Ensuring Safety and Efficacy: Protocols and Challenges in Medicinal Plant Utilization

CHAPTER 07

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SUMMARY

Herbal medicine, commonly referred to as herbalism or phytotherapy, utilizes plant-derived compounds for medicinal intentions. The effectiveness and as well as safety of herbal remedies are greatly influenced by the quality of the source materials utilized in their preparation. Both intrinsic (genetic) and extrinsic factors, such as environmental conditions, good agricultural practices, and good collection practices (GACP) for medicinal plants, including plant selection and cultivation, generally influence the quality of source materials. Medicinal plants have been utilized for an extended period to enhance human health. As pharmaceuticals, supplementary and alternative therapies, dietary supplements, cosmetics, and, shockingly, medical gadgets, they are now enjoying a boom in worldwide significance. Significant quality Difficulties arise from the complexity of herbs and extracts, which are delivered to a wide range of markets and regulatory settings. Consequently, the necessity for suitable analytical methods to identify and standardize these substances, as well as to detect adulterants and contaminants, is exacerbated. The primary objective of evaluating the quality of the ingredients in commercial herbal remedies is to guarantee their safety. Nevertheless, herbal remedies only work if they keep their overall phytochemical consistency since they are made up of many different plant secondary metabolites. The maintenance of phytochemical consistency in commercial products is contingent upon strict physical processing and extract manufacturing protocols, as well as the authenticity and homogeneity of the botanicals. Additional requirements for quality assurance include the establishment and application of harmonized multi laboratory-validated analytical methodologies, as well as transparency in the supply chain through vendor audits.

INTRODUCTION

Herbal medicine, commonly referred to as herbalism or phytotherapy, utilizes plant-derived compounds for medicinal intentions. This tradition originated in ancient cultures, where plants were highly respected for their therapeutic qualities. Ancient medicinal systems such as Ayurveda, Traditional Chinese therapy (TCM), and Native American cures completely attest to the ancient importance of herbal therapy. Herbal medicine has consistently been an essential component of primary healthcare. An estimated 82% of the world's population is believed to utilize herbal medical goods for their therapeutic advantages (Aware et al., 2022; Islam et al., 2021).

Currently, the primary focus in evaluating the substances found in commercially available traditional and modern herbal medicines, nutritional supplements, functional foods, and "super" foods is to ensure their safety by assessing their quality. Nevertheless, there is a requirement for a robust quality assurance framework for botanicals that would encompass both safety and effectiveness (Wang et al., 2023). The effectiveness and safety of herbal medicine finished products rely directly on the quality and chemical composition of the raw materials derived from medicinal herbs. Nevertheless, the phytochemical compositions of the raw materials derived from medicinal herbs exhibit qualitative and quantitative variations. It is crucial to establish precise quality standards that are closely connected to the consistency of phytochemical profiles. Adhering strictly to the standardized quality valuations would ensure consistent pharmacological activity and make it easier to compare and analyze clinical data in a meaningful way (Govindaraghavan & Sucher, 2015).

SAFETY PROTOCOLS FOR MEDICINAL PLANTS USAGE

There are some challenges to the safety monitoring of plant medicines. Given the significant global consumption of plants products and medications, pharmacovigilance systems must incorporate them. It is crucial to assess the threats connected with the use of herbal treatments just based on population exposure. As a result, the safety of these goods has emerged as a major public health issue (WHO, 2004). In recent years, there have been a rising number of poisoning incidents worldwide. This has brought attention to the necessity of conducting a

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complete toxicity evaluation and maintaining active pharmacovigilance about these products. This is necessary to guarantee its safe usage and protect the general public's health (Zhou et al., 2013).

National drug regulatory agencies frequently deal with and share common challenges, such as those pertaining to regulatory status, safety and efficiency assessment, quality control, safety monitoring, and insufficient or limited information of herbal, balancing/alternate and traditional medicine (WHO, 2005).

