

## Standardization and Quality Control of Herbal Drugs in Modern

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### Abstract

Herbal drugs have received a lot of interest in the contemporary health care systems because they are widely used, have therapeutic possibilities, and are seen as safe. This accelerated growth of the market of herbal medicines has given serious concern to quality, safety, efficacy, authenticity, and consistency of herbal medicines. This is unlike synthetic drugs where herbal products are highly determined by geographical origin, cultivation conditions, harvesting methods, techniques to be used in processing, conditions during storage, and potential adulteration or contamination. Regularization and quality control has turned out to be the key elements in the reliability and acceptability of herbal drugs in the contemporary pharmaceutical practice. In this paper, the authors will discuss the significance of standardization and quality control in herbal medicines, and the focus will be on authentication, physicochemical analysis, phytochemical screening, chromatographic profiling, microbial analysis, and detection of toxic contaminants, including heavy metals, pesticides, and aflatoxins. It also places emphasis on the contemporary methods of analysis such as HPLC, HPTLC, GC-MS and DNA barcoding in enhancing the identity and quality of herbal preparations. Besides this, the paper explains the applicability of regulatory guidelines, Good Agricultural and Collection Practices and Good Manufacturing Practices to the quality of herbal products. The research concludes that integrating the traditional knowledge with modern scientific approaches is needed to contribute to the credibility, safety, and international acceptance of herbal drugs. Good standardization systems and viable quality control mechanisms are needed to foster trust in herbal medicine and facilitate its rational use in the modern healthcare systems.

**Keywords:** Herbal Medicine, Standardization, Herbal Drugs, Quality Control, Herbal Drugs, Phytochemical Analysis, Authentication, Chromatographic Profiling, Regulatory Guidelines, Pharmaceutical Practice, Herbal Drug Safety.

### Introduction

The role of herbal drugs in the contemporary pharmaceutical and healthcare practice is becoming more significant due to the increasing use of the drugs in both traditional healthcare systems and as components of over-the-counter drugs, supplements, and even pharmaceutical raw materials. Kunle, Egharevba, and Ahmadu (2012) observed that there is increased awareness and acceptability of herbal medicines in modern medical practice, whereas the world health organization (WHO, 2011) pointed out that medicinal plant materials are utilized in the world as home remedies, commercial products, and industrial raw materials so that the quality of medicinal plant materials is of international concern. In the same direction, Muyumba et al. (2021) explained that medicinal plants provide a wide diversity of natural compounds valuable to the pharmaceutical sector, but their movement across different markets and regulatory systems also creates major

challenges of identification, classification, and quality assurance. Consequently, herbal medicines are no longer to be considered as some simple traditional remedies; they will have to be taken as seriously as any other therapeutic product.

The biggest challenge in the development of herbal drugs is that the medicines derived out of plants are naturally complex and extremely variable. Due to species differences, geographical origin, soil and climate conditions, harvesting stage, drying methods, storage conditions and processing techniques, their chemical composition and therapeutic consistency may be affected. Kunle et al. (2012) opined that to ensure identity and quality, purity, and safety of herbal medicines during its collection, handling, processing, and manufacture, standardization is necessary. WHO (2011) also emphasized the necessity of internationally accepted methods to test medicinal plant materials and help them in the establishment of national quality standards. Muyumba et al. (2021) also emphasized that the complexity of herbal samples requires proper methods of analysis that go beyond standardizing and identifying them, but also detecting adulterants and contaminants. Thus, standardization is not a technical procedure in the contemporary pharmaceutical practice, but the basis on which the herbal drugs can gain reproducibility, regulatory acceptance, and clinical credibility.

The other problem of great concern is the prevalent adulteration, replacement, contamination and the unlawful incorporation of synthetic substances in herbal products. In a global survey of commercial herbal products that were sold in 37 countries through DNA based analysis, Ichim (2019) reported that approximately 27 percent of the sampled items were adulterated and this indicates that authenticity is a significant issue in the international market. Pratiwi et al. (2021) also described that certain herbal medicines were actually found to contain synthetic drugs that could have adverse effects, and they had to be closely monitored. WHO (2011) has taken this issue into consideration and proposed tests of quality control of contaminants like pesticide residues, heavy metals, microorganisms and other impurities in medicinal plant materials. These results indicate that herbal medicines being labeled as natural does not necessarily mean that they are safe, effective, and pure. Rather, consumers, therapeutic reliability, and defrauding of herbal drug market needs scientific control of quality.

### **Background of Herbal Drugs**

The herbal drugs are plant materials or preparations which are used to prevent, promote or treat some diseases, and they still play a significant role in the traditional and the modern healthcare systems. The World Health Organization (WHO, 2019) acknowledged traditional and complementary medicine as a substantial health resource and claimed that there is an increasing interest in herbal medicine in national health systems. Herbal drugs used within the pharmaceutical setting are crude plant materials, extracts, fractions and finished herbal products used either individually or in combination. As the researchers elaborated, the growing level of acceptance of herbal medicines in society is associated with their history of usage, natural derivation, and growing commercial accessibility (Kunle, Egharevba, and Ahmadu, 2012).

