticals, and cosmetics. They can be purchased over the counter in health food stores and pharmacies for self-medication or as medications recommended by non-allopathic doctors[1]. Humans prioritize quality above all else in all facets of life. It is crucial that human medications are of high quality because they are utilised to ensure the welfare of the human race [2, 3]. The quality control of medications made from synthetically produced chemicals is subject to strict rules and regulations. They must successfully pass a number of tests and quality standards before being marketed and consumed by patients and consumers. This regulatory rigour ensures the safety and effectiveness of pharmaceutical goods by ensuring that the quality of medications produced synthetically is up to the mark [4, 5].

Herbal medications are defined as plant materials or plant parts that have undergone basic harvesting, drying, and storage procedures been transformed into phytopharmaceuticals. Include other plant-derived crude products that no longer exhibit any organic structure, such as essential oils, fatty oils, resins, and gums, as a useful addition to the term [6]. For quality monitoring of both raw materials and final herbal products, analytical separation techniques such as high-performance liquid chromatography (HPLC), gas chromatography (GC), and mass spectrometry (MS) were among the most often utilised. Because of its simplicity and dependability, the fingerprint analysis method utilising high-performance thin-layer chromatography (HPTLC) has emerged as the most effective instrument for quality control of herbal medicines. It can serve as a tool for identification, authentication, and quality control of herbal drugs [7, 8].

STANDARDIZATION OF HERBAL DRUG:

A procedure called standardisation assures that each dose of chemicals has a specific amount, level of quality, and therapeutic effect. If the medicine examined has not been authenticated and characterised in to ensure reproducibility in the product's manufacturing, then a herbal product cannot be declared scientifically genuine [8]. In addition, numerous harmful and fatal side effects, including as acute toxicity, adverse reactions, impacts from impurities, including interactions with herbal medications, have lately been recorded. The phytochemical components of a herbal preparation determine its therapeutic activity. Scientists face a significant difficulty in developing reliable analytical techniques that can quantitatively analyse marker/bioactive chemicals and other important ingredients and reliably profile the phytochemical makeup[9]. Calculating the absolute or relative abundance (typically stated as a concentration) of one,

several, or all of the specific compounds contained in a sample is known as quantitative analysis of herbal medications [10]. Markers are components of herbal medicines that are chemically identified and used for quality control. whether or if they possess any therapeutic effect. Markers may be used to determine how much of a herbal medicine's active ingredient is present in the final product. Marker compounds are pure, isolated compounds, secondary metabolites mostly with terpenes, steroid, alkaloid, flavonoid aromatic hetero aromatic frameworks, and glycosides with alcoholic, carbonyl, olefinic, acid, ester, and amide functionalities that are very helpful for individual crude drugs, possibly not survive in goods made of multiple herbs. Use precise, easily analysed markers to differentiate between kinds in quantitative investigations [11].