Regulatory Status of Herbal Medicines

The classification and definition of plant remedies are subject to variation among countries. Depending on the regulations governing foods and medicines, different countries may classify a single medicinal plant as a food, a functional food, a dietary supplement, or an herbal medicine. This creates a significant challenge in the definition of the term "herbal medicines" for national drug regulation, while also confusing patients and consumers (WHO, 2005). For example, the Dietary Supplement Health and Education Act (DSHEA) of 1994 regulates natural products in the United States (U.S. Food and Drug Administration, 2012). A major obstacle in many countries is the frequent absence of communication and exchange of regulatory information on homeopathic drugs among regulatory bodies and safety monitoring (WHO, 2004).

Evaluation of Safety and Challenges

It is indisputable that the criteria, procedures, regulations, and research methodologies required to assess the efficacy and safety of herbal remedies are complicated (WHO, 2005; Zhou et al., 2013). A solitary herbal remedy encompasses numerous natural components, whilst composite herbal medical product may comprise many folds more. Isolating each active ingredient from the specific herb used in herbal medicine formulation or production would entail significant time and resources. Particularly in cases when a botanical product consists of a combination of two or more herbs, conducting such an examination may be exceedingly difficult (WHO, 2005).

Quality Control and Challenges

Quality of source materials for medicinal plants is often influenced by both internal (genetic) and extrinsic factors which include plant collection and farming. The intricacy of doing quality assessments on the raw ingredients of herbal treatments arises from the amalgamation of these factors (WHO, 2005). Key prerequisites for ensuring the quality control of beginning materials encompass accurate identification of medicinal plant species, meticulous storage procedures, and stringent sanitation and cleansing techniques for diverse materials, in accordance with established Good Manufacturing Practice (GMP) guidelines.

The challenge of verifying the presence of all plants or starting materials is one of the most significant obstacles frequently met in the quality regulator of finished herbal medicinal products, particularly a combination of herbal products (WHO, 2005). As a result, the specific criteria and approaches for ensuring the quality of final herbal products are considerably more complex compared to those for other medications (WHO, 2004).

Safety Monitoring of Herbal Medicines

The rise of prominent safety issues, the reliance of numerous individuals in developing nations on plants as their main medicinal resource, and the lack or inadequate regulation of herbal medicines in many countries have emphasized the necessity to closely monitor safety and further investigate the potential advantages and disadvantages associated with their utilization (Rodrigues & Barnes, 2013). The consumption of herbal medicines can lead to adverse events due to various factors, such as the unintentional use of incorrect plant species, the adulteration of herbal products with undisclosed medications, contamination with toxic or hazardous substances, excessive dosage, misuse by healthcare providers or consumers, and the simultaneous use of herbal medicines with other medications (Kamble et al., 2019).

Herbal medicine will probably be identified and associated with acute symptoms and short-term harmful effects, including dermatological effects and gastrointestinal disturbances. As a result, the absence of such observations provides some evidence of safety at these specific endpoints. However, unless a prospective cohort study is done, it is unlikely that the widespread use of a drug will be linked to long-term problems like cancer, liver and kidney damage, problems with reproduction, birth defects, and other conditions that are tougher to detect. (Eruaga et al., 2024).

Drug-Herb Interactions

The relations among herbal medicines and conservative drugs can have a substantial impact on patient safety and the success of treatment. Herbal remedies are extensively utilized. The interactions between botanicals and medications may increase or decrease the pharmacological or toxicological effects of either substance (Fig. 1). Numerous medical experts are unaware of the possible damaging effects of herb-drug recipes, and a lesser amount of than 42% of patients inform their physicians that they use herbal supplements. A study of 1,500 old patients revealed that 638 of them experienced 1,097 interactions, and 35 of them experienced adversative effects (Neergheen-Bhujun, 2013).

Drug-drug, food-drug, and herb-drug interactions (HDIs) occur due to the specificity of substrates in bio transformational pathways. Pharmacodynamic medication interactions occur when chemical components interact with receptor sites, while pharmacokinetic interactions occur due to changes in absorption, distribution, metabolism, and excretion processes. Both types of interactions can affect the physiological environment. The pharmacokinetic drug interactions (HDIs) are determined based on their impact on metabolic enzymes, particularly those belonging to the cytochrome P450 (CYP) family, found in liver and intestines. They also have similar impacts on efflux proteins and drug transporters (Meijerman et al., 2006; Brown et al., 2008). The systemic activation of CYP and efflux proteins can change

how bioavailable a drug is when taken by mouth. This can cause drug levels to go up or down significantly when botanical products are also taken (Patsalos & Perucca, 2003).

