REVIEW ARTICLE

Elevating Herbal Therapies: A Deep Dive into Standardization

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ABSTRACT

Around 80% of the global population incorporates medicinal products made from herbs. Herbs play a major role in conventional medicine and are also frequently employed in naturopathic, homeopathic, ayurveda, and other healthcare practices. The herbal products are vulnerable to intrusion from numerous paths, degradation, and changes in their chemical structure because they are predominantly organic (plant-based). Hence, it is crucial to establish and implement quality control criteria for medicinal products made from herbs to guarantee both their safety and effectiveness. There are numerous factors in standardization alone, including gross morphology, microscopy, physical characteristics, and chemical, chromatographic, and spectroscopic fingerprinting. Standardization of herbal medications increases their security and therapeutic efficacy while potentially gaining global popularity. Because herbal remedies are derived from natural sources, adverse reactions, counterfeiting, and tampering are less likely. From this review, the concept of standardization of herbal drugs, as well as their classification, advantages, and limitations, is described. It also includes the need and scope for standardization of herbal drugs, its standardization method, and pharmacopeial standards.

Keywords: Standardization, Herbal medicines, Chromatographic approach, Quality, Evaluation.

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INTRODUCTION

Establishing an ensemble of criteria or fundamental features, consistent variables, and specific qualitative and quantitative results that guarantee quality, efficacy, safety, and repeatability is the manner of standardizing medicinal products made from herbs. It is the method by which technical norms are created and approved. Through trial and observation, particular expectations are developed, which eventually culminate in the act of recommending an inventory of qualities that the specific medications display. Standardization thus serves as an arsenal used in quality control.[1, 2] According to the American Herbal Product Association, standardization is the collection of guidelines and data required to produce relatively uniform commercial material. This was accomplished by decreasing the inherent diversity in the makeup of plant-based goods by implementing quality assurance techniques in farming and industrial operations.[3] The term "standardization" refers to any actions performed during quality assurance and manufacturing that result in a repeatable level of quality. It additionally covers all aspects of investigation from the time a plant is born until it is used in a medical environment. Furthermore, it refers to mixing herbal medications or herbal drug preparations or administering additives to bring the herbal medicine composition to a certain amount of an element.[4] "Evaluation" of a medicinal product involves verifying its authenticity, assessing its potency and simplicity, and identifying any corruption.[5]

All factors that affect the nutritional value of herbal medicines should be taken into account by standardization techniques, including accurate sample identification, organoleptic assessments, pharmacognostic review, volatile matter, quantitative assessment (ash values, extractive values), phytochemical evaluation, xenobiotic appearance examination, microbial load investigation, toxicological analysis, and biological functioning. The phytochemical composition holds particular importance because it directly influences the efficacy of herbal remedies.[1, 6] Phytochemical standardization includes any information that may be produced on the chemical components that make up a herbal remedy. Therefore, the following are accounted for in the phytochemical evaluation for standardized purposes:

- Initial analysis to check for the existence of various chemical groups.
- The measurement of the chemical categories of passion, such as the overall quantity of tannins, triterpenic acids, phenolics, and alkaloids. Creation of configurations for fingerprints.

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- Numerous fingerprint patterns based on markers.
- Measurement of significant chemical components.[7]

Herbs or components of plants that may have been transformed into phytopharmaceuticals through straightforward procedures, including collecting, drying, and preserving, are referred to as "herbal drugs." First of all, crude plant material such as leaves, flowers, fruit, seeds, stalks, wood, bark, roots, Rhizomes, also or other plant parts which can be complete, split up, or powdered is considered an herb. Herbal materials comprise fresh juices, gums, fixed oils, essential oils, resins, and dry powdered herbs, and actual herbs. These materials may be processed using a variety of regional techniques within certain jurisdictions, like stir-baking, roasting, or steaming with honey, alcoholic beverages, or other ingredients.[8,9] Medications derived from organic compounds are known as herbal medications. Medications that originate in plants are known as herbal medicines. Ayurvedic thought first emerged and progressed between 2500 and 500 BC. The components of plants like roots, shoots, stems, and flowers were used for health purposes. They administered their juice churn and leaped straight to the injury. However, as decades passed, the necessity for standardization grew, which resulted in the development of safe and high-quality traditional therapeutics. Many businesses are concentrated on standardizing their goods to gauge their effectiveness and safety. Regulations for the standardization of herbal remedies have been drawn up by numerous governing bodies, including the World Health Organization (WHO).[10]

Classification of Herbal Drugs

Classification of herbal drugs is categorized as follows:

Ayurvedic herbalism

The term "Ayurveda" originates from Sanskrit and means "The science of life." It had its beginnings about 4,000 years ago in India.