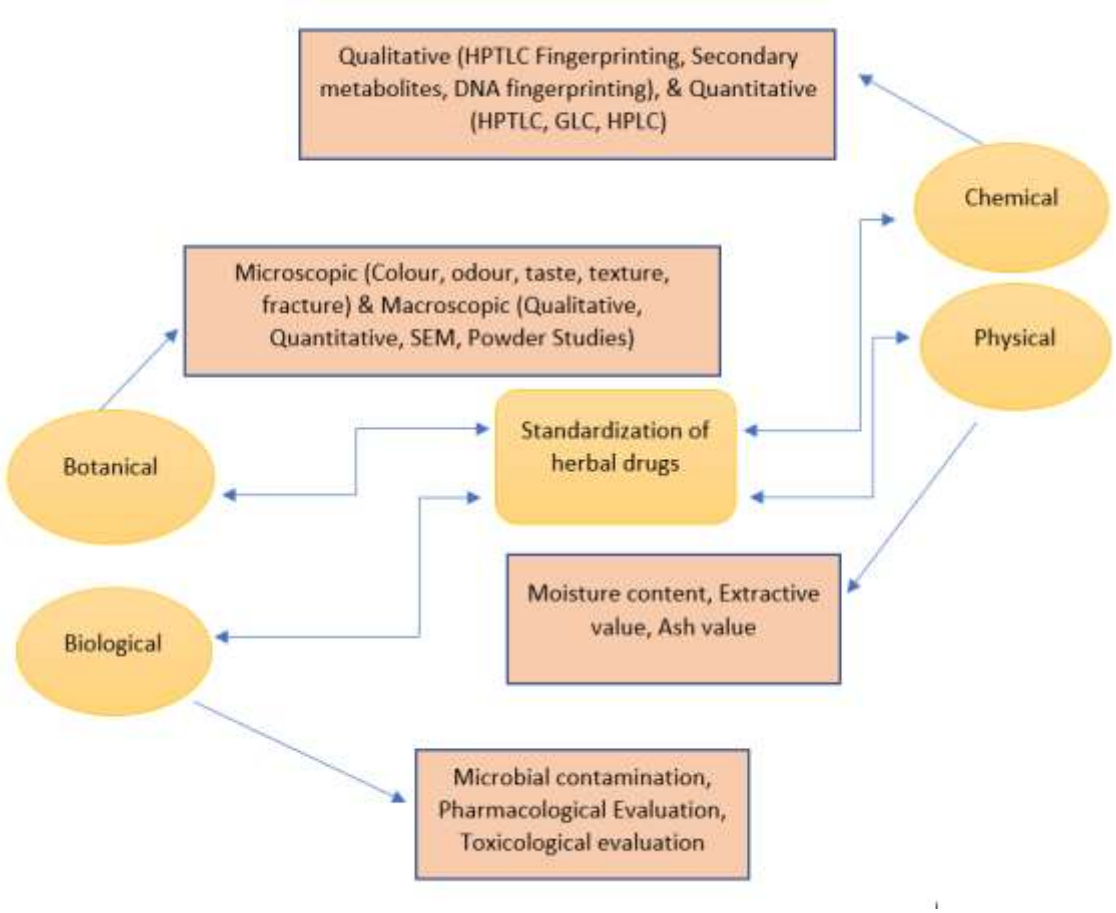

Figure 1: Block diagram of different evaluation parameter for standardization of herbal drugs.

ANALYTICAL TECHNIQUES USED IN HERBAL DRUG IDENTIFICATION AND QUANTIFICATION:

TLC:

Before instrumental chromatography techniques like gas chromatography and HPLC were developed, thin layer chromatography (TLC) was the most popular, adaptable method of choice for herbal examination. Because numerous pharmacopoeia, including the Chinese pharmaceuticals monographs, American herbal pharmacopoeia, Indian herbal pharmacopoeia, and Ayurveda pharmacopoeia, TLC is still extensively employed today for the examination of herbal medications. While there is comparatively less change in the straightforward TLC separation of herbal medicines than with instrumental chromatography, TLC is utilised as an easier method of first screening with a semi-qualitative evaluation in addition to other chromatography techniques. The observation of spots on the sample plate that were produced by the chromatography of an unknown and a reference sample, respectively, and had identical Rf values and equivalent magnitudes can help with identification. Semi-quantitative estimate is typically accomplished by visually comparing the size and intensity of the spots [12]. TLC has the benefit of having a wide range of options for finding and analysing herbal medications. TLC can also be used for multiple sample analysis and is rather straightforward. More than 30 sample sites can be examined for each plate. TLC QA-UV techniques and the CA MAG video storage system The constructed TLC plates can be used to obtain insightful qualitative and quantitative data [13].

A high-performance TLC (HPTLC) scanner may record data for TLC fingerprinting, including the chromatogram, retardation factor (Rf) values, colour of the separated bands, their absorption spectra, and the maximum and shoulder inflections of all resolved bands. All of them depict the sample's TLC fingerprint profile, along with the profiles on derivatization with various reagents. The data produced in this way may be used to identify genuine pharmaceutical products, weed out adulterants, and preserve the product's quality and consistency. To determine the amount of piperine in the methanolic extract of Sitopaladi churna, TLC fingerprinting was performed using a Silica Gel G plate with a mobile phase of toluene, ethyl acetate, and formic acid (5:3.5:0.5 v/v/v). Piperine's retention factor was determined to be 0.69 (shown by peak 7) at 342 nm [14].

HPTLC:

The HPTLC approach is frequently used in the pharmaceutical sector for process development, adulterant identification and detection in herbal products, as well as for pesticide and mycotoxin content determination and quality control of herbal and health food products. It has been widely documented that using less mobile phase than in HPLC allows for the simultaneous running of many samples. Additionally, mobile phases with a pH of 8 or higher have been said to work with HPTLC. The repeated detection (scanning) of the chromatogram under the same or different circumstances is another benefit of HPTLC. In order to simultaneously test many compounds in a multi-component composition, HPTLC has been researched. This method makes it feasible to authenticate distinct plant species and assess the uniformity and stability of their preparations coming from various sources [15].