HERBAL DRUGS AND THEIR PREPARATIONS

Traditional therapeutic herbal pharmaceuticals consist of a variety of plant parts, including aerial parts, flowers, fruits, leaves, seeds, stems, and subterranean components such as roots, bulbs, tubers, and rhizomes (Fu et al., 2018; Zhao et al., 2013). These materials are available in a variety of forms, such as raw, fresh, dried, and extracts. Occasionally, researchers employ entire desiccated plants (Dori et al., 2020; Sahoo et al., 2010). It is imperative to guarantee the safety and efficiency of these goods by ensuring their quality (Zhao et al., 2013; Muyumba et al., 2021).

Quality of Herbal Drugs

A variety of factors, including abiotic, biotic, and genetic, can influence the expression of secondary metabolites in a specific plant. The genetic constitution of each taxon is the determining factor in its specificity. It is important to consider the plant's phenological stage (beginning, end of flowering, etc.), the time among the moment of harvest and the moment of analysis, and the harvest conditions (hygrometry, location, etc.). Storage conditions significantly influence the preservation of secondary metabolites, the preservation of herbal medicines, and the quality of microbiological samples. Keeping the samples dry is the most straightforward approach, given their fragility and susceptibility to rapid degradation (Vongsak et al., 2013). Biological contamination, atmospheric oxidation, photo-decomposition, or deterioration may result from inadequate storage and drying. This can also affect the composition and quality of the final product, as impurities can occur during the production stage (Sahoo et al., 2010; Thevenin, 2017). It is customary to address these sources of variation by establishing rigorous guidelines for good agricultural and collection practices (GACP) and good laboratory and manufacturing practices (GLP/GMP) (WHO, 2003).

Nature of Herbal Medications

Deploying efficient identification systems and resilient detection methods for foreign material is crucial to ensure the purity and quality of pharmaceuticals. These measures effectively identify and reduce the risks associated with such issues (Sahoo et al., 2010). Numerous genomic, proteomic, chemical, and taxonomic markers can authenticate and identify components of herbal medications. Several of these methods are morphologic identification, molecular marker analysis (for example, proteins or DNA) (Sahoo et al., 2010; Gautam et al., 2010), and secondary metabolite analysis or profiling using HPTLC, HPLC, GC, and CE. Mass spectrometry can also hyphenate these methods (Sahoo et al., 2010; Moller et al., 2009; Kim et al., 2010). These markers can be specific to a tax on (family, species, or occasionally variety); they enable the identification of a particular herbal material or can convey its proportionality in a composite (Sahoo et al., 2010).