Chinese herbalism

One component of connected conventional health care is Chinese herbalism.

Western herbalism

First practiced in Rome and Greece, it later spread to North and South America.[11]

Categorization of medicinal products according to their origins, the evolution of life, and present applications:

- Group 1: Indigenous herbal medicines.
- Group 2: Systems containing herbal medicines
- Group 3: Adapted herbal remedies
- Group 4: merchandise that is imported with a foundation in medicinal herbs.[12]

Drugs That are Single or Crude

Mostly entire, dispersed, or shredded plants; plant components usually exist in dried forms, though they can occasionally be fresh. Additionally, it consists of lichen, fungus, and algae.

Multiple Blends of Herbs

The botanical components are transformed by extraction, the distillation expression procedure, divided into fractions, partitions chromatography, and compounding to create diverse compositions.[13]

Positive Aspects

- A broader period of utilization and improved patient acceptance and tolerance characterize herbal remedies.
- The only reliable source of affordable, long-term medical supplies for the globe's expanding population is the inexhaustible reservoir found in medicinal plants.
- Access to medicinal plants is not an issue, particularly in emerging nations with significant agroclimatic, social, cultural, and linguistic varieties, such as India.
- The development and commercialization of medicinal plants and herbal derivatives are eco-friendly.
- Extension of and relatively unremarkable employment of ayurvedic remedies provides yield assurance of both safety and effectiveness.
- Herbal medicine has contributed a great deal of the world's most effective medications to the enormous supply of pharmaceuticals that medical science currently has at its disposal, both as synthetic substances and in their raw forms, which serve as the foundation for contemporary treatments.[14-16]

Negative Aspects

- Insufficient dose guidance
- The possibility of poisoning from wild medicines
- May interfere with other medications
- Unsuitable for multiple circumstances
- Some can't be employed safely[11]

The Necessity of Standardization

- To assist in the production of high-quality pharmaceutical products based on their active components.
- To ascertain the *in-vivo* characteristics.
- To illustrate what is deemed acceptable in the contemporary medical system.
- To assess the herbal medicine's quality and purity.
- Measuring medication quality using analytical, physical, chemical, morphological, and biological techniques.[10]

The following succinctly describes the necessity of quality control and standardization for herbal products

- The idea of standards and technology was very different when conventional medications were invented.
- The constantly changing process of adaptation during the last millennium may have altered the distinct characteristics of plant components.
- The procurement of authentic fundamentals has grown more difficult as a result of marketing.
- The surrounding environment and time may have changed a plant's features.[17]

Numerous factors can cause substantial discrepancies in organic raw materials. These include plant identity, variation in

the season that affects when to harvest, genotypic, phenotypic, and ecotypic variations, drying and storage circumstances, and the presence or absence of xenobiotics.[18] Significant variations in product quality and plant chemical concentration can be caused by a variety of different environmental factors, including natural light, rainfall, altitude, temperature, soil, and shelf life. Additionally, distinct harvesting techniques, gathering periods and techniques, and production procedures, including decision-making, being dried, the purification process, and extraction, can also contribute to fluctuation. Environmental factors like devouring insects and infections caused by bacteria can impact secondary metabolites, which can alter the plant's chemical makeup.

Nevertheless, fluctuations in the seasons and daylight hours (such as paclitaxel and opium alkaloids) add to the unpredictability of herbal remedies. The elements of the plant utilized and their maturity stages determine which parts of the plant are hazardous or beneficial.[19] Goods from different vendors differ greatly from one another, and it is impossible to manage every element that influences a plant's chemical makeup.[20,21] The majority of herbal remedies, particularly those found in conventional medicine's classical compositions, are polyherbal. A lot of preparations are semisolid or liquid. It is particularly challenging to set quality control parameters for such mixtures.