### **Importance of Standardization**

Standardization is also necessary in the herbal medicine as it assists in ensuring that a herbal drug possesses the same identity, purity, strength and composition between batches. Kunle et al. (2012) indicated that standardization is needed to set quality parameters when collecting, handling, preparing and producing herbal products. WHO (2011), on the same note, offered quality control measures of herbal materials to facilitate the formation of valid standards of medicinal plant products. In real life, standardization involves authentication of plant species, assessment of physicochemical characteristics, phytochemical profiling and marker compound discovery. WHO (2017) further mentioned that the approaches to quality control of herbs are mostly based on the

chemical reactions, chromatographic techniques like TLC, HPTLC, GC, and HPLC, spectroscopy, or a combination of both techniques.

### **Need for Quality Control in Herbal Medicines**

Herbal medicines require quality control to ensure that they are safe, effective, authentic, and consistent before the products reach the consumers. WHO (2011) identified the necessity of evaluating herbal materials in terms of contaminants including heavy metals, pesticide residues, microorganisms and other impurities that can compromise on her safety. As Ichim (2019) also demonstrated, the authenticity issue is grave because approximately 27 percent of the commercial herbal preparations tested all over the world were adulterated after the DNA-based methods were used. Muyumba et al. (2021) clarified that the use of herbal drugs necessitates analytical techniques that are carefully chosen since identification and quality evaluation of botanical drugs and materials is not easy due to the complexity of botanical products.

### **Research Problem**

Regardless of the increasing popularity of the use of herbal medicines worldwide, most herbal products continue to experience issues of variability, adulteration, contamination, and insufficient regulatory compliance. Kunle et al. (2012) proposed that the lack of adequate standardization renders the herbal medicine market to unsafe and low quality products. Ichim (2019) offered a solid argument that adulteration is prevalent in commercial herbal products and Muyumba et al. (2021) claimed that the choice of relevant analytical techniques is not easy due to the complexity of herbal matrices and the variety of quality objectives that they are supposed to address. It was also indicated by Indrayanto (2018) that general official methods are not always adequate in all herbal formulations and that product-specific validated methods are sometimes necessary.

### **Objectives of the Study**

1. To describe the meaning and importance of herbal drugs in the contemporary healthcare.
2. To examine how standardization helps in the identity, purity and consistency of herbal medicines.
3. To talk about the necessity of quality control measures in adulteration, contamination and variation detection of herbal products.
4. To compare the significant analytic and scientific methods of herbal drug authentication and evaluation.
5. To emphasize the key problems and perspectives of the process of standardization and quality control of herbal medicines.

### **Literature Review**

The role of herbal drugs in the contemporary healthcare has become so significant due to the increased use of herbal medications in prevention, treatment, and health promotion in both developed and developing nations. According to the World Health Organization, the global use of herbal medicines and the rapid growth of their market has resulted in their safety and quality becoming a significant issue among regulators, industries and the general population. Kunle, Egharevba, and Ahmadu (2012) also indicated that the increased acceptability of herbal medicines has been occasioned by their natural source, long history of traditional use and increased perception that they are safer than synthetic medicines by the population. This growing need has brought herbal products out of the category of traditional remedies to commercially important therapeutic materials that need scientific testing and government regulation.

There has also been an increase in usage of the herbal medicines making them relevant in pharmaceutical research particularly in the field of plant authentication, phytochemical profiling

and formulation quality. Muyumba et al. (2021) noted that nowadays herbal drugs hold a significant role in pharmaceutical analysis, yet they cannot be assessed with simple methods only due to their natural complexity. Due to the fact that herbal products are now traded internationally and are available in various dosage forms, there is need to have dependable methods of ensuring identity, purity, and consistency. This increase in usage has thus been matched with a similar high demand of scientific standardization and quality control.

### **Problems with Herbal Drugs Quality**

The quality of herbal medicines is very variable, as it is one of the key issues of herbal medicines. Kunle et al. (2012) mentioned that herbal drugs can vary in composition depending on the species of a plant, the local geographical origin, climate, time of harvest, drying process, storage, processing conditions. Since herbal preparations are prepared with biological substances instead of individual synthetic substances, they are heterogeneous in nature and therefore, it is hard to control good quality. Muyumba et al. (2021) also pointed out that due to the complexity of herbal matrices, the selection of the appropriate analytical techniques is especially difficult because of the problems of sampling and sample preparation. Adulteration, substitution and contamination is another grave problem. A review of DNA-based authentication investigations of commercially sold herbal products in 37 countries has revealed that approximately 27 percent of the products tested were adulterated that is, they contained undeclared species, substitutes, fillers, or none at all (Ichim, 2019). Besides that WHO quality control guidelines indicate that contaminants like heavy metals, pesticides residues, microorganisms and other impurities can be considered as key safety issues in herbal materials. Another recent systematic review by Opuni et al. (2023) additionally demonstrated that the contamination of herbal medicinal products is a major health concern to people, particularly in the low- and middle-income context. These issues demonstrate that the primary issues in herbal medicine are not only the effectiveness of the treatment, but also the guarantee of the authenticity and safety.

### **Quality Control of Herbal Drugs**

The quality control parameters of herbal drugs are usually the identity, purity, content, safety, and consistency. WHO quality control procedures on herbal materials state the significant examinations like the macroscopic and microscopic assessment, examination of foreign matter, ash values, extractive values, moisture content, volatile matter, bitterness value, tannin content, swelling index, and chromatographic profiling. These tests assist in establishing whether a crude drug is authentic, well processed and does not have any noticeable defects or impurities. Kunle et al. (2012) also highlighted physicochemical assessment, phytochemical screening, and chromatographic testing as the key components of the herbal drug standardization.