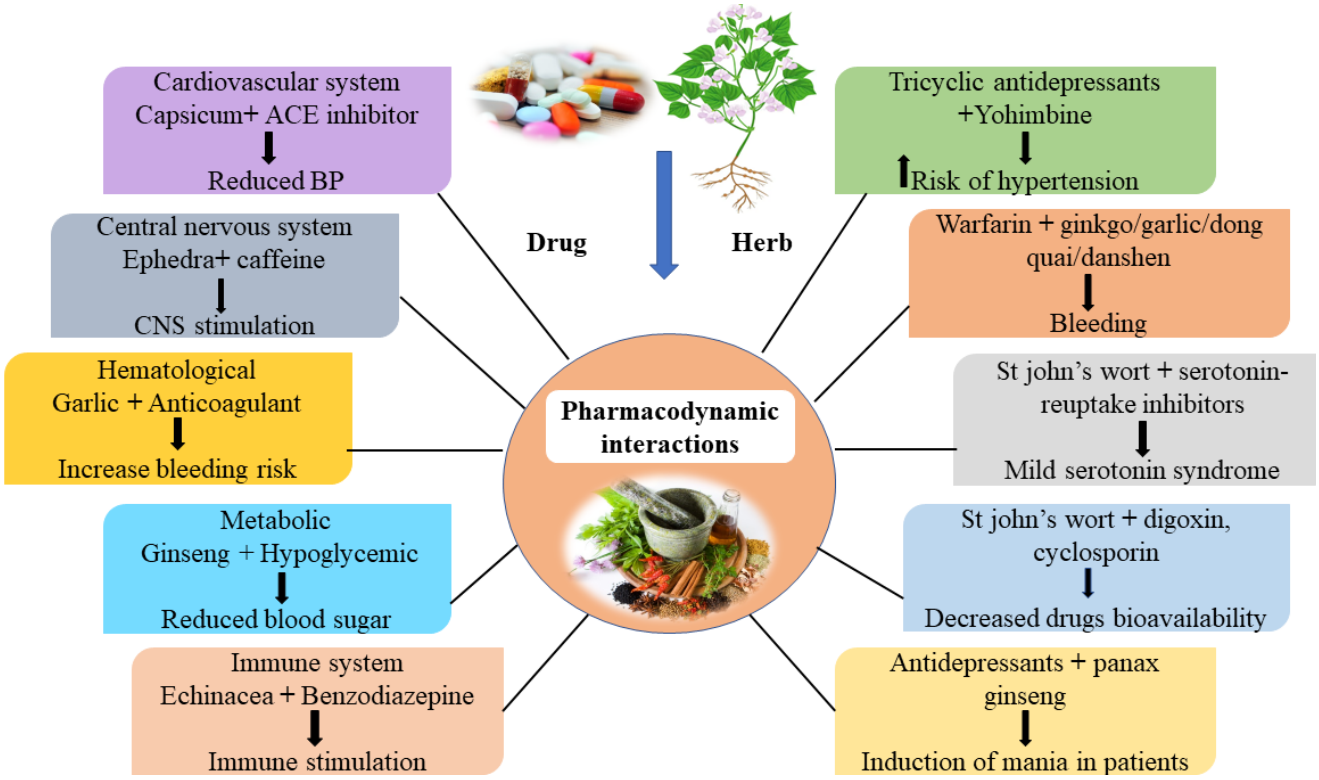

Fig 1. Impact of drug-herb interactions**.** ACE, angiotensin-converting enzyme; BP, blood pressure; CNS, central nervous system (Balkrishna et al., 2024)

SAFETY AND POTENTIAL TOXICITY OF HERBAL REMEDIES

Definition of "toxicity" is naturally influenced by individual viewpoints. Several widely consumed foods have constituents that have the potential to induce allergies or satisfy certain criteria for toxicity classification. Gluten extracted from wheat, oats, and rye contains alpha-gliadin. Fruit seeds of several kinds contain cyanogenic glycosides. Vegetables that are Brassica in color contain thiocyanates. Plants in the Solanaceae family contain alkaloids. Certain legumes, including soy and red kidney beans, contain lectins (George, 2011). The fact that even essential elements like oxygen and water may be fatal when consumed in excess emphasizes how important dose is (Boullata & Nace, 2000; Ernst, 2007). However, it is possible to divide botanicals into three distinct categories from a safety perspective.

The initial group consists of a limited herbs that encompass significant concentrations of potentially injurious materials, similar to pharmacological compounds. With the exception of homeopathic preparations, untrained individuals should never consume them. The second group comprises botanicals that have potent effects and may occasionally induce symptoms such as seasickness or queasiness (Steinhoff, 2019). Herbs that manifest specific types of poisonousness, as supported by scientific evidence, comprise the third group. It is important to note that plants that contain pyrrolizidine alkaloids (George, 2011).

When it comes to herbal medicine and nutritional supplements, misuse is frequently the cause of side effects and toxicities. These instances may stem from various causes, including improper use of botanical plants and supplements, improper preparation, high dosages, or prolonged use (Mulholland & Benford, 2007). Similar negative effects, such as osteoporosis and hepatotoxicity, can arise from chronic and excessive vitamin A use (Jacobus et al., 1992; Huang et al., 1997). Healthcare practitioners should therefore be wary of items that make claims about providing quick symptom relief because this could indicate deliberate adulteration with pharmaceuticals. Adulteration of this kind can result in hazardous outcomes (Liu et al., 2018). Using a more affordable or easily accessible plant instead of another, even if it has a lower safety record, is a different type of adulteration (Haung et al., 1997; Ernst, 2002; Yee et al., 2005; Ariffin et al., 2021).