Herbal product standardization can be separated into two distinct groups: First, a concentrate of active components with designated biochemical fundamentals and beneficial principles, and second, an extract of marker components without recognized biochemical principles, which is employed as a marker to determine the existence of other biochemical elements with medicinal properties.[22] Quality control is crucial for organic crude drugs and their preparations to be accepted in the contemporary medical system. Standardization of artificial drugs presents no issues when the analysis's assumptions are well specified. It is not unusual for a single mixture to have five or more distinct botanical components. When there is no established norm for verification, batch-to-batch diversity begins with the initial ingredient acquisition alone. WHO has underlined the importance of guaranteeing quality control of goods made from medicinal plants by applying appropriate criteria and specifications and employing contemporary methodologies. Standardized goods and services are beneficial because they boost consumers' perceptions of well-being and safety, assurance, superior quality, and flexibility. For enterprises, standardization offers significant advantages, such as creating a strong base for the establishment of fresh innovations and facilitating collaboration and improvement of current procedures. Because standardization supports laws, regulations, and policy initiatives, it also plays a critical role in supporting legislatures, government agencies, officials, and legal community members.[23, 24]

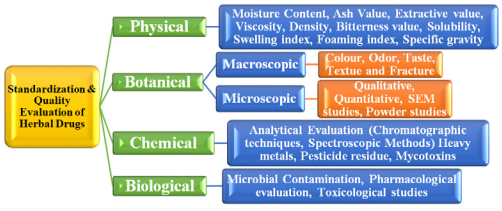

Figure 1: Method of standardization[8]

Methods of Standardization

Standardization & quality evaluation of herbal drugs can be done by physical, botanical, chemical and biological methods (Figure 1).

Scientific Investigation

Scientific investigation is done using physical, botanical, chemical, and biological methods.

Physical examination

Every monograph includes comprehensive botanical, macroscopic, and microscopic details and in-depth images and drawings that offer tangible evidence of precisely recognized content. A microscopic examination verifies the substance's authenticity and serves as an initial detection test for contaminants.

- *Loss on drying/moisture content*

Removing moisture from crude medicinal products as much as possible is necessary as it is an essential element. Drying the crude medication is crucial for conservation, limiting the hydrolytic breakdown of its therapeutic components and facilitating the simple diminution of its dimensions after it has been retrieved. Medication deterioration resulting from microbial development is caused by either excessive moisture or inadequate drying. As a result, the drying procedure should lower the drug's moisture content below a certain threshold. Azeotropic distillation, Karl Fisher reagent method, loss on drying, halogen balance, and other techniques are used for assessing it.[12]

- *Ash values*

Ash value serves as a means for recognizing the substance and evaluating its nature, quality, and purity. For example, phosphates, carbonates, and silicates of calcium, magnesium, potassium, sodium, and other elements are found in ash. They assist in standardizing a given crude medication because it exists in certain quantities, which can be evaluated quantitatively by employing different ash values. When material from plants undergoes combustion, the amount of persistent ash left behind is quantified, accounting for both entire and acid-insoluble ash. Acid-insoluble ash and ash from the plant are accounted for in total ash, which is an estimate of the entire quantity of matter remaining after combustion. The residue left over after burning the rest of the insoluble stuff and boiling the entire ash in diluted HCL is the latter. The following procedure counts the quantity of silica, particularly in the manner of siliceous earth and sand.[12,25,26]

- *Acid insoluble ash*

After extracting all of the ash using HCL, the residual ash that is insoluble in HCL gives the impression of earthy stuff. 25 mL 2M HCL solution using the IP technique. BP method: 15 mL water + 10 mL HCL; USP method: 25 mL 3N HCL solution.

- *Water insoluble ash*

The material that dissolves in water accurately represents the drug's prior extract of salts that dissolve in water or the quantity of inorganic substances present.[10]

- *Extraction value*

Measuring the extractive matter that is dissolved in ethanol or water is one way to assess medications. The extractive value assessed the total quantity of beneficial compounds in a particular volume of medicinal botanical material after it had been extracted with a solvent. It is used for materials for which there isn't a chemical or biological assay technique. It can be identified as either a substance that dissolves in water extractive or a substance that is alcohol soluble extractive.[12]

- *Foaming index*

The foaming index is used to quantify the foaming capacity of herbal medications and their extracts. Whenever saponins are mixed in water, they produce a continuous foam. Therefore, the foaming capability of plant-based matter or extract comprising saponins is gauged using the foaming index.[12] When an aqueous infusion is stirred, the saponin-containing plant's tendency to produce an enduring foam is what triggers the foam. The mathematical equation for calculating the foaming index is 1000/a, where a is the volume in milliliters of the decoction required to make the dilution in the tube where 1 cm of foaming is observed. This is how foaming ability is tested.[10]

- *Swelling index*

Due to their swelling characteristics, most herbal medications, particularly those for gums and those featuring significant quantities of mucilage, pectin, or hemicelluloses, have particular medicinal or pharmacological value. The volume in milliliters occupied by the swelling of one gram of vegetative matter beneath given circumstances is known as the swelling index. The insertion of water or a swelling agent, as indicated in the examination protocol for every distinctive plant-based substance, is what establishes it. It is essential in assessing crude medications, including mucilage, since it provides an estimate of the drug's composition.[12]

- *Viscosity*

A liquid's viscosity, which serves as a composition index, remains constant at a particular temperature. As a result, it can be applied to standardize liquid medications.