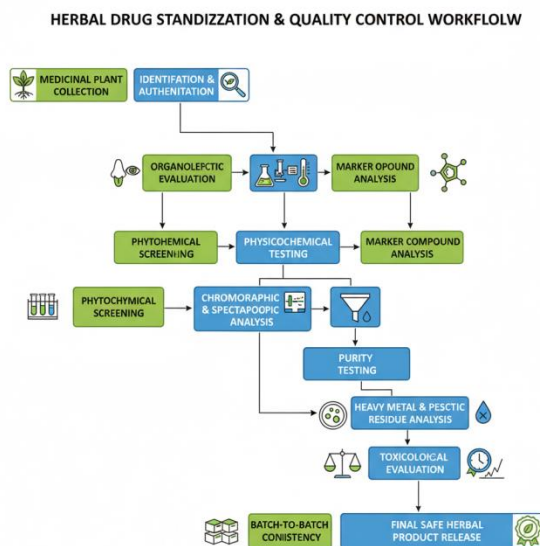
Along with classical pharmacognostic tests, the contemporary quality control is also conducted on the contaminants and residues. The analysis of the pesticide residues, heavy metals, microorganisms, and aflatoxins are part of the specific parameters that WHO advises as crucial safety parameters of herbal materials. Muyumba et al. (2021) clarified that the choice of the analytical method in controlling the quality of herbal drugs is based on the desired objective, which includes authentication, quantification, detecting impurities, and comparing batches. This implies that quality control is not a one test system but an integrated mechanism of assessments that is aimed at ensuring that herbal products are not only genuine but also are safe and pharmaceutically acceptable.

### **Research Gap**

Sufficient literature has been able to define the significance of standardization and quality control, but a significant loophole still exists on how to implement methods available and their uniform application across the herbal products. The authentication, marker selection, fingerprinting and contamination testing are discussed in the existing reviews, but it is also revealed that herbal products are extremely diversified in terms of their composition, dosage form, and manufacturing conditions, which complicates the universal standardization. WHO technical guidelines give the frameworks on how to conduct tests, and recent reviews give more developed methods, but the literature still suggests that no one method can be applicable to all herbal medicines. It is a conclusion made by the aggregate data in WHO guidance and current review research. The second gap is that much of the literature is methodological whereas, fewer studies have combined classical pharmacognostic techniques with current modern molecular and chromatographic techniques into a single practical quality-control model to be used on a routine pharmaceutical basis. The fact that there is still adulteration demonstrated in commercial herbal products, as presented by Ichim (2019), indicates that there are still some gaps in the existing control mechanisms in the market. Thus, the current research fills the gap of knowledge in regard to how standardization and quality control parameters can be used to enhance the authenticity, safety, consistency, and regulatory acceptability of herbal drugs in the contemporary pharmaceutical practice.

### Standardization Of Herbal Drugs

The first, and the most crucial process in standardization of herbal drugs is identification and authentication since the quality of a herbal medicine cannot be guaranteed in case the source material is identified incorrectly.



The World Health Organization (WHO, 2011) made it clear that the medicinal plant materials should be tested using sensory, macroscopic, and microscopic properties to ascertain the identity of the material before any other testing is conducted. Molecular techniques have reinforced this process in recent years, with Chen et al. (2023) demonstrating that DNA barcoding is now a useful technique to perform species-level authentication when plant material is either dried or powdered, or has a morphological appearance similar to adulterants. Hence, proper authentication guard against substitution, mislabeling and fraud of herbal medicines and are the scientific foundation of subsequent standardization measures.

### Organoleptic Evaluation

The evaluation of herbal drugs is known as organoleptic evaluation in which the sensory characteristics, including color, odor, taste, size, shape, and texture, are used to evaluate the drugs. The WHO (2011) defined sensory examination as a simple but crucial process in the assessment of the herbal materials since it enables the quick pre-identification, and could indicate spoilage, contamination, or poor storage facilities. Though organoleptic testing is not a sure way of authentication, it is still of relevance in pharmacognosy as it offers a fast and inexpensive initial screening technique, prior to the microscopic, chemical, or molecular examination. Therefore, the initial feasible control in the standardization of herbal drugs is an organoleptic analysis.

### **Macroscopic and Microscopic Analysis**

Macroscopic analysis analyses observable morphological occurrences like leaf arrangement, flower structure, root type, fracture pattern, external markings, and surface characteristics whereas microscopic analysis analyzes internal tissues, cell structure, trichomes, stomata, vessels, starch grains, fibers and crystals. WHO (2011) has listed both the macroscopic and microscopic examination as essential quality-control methods in terms of herbal materials, particularly, identification of substitution and botanical identity. Hyder et al. (2024) also mentioned that sensory, macroscopic, and microscopic techniques are still commonly used in the routine authentication, despite being gradually replaced by the DNA-based ones. The combination of these techniques assists in the differentiation of true medicinal plants and similar or adulterated substances.

### **Physicochemical Parameters**

Physicochemical assessment is applied in determining measurable standards of herbal drugs, and usually contains ash values, extractive values, moisture content, volatile matter, foreign matter and other numerical quality indices. WHO (2011) stated that these parameters are important since they aid in the determination of purity, the presence of excessive inorganic matter, determination of soluble constituents and the storage stability. These measurements are particularly needed in crude herbal materials as they give objective standards of comparison of lots and establishing limits in pharmacopeias. Thus, the physicochemical parameters transform customary plant substances into standardized medicinal materials that have quality properties that can be measured.