HPLC:

For the isolation and purification of herbal components, pharmaceutical companies frequently use preparative and analytical HPLC. Low pressure HPLC (usually < 5 bar) and high pressure HPLC (pressure > 20 bar) are the two main categories of preparative HPLC. In preparative HPLC (pressure >20 bar), bigger stainless-steel columns and packing materials (particle size 10-30 m) are required. In analytical HPLC, resolution, sensitivity, and quick analysis time are the key factors to be taken into account. Kromasil 10 m, Kromasil 16 m, and Chiralcel AS 20 m are examples of silica columns for normal phase, while Chromasil C18, Chromasil C8, and YMC C18 are examples of columns for reverse phase. Compounds are to be isolated or purified, but in analytical work, information about the sample is what is sought after. This is crucial in the modern pharmaceutical sector because new products—natural and synthetic—must be released onto the market as soon as feasible. Spending less time on the synthesis conditions is made possible by having access to such a potent purification method [16].

Liquid Chromatography- Nuclear Magnetic Resonance (LCNMR):

The domains of pharmacokinetics, toxicity research, drug metabolism, and the drug development process have all found usage for LC-NMR, which increases speed and sensitivity of detection. One of the most effective and time-saving methods for the separation and structural elucidation of unknown compounds and mixtures, particularly for the structure elucidation of light- and oxygen-sensitive substances, is the coupling of chromatographic separation technology with NMR spectroscopy. Automated data capture and processing in LC-NMR improves the speed and sensitivity of detection. The online LC-NMR technology enables continuous registration of temporal changes as they emerge in the chromatographic run. The recent development of the three-dimensional approach and the pulsed field gradient technique in high-resolution NMR increases the applicability in structure elucidation and molecular weight data. The domains of pharmacokinetics, toxicology research, drug metabolism, and the drug discovery process can all benefit from these novel hyphenated approaches [17].

GAS CHROMATOGRAPHY (GC-MS):

Direct connections between many types of rapid scan mass spectrometer and GC equipment are possible. Due to their sensitivity, stability, and great efficacy, GC and GC-MS are universally recognised procedures for the analysis of volatile components of herbal medicines. For the qualitative study of the complicated elements, the hyphenation with MS in particular offers trustworthy information. In most cases, the capillary column's flow rate is low enough for the column output to be fed directly into the MS's ionisation chamber. The Ion Trap Detector is the GC's most basic mass detector (ITD). By electron impact or chemical ionisation, ions are produced from the eluted material in this instrument and stored in a radio frequency field. The trapped ions are subsequently released from the storage area and land on an electron multiplier detector. Controlled ejection makes it feasible to scan on the basis of mass-to-charge ratio. In comparison to quadrupole devices, the ions trap detector is remarkably small and less expensive. Numerous constituents that are present in natural and biological systems have been identified using GC-MS equipment [18].

DNA FINGERPRINTING:

It has been established that DNA analysis is a crucial tool for standardising herbal medicines. This method can be used to differentiate between genuine drugs that are phytochemically indistinguishable and replaced or falsified drugs. It has been found that while the phytochemical content varies depending on the plant part utilised, physiology, and environment, the DNA fingerprint genome remains constant regardless of the plant part used. All living cells are fundamentally made up of deoxyribonucleic acid (DNA)[19]. The exact arrangement of DNA base-pair sequences in the cell determines our traits, attributes, and physical qualities. The Central Dogma Theory explains how this particular configuration of adenine, guanine, thymine, and cytosine (referred to as DNA nucleotides) controls the synthesis of particular proteins and enzymes. The central dogma idea, which states that genetic information passes from DNA to RNA to proteins, is a key theory of molecular biology. Over the past few decades, the idea of fingerprinting has been used more and more to identify the lineage of different microorganisms, plants, and animals. Since most plants can exhibit significant diversity between strains despite sharing the same genus and species, genotypic characterisation of plant species and strains is helpful. The availability of intact genomic DNA from processed plant materials is another reason to use DNA fingerprinting on commercial herbal medications. Even in processed samples, adulterants can be identified, making it possible to authenticate the medicine[20]. The presence of intact genomic DNA specificity in commercial herbal medications, which aids in identifying adulterants even in processed samples, is the other beneficial application of DNA fingerprinting [21].