Such adulterations can have disastrous results because the additional medications frequently pose serious toxicity hazards. For example, drugs such as corticosteroids, phenylbutazone, phenytoin, and sulfonylurea might have serious side effects that may even be fatal (Yee et al., 2005). Further people who use nitrates to treat heart ischemia may become hypotensive if they accidentally use products tainted with sildenafil. Furthermore, careless use of sulfonylurea-containing medications can lead to fatal or extremely severe hypoglycemia (Haung et al., 1997; Chamsi-Pasha & Sildenafil, 2001; Kerchner & Farkas, 2020). Other than this, species substitution and adulteration are the main causes of quality issues in the market for herbal therapeutic products (Msomi & Simelane, 2019).

Furthermore, because Aristolochia fangchi contains aristolochic acid, replacing Stephania tetrandra in TCM products may cause cancer and kidney damage. According to Han et al. (2011), Pandey et al. (2016), and Msomi & Simelane (2019), the adulteration of Datura stramonium with Brugmansia arborea poses significant hazards. Given the aforementioned difficulties, it is critical to accurately identify medicinal plant components to guarantee their safety. Furthermore, makers of herbal medicines often overlook or undervalue the importance of taxonomic botany and documentation, leading to special difficulties in classifying and assembly the medicinal plants used in herbal remedies. Adopting commonly used binomial names for medicinal plants, along with their synonyms, is critical to addressing common name misunderstandings (Pandey et al., 2016)

Therefore, effective management of herbal drugs safety requires strong collaboration between pharmacologists, Phyto chemists, botanists, and other relevant parties (Ifeoma & Oluwakanyinsola, 2013). To protect consumers, it is still necessary to authenticate the final commercialized products as well as the original herbal ingredients (World Health Organization, 2007).

QUALITY CONTROL MEASURES IN HERBAL MEDICINES

Organizations like the WHO have a crucial role in setting strategies and ethics for the manufacturing of herbal medicines (WHO, 2007). Herbal goods don't always have the same consistency and quality because of differences in cultivation, harvesting, processing, and storage, unlike pharmaceuticals that go through extensive premarket testing. In order to solve these issues and protect consumer welfare, regulatory measures must be enforced. There are difficulties in attaining uniformity since factors including climate, soil composition, and geographic location affect the diversity in phytochemical compositions. The escalating problems of adulteration and substitution of herbal treatments, which are frequently associated with a rise in deforestation, further undermine the safety and effectiveness of these products (Wang et al., 2023). The WHO has set forth recommendations for the standardization of herbal drugs, which comprise chromatographic and spectroscopic analyses, microbiological contamination, moisture content, ash levels, and organoleptic quality examinations (Nazim et al., 2018; Marchese et al., 2017)

For the purpose of authenticity and standardization, physicochemical analyses, pharmacogenetic systems, and organoleptic testing are essential. The information obtained from microscopic and macroscopic investigations helps to identify and prevent the adulteration of real herbal items. Additionally, a useful technique for standardization is the identification of secondary metabolites such alkaloids, tannins, glycosides, saponins, and flavonoids (Shaheen et al., 2018; Liu et al., 2018). The current assessment of the quality of herbal medicines often depends on the identification of one or two

specific indicators or pharmacologically active compounds. Nevertheless, these methods may not offer a whole comprehension of a product's therapeutic impacts, as many components frequently collaborate synergistically (Deogade & Prasad, 2019).

It is thus essential to use chromatographic methods. Chromatographic fingerprints, which show the distinctive chemical components, may be used as a comprehensive method to evaluate the efficacy of herbal remedies. The fingerprints need to show both the similarities and variations across different samples. When coupled with chemometric techniques, hyphenated chromatography-spectrometry methods such as capillary electrophoresis–diode-array detection, gas chromatography mass spectrometry, and high-performance liquid chromatography diode array detection offer improved separation, selectivity, and accuracy for qualitative and structural analysis. Chromatographic fingerprints are crucial for quality control because of their dimensional advantages (Kamble et al., 2019; Jitareanu et al., 2022)

Governments, regulatory bodies, and international organizations must work together to establish uniform worldwide regulatory standards, which is an ongoing challenge (Fernandes et al., 2016; Rashid et al., 2018).