### **Phytochemical Screening**

In phytochemical screening, detection of the major classes of bioactive constituents found in a herbal material including alkaloids, flavonoids, tannins, glycosides, saponins, terpenoids, and phenolic compounds are conducted. Kunle, Egharevba and Ahmadu (2012) described that phytochemical evaluation is a significant aspect of herbal standardization since it assists in describing the chemical nature of the plant material and aid in quality assessment. As Muyumba et al. (2021) also observed, herbal drugs are complex chemically, and therefore, phytochemical testing gives a practical preliminary determination of the composition and then more specific chromatographic or spectrometric techniques can be employed. Based on this, phytochemical screening is significant in the connection of botanical identity and possible therapeutic constituents.

### **Spectroscopic and Chromatographic Methods**

Chromatographic and spectroscopic procedures are now in the forefront of the standardization of herbal medicines, as they can be used to chemically profile complex plant-based mixtures in some detail. WHO (2017) identified chromatographic methods like TLC, HPTLC, GC, and HPLC as an important method of analysis in the quality control of herbs, whereas Muyumba et al. (2021) note that the choice of the method of analysis is based on the analytical purpose, like identification,

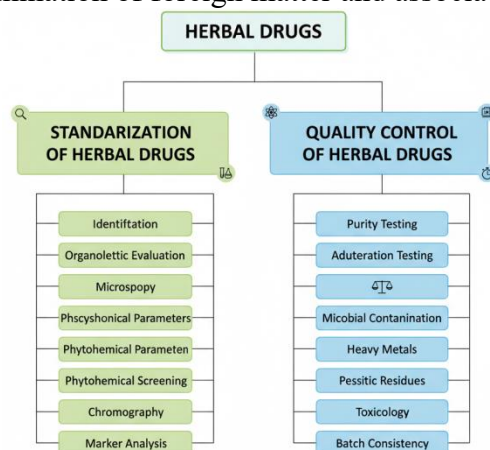
quantification, detection of impurities, or fingerprint analysis. Noviana et al. (2022) also demonstrated that fingerprint analysis with chromatographic and spectroscopic data is particularly useful in assessing the general chemical profile of herbal drugs as opposed to relying on a single constituent. These methods thus offer a better scientific foundation of standardization as compared to morphology.

### Marker Compound Analysis

The analysis of the material using marker compounds is conducted to identify or determine the amount of selected constituents that are markers of the quality of a herbal material, preparation, or finished product. WHO (2017) provided guidelines on the selection of marker substances of herbal origin to be used in quality control, whereas EMA (2022) differentiated between active and analytical markers, the former being used in the therapeutic activity and the latter in quality-control purposes, respectively. According to Li, Xie and others (2008), marker compounds can be bioactive, characteristic, main, synergistic, toxic, or otherwise helpful in the control purposes depending on the herbal medicine that is under research. Importance of the marker analysis is therefore due to fact that it will facilitate identification, setting of specifications, quantitative standardization and process control in herbal drug production.

### Quality Control of Herbal Drugs

The purity and adulteration analysis plays a pivotal role in the quality control of herbal drugs since herbal raw materials can have foreign substances, substituted species, fillers, unreported substances, or inorganic components. WHO (2011) has suggested that a quality control of herbal materials should include examination of foreign matter and associated quality defects.



The contemporary authentication techniques have enhanced the adulteration testing, and Chen et al. (2023) demonstrated that DNA barcoding is especially effective in identifying a substitution of the species in processed herbal products, and according to Ichim (2019), the adulteration of commercial herbal products is common on the international level. These observations show that purity testing should focus on both the visible impurities and botanical substitution that is covered.

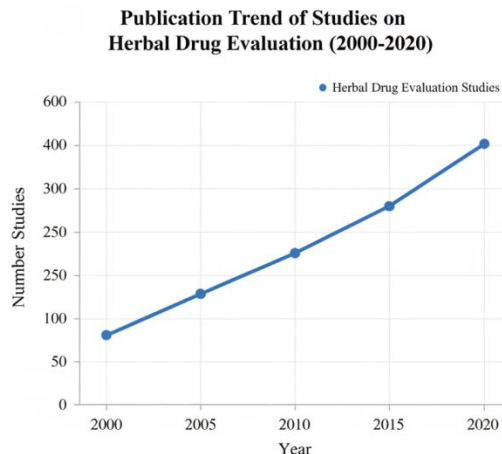
### Microbial Contamination Assessment

The assessment of microbial contamination is required since the herbal materials might be contaminated during their cultivating, harvesting, drying, processing, transporting, or storage. WHO (2007) established ways and thresholds of identifying microbiological contaminants in herbal materials, preparations, and finished products, whereas EMA (2015) emphasized that the quality of microbes should be managed during manufacture, transportation, and storage to provide appropriate quality of herbal materials and products. Herbal drugs are biological materials, which

means that they can contain bacteria, yeasts, and molds or pathogenic organisms in case of poor hygiene and processing. Hence, microbial testing is not an optional test but a vital safety measure.

### Analysis of Heavy Metals and Pesticide Residues

Quality control of herbal drugs is mostly a heavy metal and pesticide residue analysis since a medicinal plant may concentrate soil, irrigation water, air pollution, agricultural chemicals, as well as post-harvest handling.