GENETIC MARKER: A gene or DNA sequence that has a known position on a chromosome and is connected to a specific gene or trait is called a genetic marker. It can be characterised as a variation that may result from a mutation or other change in the identified genomic locus.A genetic marker could be a small DNA sequence, like the region surrounding an SNP (single nucleotide polymorphism), or it could be a large DNA sequence, like a minisatellite. Some forms of genetic markers that are frequently utilised are [22].

1. RFLP (or Restriction fragment length polymorphism)
2. AFLP (or Amplified fragment length polymorphism)
3. RAPD (or Random amplification of polymorphic DNA)
4. VNTR (or Variable number tandem repeat)
5. Micro satellite polymorphism
6. SNP (or Single nucleotide polymorphism)
7. STR (or Short tandem repeat)
8. SFP (or Single feature polymorphism)

ROLE OF GENETIC MARKER IN HERBAL DRUG TECHNOLOGY

Genetic variation/genotyping:

Geographical factors influence the active components of medicinal plants and, consequently, their activity profiles, as has been well-documented. Geographical variation has been investigated at the genetic level by numerous researchers. The development of agricultural improvement programmes, management of germplasm, and evolving conservation policies all benefit from estimates of genetic diversity. It has been discovered that RAPD-based molecular markers can help distinguish between distinct neem accessions gathered from various geographical locations. A lot of work has been done in another crucial area called germplasm analysis to explore genetic diversity. Numerous crops, including rice, wheat, chickpeas, pigeon peas, pearl millet, etc., are being fingerprinted [23].

Authentication of medicinal plants:

Plant species with therapeutic value have been authenticated frequently using DNA-based approaches. This is especially helpful for those that are frequently replaced or adulterated with other genera or varieties that are identical in terms of morphology and/or phytochemistry. RAPD markers were used to distinguish Lycium barbarum's dried fruit samples from those of related species. Yu-pingfengsan, a Chinese herbal remedy, comprises components that have been identified using the RAPD method. In this investigation, a single RAPD primer was used to detect the presence of three herbs (Astragalus membranaceous (Fisch.) Bge, Ledebouriella seseloides Wolff, and Atractylodes macrocephala Koidz) in the formulation [24].

Detection of adulteration/substitution: The separation of these plants and the detection of substitution by other closely related species have been successfully accomplished using the techniques of sequence characteristic amplified region (SCAR), AP-PCR, RAPD, and RFLP. For example, P. quinquefolius is frequently used instead of P. ginseng [25].

Medicinal plant breeding:

It has been discovered that ISSR-PCR is an effective and trustworthy method for identifying zygotic plantlets in citrus interploid crosses. To confirm sexual and apomictic offspring of intraspecific crossings in the well-known antihelminthic and diuretic Hypericum perforatum, molecular markers have been used. With the aid of RAPD markers, an effort has been undertaken to select fertile garlic clones with the aid of markers. For the purpose of choosing Piper longum micro propagated plants for conservation, RAPD markers have been utilized repeatedly [26].

Quality control and standardization of medicinal plant materials:

Even though there are numerous known chemotypes of a plant species, choosing the right chemotype to which therapeutic effects are attributed is challenging. However, choosing the right chemotype of the plant is essential to ensuring efficacy. DNA markers are trustworthy for informative polymorphism since each species' genetic makeup is distinct and unaffected by ageing, physiological conditions, or environmental influences [26]. Since DNA may be extracted from both fresh and dried organic plant tissue, detection is not limited by the physical form of the sample. DNA polymorphism is assessed using several DNA-based molecular methods. These include procedures based on hybridization, polymerase chain reaction (PCR), and sequencing [26].

CONCLUSION:

The herbal products market in India is aggressively expanding. There are now more herbal products available on the market. The standardisation of these herbal medications is necessary for the safety and effectiveness of herbal goods. There is a need for more sophisticated standardisation approaches because the conventional methodology is insufficient for the contemporary herbal industry. The total of all elements that directly or indirectly affect the product's security, efficacy, and acceptance constitutes the quality of herbal medicines. Many techniques, including botanical, chemical, spectroscopic, and biological methodologies, are utilised to estimate the active components contained in crude medications due to advancements in our understanding of the chemistry of these substances. All factors affecting the quality of herbal drugs should be taken into account when standardisation techniques are used. It is impossible to overstate the importance of the development of contemporary analytical instruments for testing the many quality factors for an efficient quality control herbal product. Monitoring the quality of the product from collection through processing to the completed packaged product is necessary to ensure the safety and efficacy of herbal medication.

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