EFFICACY AND RISK ASSESSMENT OF MEDICINAL PLANTS

Modern herbal remedies have limited use of powdered medicinal herbs, except traditional herbal formulations. Soft or dry extracts comprise the majority of herbal constituents in the global marketplace. At the supply chain's extraction ingredient level, chemo profiling is the sole technique for identification that is accessible. These factors will determine the extraction chemo profile used as an ID.

- Harvest time is used to regulate temporal variations
- While plant parts and compositional ratios are used to regulate spatial variations.
- Solvents used in the extraction process
- The manufacturing process that was implemented.

Medicinal plants produce a substantial quantity of phytochemicals with varying degrees of polarity. Several additional chemicals are eliminated and the chosen ingredients (based on polarity) are enhanced by the solvents employed in the extract production process. The decrease of the phytochemical complexity and diversity of extract constituents is made easier by this selective enrichment. It divides preparations of medicinal plant extracts into nontargeted (non-standardized) and targeted (standardized) categories. In extracts that are not standardized and are prepared using a consistent extraction procedure, the chemo-profile differences are solely associated with the variation in the configuration of the starting substantial (Chen et al., 2019).

On the other hand, the variable phytochemical configuration of the raw material and the manufacturing technique used to enrich the extract with one or more particular components assumed to be bioactive or markers have an impact on the chemo profiles of standardized extracts. This is mostly because various herb-starting materials from different places and seasons have variable "marker/active" concentrations. To get the right concentration, certain materials could need different degrees of enrichment. This "marker/active" quantitative variance is taken into account by allowing a range in the native extract ratio. For example, rather of using an exact ratio of 100:1, we use a range of 95–105:1 (Iakovenko, 2014).

For standardizing herbal extracts and preparations, there are no standard guidelines for selecting markers or actives. In most cases, they are significant components of an active extract or preparation. Additionally, the standardization of active extract ingredients to a single active constituent may partially contribute to the overall efficacy (Abdullah et al., 2017).

Using chemometrics and pattern-oriented multicompound (or holistic) chromatographic profiling gives us information on how to identify extracts (to plant parts and species). Chemometrics was used to look at Equisetum arvense extract profiles from different parts of the world and found subspecific differences in profile patterns, which were explained by phytogeographical factors (Cook et al., 2013). It also showed very clearly how important it is to get the same subspecific chemotype to make sure that profiles and efficacy are consistent in species that have larger subspecific variations. When identifying unknown impurities, principal component analysis provides indicators for adulteration identification. Furthermore, the method effectively produces data on the stability of "multicompound" extracts during storage, a feature previously unavailable in the industry (Zhang et al., 2012).

STANDARDIZATION OF MEDICINAL PLANT PRODUCTS

The process of ensuring the excellence and standardization of herbal medicines consists of multiple stages (Fig. 2). The basis and quality of raw materials are crucial issues in ensuring the quality and stability of herbal remedies. Various aspects, including the utilization of fresh plants, temperature, light exposure, water availability, nutrients, collection period and time, collection method, drying, packing, storage, and transportation of raw material, as well as the age and part of the plant collected, can significantly impact the quality and therapeutic efficacy of herbal medicines. Certain components found in plants are sensitive to heat and can be easily destroyed. Therefore, plants that contain these components must be dried at low temperatures. In addition, enzymatic reactions persist for extended periods of time following plant collection, leading to the degradation of other active compounds. This is the reason why the content of herbal medications often varies. Hence, it is imperative to consistently conduct thorough standardization and quality control procedures for both the raw materials and the herbal medicines (Cook et al., 2013).