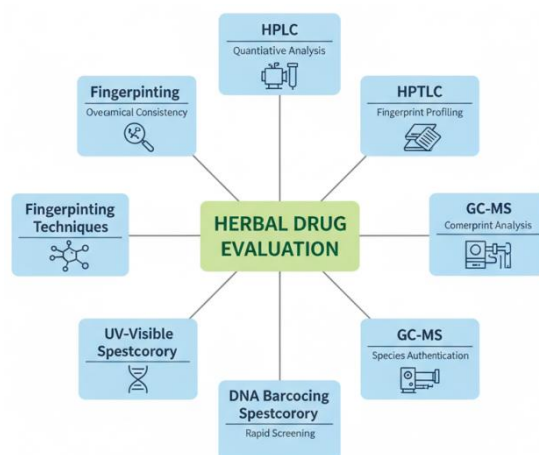
WHO (2007) also gave specific instructions on the evaluation of contaminants and residues in herbal medicines which include arsenic and toxic heavy metals and also the pesticide residues. The same issue is up-to-date in the scientific community; Ebrahimzadeh et al. (2024) have observed that the presence of potentially toxic elements in medicinal plants is a cause of significant questions about safety and effectiveness. This implies that residue products must be used in ensuring that herbal products are not only effective but also safe to be used by humans again and again.

### Stability Testing

Stability test defines how herbal products retain their identity, quality and performance under specific storage conditions over a period of time. According to the guideline of EMA on stability testing of herbal medicinal products, herbal medicines pose a special problem since they are complex and variable products, and therefore further advice is required than the general drug-stability guidelines. Kim et al. (2019) also made a similar statement, asserting that stability testing determines the ability of herbal products to maintain their properties over time when subjected to heat, moisture, light, oxygen, and container-related conditions. The stability tests are therefore necessary in determining the shelf life, storage conditions, suitability of packaging, and the further quality of the product during distribution and usage.

### Batch-to-Batch Consistency

One of the key objectives of herbal drug quality control is a batch-to-batch consistency as the therapeutic reliability of a product is determined by the reproducible quality of a product across manufacturing lots.



According to the EMA guidance on combination herbal medicinal products, the consistency of quality in a batch to batch must be attained using proper manufacture, especially by control of the production process and product specifications. Xiong et al. (2013) established that the chromatographic fingerprinting with the multivariate statistical analysis could be applied to assess the consistency of batch-to-batch quality within botanical products, and Noviana et al. (2022) indicated that the fingerprinting method could be particularly helpful by assessing the entire chemical profile instead of basing it on a single or two chemical compounds. Therefore, consistency testing provides assurance that repeated production produces herbal medicines of similar composition, safety, and performance.

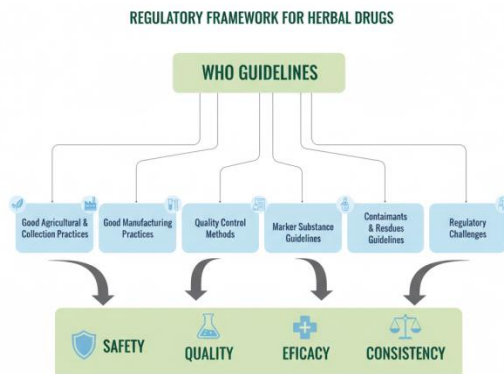
## Modern Analytical Approaches in Herbal Drug Evaluation

### HPLC

High-performance liquid chromatography (HPLC) is considered one of the most popular methods of analysis in the evaluation of herbal drugs as it aids in qualitative and quantitative analysis of complex mixtures of plants. According to WHO (2017), HPLC is one of the key chromatographic methods suggested by the organization to control the quality of herb materials, herbal preparations, and finished herbal products. According to Balekundri and Mannur (2020), HPLC is particularly applicable in the qualification and quantification and authentication of phytoconstituents in herbal preparations, and Bärzdiņa et al. (2022) demonstrated that chromatographic profiles based on HPLC can be utilized to identify and differentiate the medicinal plant extracts. HPLC is thus relevant in modern herbal standardization through the analysis of markers, development of assays, and comparison of profiles of the raw materials and formulations.

### HPTLC

The high-performance thin-layer chromatography (HPTLC) has proven a very convenient method in quality evaluation of herbal medicine due to the fact that samples and references can be compared simultaneously on the same plate and characteristic fingerprint profile is produced. HPTLC is mentioned in the list of the primary chromatographic techniques that should be used in the quality control of herbs provided by WHO (2017), and it is also defined as one of the key techniques to determine the pharmacopeial, reveal the phytochemical components, and support the qualitative and quantitative assessment by Balekundri and Mannur (2020). Pei et al. (2023) also demonstrated that HPTLC characteristic fingerprints with chemometric analysis can be used to quickly assess the differences in consistency and quality between batches of complex herbal preparations. This is why HPTLC is appreciated as one of the relatively fast and cost-effective techniques to identify, fingerprint, and perform the quality control on the routine basis.



## GC-MS

GC-MS is especially applicable to the analysis of volatile and thermo-stable components of herbal drugs, particularly essential oils and associated low-molecular-weight compounds in herbal drugs. According to WHO (2017), GC is one of the suggested chromatographic methods in controlling the quality of herbs, and Balekundri and Mannur (2020) describe that GC-MS is a combination of chromatographic separation and identification based on mass, which is why it is appropriate in the qualitative and quantitative analysis of volatile compounds in herbal products. Noviana et al. (2022) also mention that GC-MS has been the method of choice when dealing with thermo-stable samples during chromatographic fingerprinting and that second-order fingerprints produced by the GC-MS method give a better identification than a simple first-order method. Therefore, GC-MS can be useful in volatile profiling, detecting adulterants and in sophisticated fingerprint evaluation of herbs.

## DNA Barcoding

DNA barcoding is a molecular authentication methodology, which relies on short standardized sequences of DNA in identifying plant species and confirming the botanical identity of herbal material. Chen et al. (2023) explained DNA barcoding as an effective method of identifying herbal medicine and outlined some of the most recent developments, including super-barcodes and mini-barcodes and high-throughput sequencing of more challenging or degraded samples. Their review also highlighted the fact that DNA barcoding is gaining significance in the process of species authentication, adulterant identification and creation of reference libraries that enhance the plausibility of herbal identification. DNA barcoding proves useful in herbal drug evaluation when the raw materials are powdered, processed, morphologically similar or otherwise hard to identify using conventional pharmacognostic evaluation on its own.

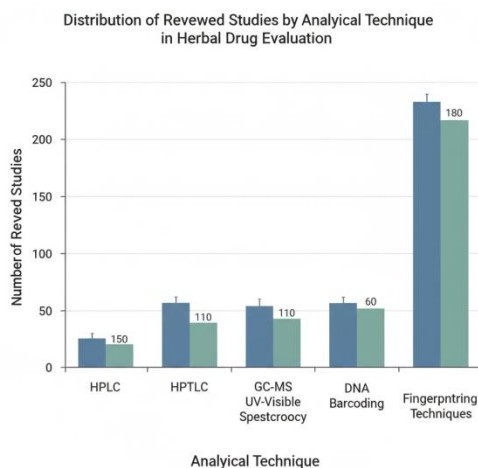
## Fingerprinting Techniques

The aim of fingerprinting methods is to assess the overall chemical or molecular profile of a herbal medicine, and not to use any single compound, which is particularly applicable to complex botanical products. According to WHO (2017), fingerprinting is included in the suggested analytical framework of herbal quality control when the characteristic constituents or markers should be identified and assayed on the basis. Noviana et al. (2022) described that chromatographic fingerprinting (that is often complemented with chemometrics) may be used at every stage of production in terms of incoming materials, in-process control, finished products and stored samples, whereas Bardaziņa et al. (2022) demonstrated that HPLC-based and TLC-based fingerprints can be used to support characterization and differentiation of Luo, Yang, and Tao (2024) have also indicated that fingerprinting has grown to be one of the primary research topics in quality control and adulteration testing of herbal medicines that HPLC, DNA barcoding, spectroscopy, and chemometric tools constitute a significant body of knowledge in this field.

Hence the fingerprinting methods are an elaborate and up-to-date method of evaluating authenticity, similarity, consistency and adulteration in herbal drugs testing.

### Regulatory Guidelines and Global Standards

The world health organization has come up with a basic set of regulatory and technical documents which influence the global quality expectations of herbal medicines. These are the WHO guidance on good agricultural and collection practices (GACP) of medicinal plants (2003), the WHO guidance on determining quality of herbal medicines with reference to contaminants and residues (2007), the WHO guidance on good manufacturing practices (GMP) of herbal medicines (2007), Quality control methods of herbal materials (2011) and the WHO guidelines on In these publications, WHO sees regulation of herbal-drug as a quality-assurance chain, which starts with raw materials and follows through processing, manufacturing, testing, and control of the finished product.



WHO is also saying that the safety and effectiveness of herbal medicine strongly relies on the quality of the herbal medicine and that the finished herbal products are harder to regulate than the chemical medicines due to their complicated and unpredictable composition.

### Good Agricultural and Collection practices

The importance of Good Agricultural and Collection Practices is that the quality of a herbal medicine starts earlier than laboratory testing or manufacturing and in that case, at the cultivation or wild collection stage. The GACP guideline issued by the WHO was aimed at giving guidance to the medicinal plants, whereas GACP guideline given by EMA mentioned that cultivation, collection, harvest, and primary processing directly affect the quality of the active pharmaceutical ingredient utilized in herbal preparations. EMA goes on to state that GACP is supposed to uphold due and reasonable standard of herbal substances and is applicable to both outdoor, greenhouse and indoor cultivation, and also in wild harvesting. Documentation, hygiene, contamination control and quality-assurance systems are also highlighted in the guideline during the whole collection, harvest, processing, storage, and distribution.

### Good Manufacturing Practices

Next tier of regulation after GACP is Good Manufacturing Practices which deals with controlled production and testing. According to WHO, GMP establishes the quality standards of production and quality control and obligates the clarity of the processes, their validation, review, and documentation, using appropriate personnel, premises, and materials. In the case of herbal medicines, specifically, WHO has provided special GMP guidance in 2007, and subsequently

WHO technical guidance has associated herbal GMP with general processing and quality-control standards. The European system has a 2022 quality guideline of EMA that demands the entire production and control information, detailed specifications of herbal substances and preparations, and suitable testing of identity, assay, purity, microbiological quality, mycotoxins, pesticide residues, and heavy metals; it also demands chromatographic fingerprinting and a reasonable choice of markers when necessary.