When the active components are not known, it is necessary to establish marker substances for analytical reasons. Nevertheless, it is common for these markers to remain untested in order to determine their actual contribution to the

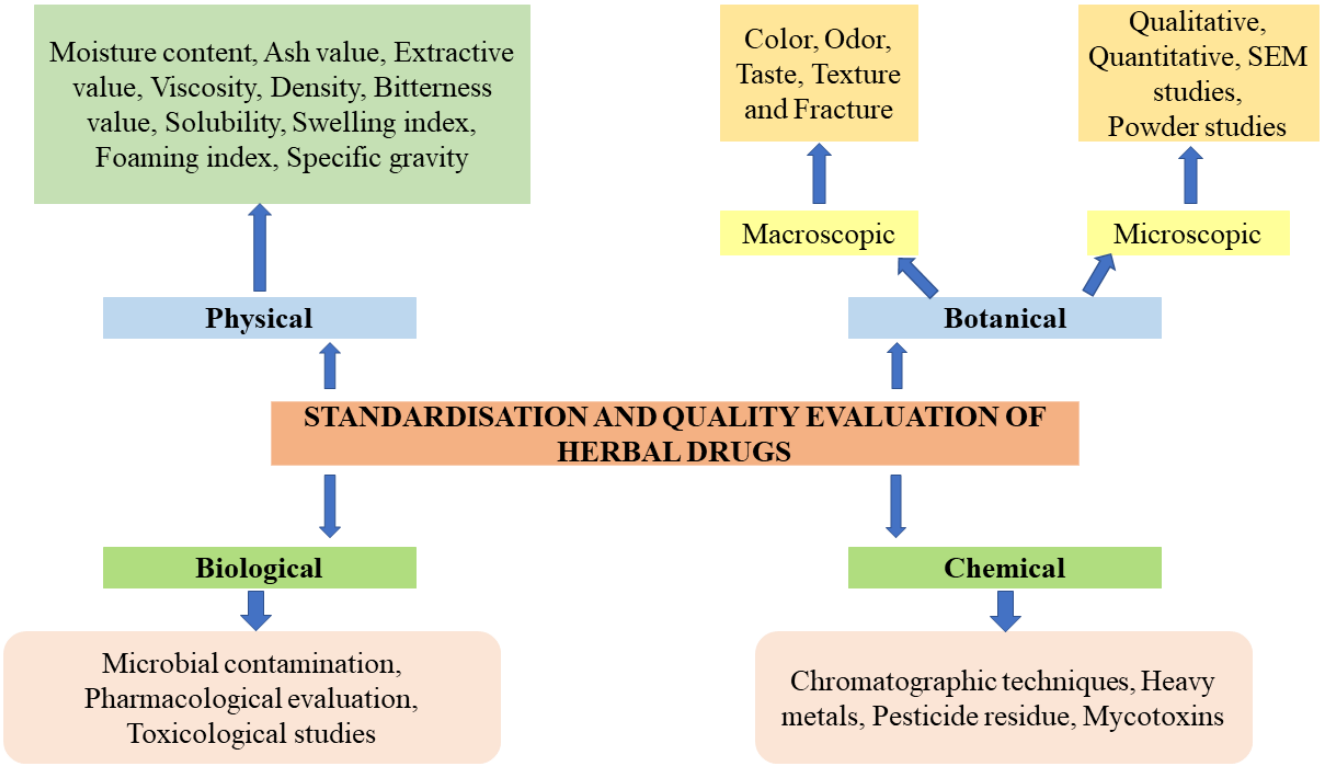

Fig. 2. Standardization and quality evaluation of herbal drugs

stated therapeutic effects of herbal medications. In addition to the aforementioned variable aspects, other elements such as the extraction technique and contamination with microbes, heavy metals, pesticides, and so on, can potentially disrupt the quality, safety, and effectiveness of herbal remedies (Sharma & Yadav, 2023; Whaley et al., 2023).

ADVANCEMENTS IN MEDICINAL PLANT RESEARCH

Transcriptome sequencing of medicinal plants is so crucial. Proteomics, genomics, and transcriptomics have gained popularity with the emergence of the post-genomic era. Because it allows for the study of both functional and differentially expressed genes (DEGs), transcriptomics is now a field with much research and application (Jia et al., 2015). There are some distinctions between transcriptomics and genomes in medicinal plant research.