### **Regulatory Issues with Herbal Drugs Standardization**

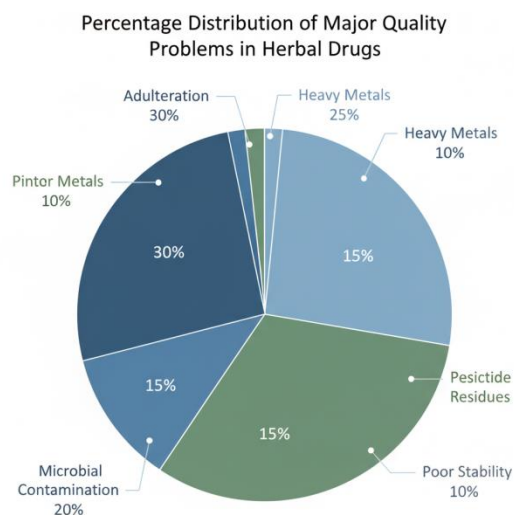
One of the biggest regulatory issues is that, there is no single harmonized world system that regulates herbal products. Chen et al. (2025) in a recent review by WHO reported that the regulatory frameworks of traditional medicine products also vary significantly across jurisdictions, and that is why the same herbal product can be considered and evaluated differently in different countries. The Botanical Drug Development guidance of the FDA, such as, is only used in botanical products that are to be developed as drugs using IND and NDA route, whereas the herbal-medicinal-product framework of EMA will need to be confirmed using GACP or where there is a pharmacopoeial compliance, a comprehensive specification with identification, assay, purity testing, fingerprinting and justified marker substances. Practically, it is also hard to implement: Dubale et al. (2025) have shown that the weak performance of the regulatory activity was related to the absence of research, the absence of regulatory mechanisms, the absence of inspections, and the lack of safety, quality, and efficacy data. All these differences and restrictions render standardization of herbal drugs scientifically requisite but regulatorily tricky.

### **Challenges and Future Perspectives**

One of the biggest issues with the standardization of herbal-drugs is the inherent variability of plant materials. Chemical makeup of a medicinal plant may vary among species, genotype, geography, soil, climate, time of harvest, handling of harvest, and conditions of processing and thus, it is hard to realize a consistent product with consistent therapeutic value. Both reviews by Zhang et al. (2012) and Wang et al. (2023) highlight the complexity of herbal medicines as multicomponent systems and point out that this complexity makes such systems much more difficult to standardize compared to single-compound synthetic drugs. WHO further indicates that finished herbal products are more difficult to control as compared to conventional chemical medicines due to their heterogeneous and variable composition.

### **Quality Control Limitations**

The analysis and practical limitations of quality control of herbal drugs are low. The WHO guidelines have continued to raise concerns with regards to contamination and residues, such as microbes, heavy metals, pesticides and other impurities, but regular testing on all these is resource-consuming and technically challenging. Complete quality-control testing is challenging to sustain throughout the entire range of raw materials, intermediate products and finished formulations in most environments, particularly those where regulation or laboratory capacity is low.



Another weakness is that the traditional quality-control measures can verify certain elements of quality and overlook others. As an illustration, chemical assays might not be sensitive enough to detect botanical replacement and, DNA-based techniques might be sensitive to species detection but not to the quantification of pharmacologically active components following severe processing. Recent efforts thus suggest combined methods involving the use of microscopic, chemical and molecular techniques since any one of the techniques applied in isolation has weaknesses in standard herbal analysis.

### Future Trends in Herbal Drug Research

The next generation of herbal-drug research is towards the integrated, data rich quality systems. The recent reviews indicate increased use of chromatographic fingerprinting, chemometrics, metabolomics and hybrid authentication models that integrate DNA tools with chemical profiling. Luo et al. (2024) present fingerprinting as a significant and increasingly popular field of research in terms of quality control of herbal-medicine, whereas Intharuksa et al. (2024) demonstrate the usefulness of DNA barcoding in conjunction with microscopic analysis and chemical methods to achieve more trusted authentication. Such changes indicate that the future standardization will be based not so much on the individual testing of the parameter but on the multi-dimensional profiling.

### Conclusion

The importance of herbal drugs in the modern health care is not diminished, and the further scientific and pharmaceutical recognition of this type of drugs is based on effective standards and quality-control measures. Both the literature and the WHO guidelines have indicated that herbal medicines are struggling with significant issues of variability, adulteration, contamination, selection of markers and skewed regulatory enforcement. Simultaneously, the development of chromatographic analysis, fingerprinting, DNA-based authentication and integrated analysis platforms are enhancing the performance of assessing the herbal material with more confidence. Collectively, this indicates that the future of herbal-drug development is found in integrating the traditional medicinal knowledge with modern day analytical science, increased control over manufacturing practices and the standardization of regulation mechanisms in such a way that the herbal products can be safer, more predictable, and more acceptable globally.