Firstly, transcriptome analysis can track an organism's overall transcriptional activity without a reference genome, while genome assembly in plant research is more challenging and costly. Furthermore, due to the dynamic nature of the transcriptome, it encompasses data on secondary metabolic pathways and serves as a reflection of gene expression fluctuations across different temporal and spatial locations (Mironova et al., 2015).

These variations are reflected in gene expression patterns, which in turn reflect variations in time and location. According to Wang et al. (2009), the transcriptome is, therefore, better suited for finding genes linked to therapeutic components in medicinal plants. Gene expression varies both temporally and spatially among plant tissues and organs. Studies on genetic diversity, secondary metabolites, resistance genes, practical gene mining in medicinal plants, and gene regulatory networks are significantly impacted by these discrepancies. RNA sequencing technology (RNA-Seq) has replaced the outdated chip hybridization platform as the primary instrument for transcriptome analysis in recent years. This is a result of the constant improvement of sequencing techniques (Mironova et al., 2015). This process allows for whole-transcriptome analysis without requiring a genomic reference sequence.

One popular molecular biology technique for sequencing is transcriptome sequencing (Sun & Wei, 2018). Model plants like maize (Xu et al., 2014), Arabidopsis (Guo et al., 2009), and rice (Li et al., 2012) have all greatly benefited from the widespread application of this technique to date. It also gives an overview of the progress made in using transcriptome sequencing in 4 areas of medicinal plant research: finding functional genes, developing molecular markers, finding pathways for making secondary metabolites, and finding out how medicinal plants grow.

Applications of Transcriptome Sequencing Technology in Medicinal Plant Research

- Mining Functional Genes of Medicinal Plants
- Development of Molecular Markers Based on Transcriptome Sequencing
- Exploring the Biosynthetic Pathways of Secondary Metabolites
- Transcriptomics and Developmental Mechanisms in Medicinal Plants

Ensuring the Safe Use of Herbal Remedies

There has been a significant rise in the acceptability and public interest in natural therapies in both developed and developing countries over the past decade. These herbal remedies are now available in food stores and supermarkets, in addition to drug stores. Eighty percent of the world's population, or up to four billion people, live in underdeveloped countries where herbal medical goods are their main form of healthcare. The use of plants is one of the traditional medicinal practices that these nations see as fundamental to their culture (Tang et al., 2020).

Medicinal plants significantly influence the prevention and treatment of diseases (Teng & Shen, 2015). According to Huang et al. (2005), traditional Chinese medicine uses between 60% and 70% of the approximately 3000 endangered plant species for their medicinal value. The specifics of propagating medicinal plants are determined by quality, which is the direct manifestation of output value. Drought, frost, damage, and extreme temperatures are examples of environmental conditions that significantly restrict the growth and development of medicinal plants. But they may also encourage the build-up and release of secondary metabolites, or active components, in plants, such as flavonoids and alkaloids (Huang & Guo, 2007; Guo & Huang, 2008).

Due to the previous misconception that herbal medicinal products are "safe" as they come from "natural" sources, prevalence of adverse reactions has increased in recent years and is no longer debatable. The truth is that the terms "safety" and "natural" are not interchangeable. Consequently, it is imperative to establish and reinforce global regulatory policies regarding herbal remedies. In order to protect public health, regulatory bodies in many nations must continue to be proactive and take the required steps, making sure that any herbal medications that are authorized for sale are safe and of the right quality (Shaito et al., 2020).

Healthcare providers frequently possess inadequate training and comprehension regarding the health consequences of herbal medications (Teng & Shen, 2015). An appropriate knowledge base that is pertinent to the decision-making process for diagnosis and treatment is also of paramount importance. Additionally, the healthcare provider should demonstrate a sufficient level of dedication to comprehending the application of homeopathic medications. When they come across patients who are presently taking these drugs, they may do this by asking appropriate questions about the usage of these natural medicines and others. Ultimately, a drug regulatory framework in every country must regulate herbal medicines to ensure they meet the necessary standards of safety, quality, and efficacy, just like other human-use medications (Tang et al., 2020).

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