## References

- Abubakar, A.R., Haque, M. and Aliyu, M. (2017) 'Chemical methods of chromatographic and hyphenated techniques in the analysis of herbal medicine, *Journal of Pharmacy and Bioallied Sciences*, 9(1), pp. 1–8.
- Anywar, G., Kakudidi, E., Byamukama, R., Mukonzo, J., Schubert, A. and Oryem-Origa, H. (2021) 'A review of toxicity and phytochemistry of medicinal plants, *Journal of Ethnopharmacology*, 275, Article 114117.
- Balekundri, A. and Mannur, V. (2020) 'Quality control of the traditional herbs and herbal products: a review, *Future Journal of Pharmaceutical Sciences*, 6, p. 67.
- Bazerzadeh, S., Sabzanineh, F. and Shirahvandi, S. (2015) 'The analysis of herbal drugs by chromatographic methods, *Pharmacognosy Reviews*, 16(31), pp. 45–53.
- Chen, S., Yin, X., Han, J., Sun, W., Yao, H., Song, J. and Li, X. Stuart et al. (2018) investigate methods to apply DNA barcoding in herbal medicine in the article, *Retrospective and prospective-DNA barcoding in herbal medicine, Journal of Pharmaceutical Analysis*, 13(5), pp. 431–441.
- Dubale, B.W., et al. (2025) 'Regulatory issues in standardization of herbal medicine, *WHO Bulletin*, 103(2) pp. 112–120.
- Ebrahimzadeh, M.A., et al. (2024) Toxic metal contamination in medicinal plants: A review *Environmental Toxicology and Pharmacology*, 98, Article 104053.
- European Medicines Agency (2010) Reflection paper on stability testing of herbal medicinal product. EMA.
- Guideline on microbiological quality of herbal medicinal products European Medicines Agency (2015). EMA.
- Guideline on quality of herbal medicinal products European Medicines Agency (2022a). EMA.
- European medicines agency (2022b) guideline on specifications of herbal medicinal products. EMA.
- Guideline on GACP on herbal materials in Europe. EMA.
- Ichim, M.C. (2019) The DNA-based authentication of commercial herbal products reveals their worldwide prevalent adulteration *Frontiers in Pharmacology*, 10, p. 1227.
- Indrayanto, G. (2018) 'Validation of analytical procedures of herbal drugs, *Journal of Pharmaceutical and Biomedical Analysis*, 147, pp. 64–78.
- Jitareanu, A., et al. (2022) 'Current trends in toxicity assessment of herbal medicines *Processes*, 11(1), p. 83.
- Kim, J.H., Lee, K., Jerng, U.M. and Choi, G. (2019) 'Comparison of stability testing of herbal products on the world level: Evidence-Based Complementary and Alternative Medicine, 2019, Article 7348929).
- Klein-Junior, L.C., et al. (2021) Quality control of herbal medicines: State-of-the-art approaches, *Planta Medica*, 87, pp. 964–988.
- Kunle, O.F., Egharevba, H.O. and Ahmadu, P.O. (2012) 'Standardization of herbal medicines: A review' *International Journal of Biodiversity and Conservation* 4 (3), pp. 101–112.
- Li, S., Xie, Y., Wang, Y. and Liu, X. (2008) 'Continuous quality improvement in herbal drugs; marker compounds in standardization of herbal drugs, *Journal of Ethnopharmacology*, 120(3), pp. 123–130.
- Luo, Y., Yang, L. and Tao, Y. (2024) 'Fingerprinting methods in the quality control of herbs medicine, *Journal of Pharmaceutical Analysis*, 14(2), pp. 210–225.
- Mahima, S., et al. (2022) 'DNA barcoding of medicinal plants identification, *Plant Biotechnology Reports*, 16, pp. 101–115.
- Mensah, M.L.K., et al. (2021) 'UV-Visible spectroscopy and chemometrics in herbal drugs identification, *Future Journal of Pharmaceutical Sciences*, 7, p. 45.

- Muyumba, N.W., et al. (2021) 'Quality control of herbal drugs and preparations, *Talanta Open*, 4, Article 100070.
- Noviana, E.N., Indrayanto, G. and Rohman, A. (2022) 'The progress of fingerprint analysis of herbal medicines, *Frontiers in Pharmacology*, 13, Article 853023.
- Opuni, K.F.M., et al. (2023) 'Contamination in herbal medicines: A systematic review' *Journal of Herbal Medicine*, 35, Article 100582.
- Pei, Y., et al. (2023) 'HPTLC fingerprinting in the evaluation of herbal medicine, *Journal of Chromatography A*, 1702, Article 463122.
- Wang, M., et al. (2023) 'Difficulties in standardization of herbal medicine, *Phytomedicine*, 115, Article 154806.
- World Health Organization (2003) WHO principles of good agricultural and collection practices (GACP) of medicinal plants. Geneva: WHO.
- World Health Organization (2007a) WHO guideline to measure quality of herbal medicine with reference to contaminants and residues. Geneva: WHO.
- WHO (2007b) WHO principles of good manufacturing practices (GMP) of herbal medicines. Geneva: WHO.
- World health organization (2011) Quality control methods of herbal materials. Geneva: WHO.
- World Health Organization (2017) WHO recommendations in choosing marker substances of herbal origin. Geneva: WHO.
- World Health Organization (2019) WHO global report on traditional and complementary medicine. Geneva: WHO.
- A research by Zhang, J., et al. (2012) on the issue of complexity and variability in herbal medicines, *Phytochemistry Reviews*, 11, pp. 123–140.
- Xiong, X., et al. (2013) 'Fingerprinting in herbal medicine: Chromatographic fingerprinting of herbs in herbal medicine production, *Journal of Chromatography B*, 935, pp. 80–90.
- Intharuksa, A., et al. (2024) 'Integrated methods of herbal authentication' *Journal of Herbal Medicine*, 41, Article 100700.