- *Melting point*

Melting points are extremely crisp and uniform when it comes to chemical substances that are pure or phytonutrients. A specific melting point range characterizes crude pharmaceuticals derived from plants or animals because they comprise a combination of compounds.

- *Chemical examination*

A chemical examination of the medication is conducted to evaluate the therapeutic value of the plant component about its pharmaceutical properties. It addresses the chemical elements' process of purification, authentication, isolation, and method of screening. It aids in pinpointing the drug's constituent and any potential counterfeiting. Color interaction analyses are one type of chemical screening or test that can be utilized to recognize compounds in drugs as well as discover contamination.

- *Heavy metals*

Hazardous metal contamination can occur mistakenly or on deliberately. There are some reasons why herbal remedies may contain heavy metal contamination, especially environmental damage. These contaminants might present clinically significant risks to the user's health thus their use should be restricted. Heavy metal contamination in herbal treatments includes mercury, lead, copper, cadmium, and arsenic. Several pharmacopeias include a basic method for determining the presence of heavy metals. It involves the reaction of colors utilizing specific chemicals like a substance called thioacetamide or diethyldithiocarbamate, and the quantity of metals is determined by comparing it to a benchmark. When tiny amounts of the metals exist, analytical techniques must be used. Based on the product's suggested or projected quantity and the degree of the hazardous metal present, the possible consumption of the metal can be predicted. The WHO's Food and Agriculture Organization (FAO-WHO) has set forth what is referred to as provisional tolerable weekly Intake values (PTWI) for dangerous metals that can be employed to place the risk of being subjected to a toxicological context.[12]

- *Pesticides residues*

It is crucial that medicinal plants and medicinal products are devoid of pesticides and chemical fumigants or at a minimum, are managed to ensure there are no dangerous amounts present, even though there haven't been any significant observations regarding toxicity owing to these substances. Pesticide residues can build up in medicinal products as a result of farming processes like an application by spraying, preparing soils throughout cultivation, and using chemical fumigants while warehousing. Medicinal plant samples are separated using a conventional process; contaminants are eliminated by partitioning and/or adsorbing; and particular pesticides are quantified using various approaches to analysis. The European Pharmacopoeia, currently set minimum criteria for residues of pesticides in pharmaceuticals and the World Health Organization has released a few straightforward guidelines. Pesticide restrictions are determined by the Food and Agricultural Organization (FAO) and WHO. Pesticides are typically found in botanicals. When medicinal plants are being grown, such pesticides are combined with them. Pesticides such as DDT, BHC, toxaphene, and aldrin mostly create significant negative reactions in individuals when combined with raw pharmaceuticals.[12]

Analytical Evaluation

Methods for characterizing and identifying medicinal products from plants, such as spectroscopic and chromatographic approaches.

Thin layer chromatography

Currently, the most often used technique for verifying conventional herbal remedies is thin-layer chromatography (TLC). TLC can be employed in conjunction with various chromatographic methods as a simpler first-pass screening procedure that yields a semi-quantitative assessment. It offers fluorescent or UV visuals in addition to regular views. It provides an extra color element in comparison to column chromatography. Multiple specimens were determined simultaneously using this procedure. During TLC fingerprinting, the chromatogram, retardation factor (Rf) values, the color of the segregated bands, their absorption spectra, λ_{max}, and shoulder inflection(s) of all the sorted bands are among the information that may be captured with a high-performance TLC scanner. All of them, coupled with the patterns of modification using various compounds, show the specimen›s TLC fingerprint profile. The details created may be used to distinguish genuine medications from adulterants and preserve the medicine's quality and reliability. TLC includes the benefit of multiple detection opportunities while examining herbal remedies. TLC is widely used for a couple of reasons: first, it allows for the quick examination of medicinal extracts without needing specimen tidying; second, it offers semi-quantitative and qualitative data regarding the recovered chemicals. It makes it possible to quantify the components of chemicals.[27-29]

High-performance thin-layer chromatography

The high-performance thin-layer chromatography (HPTLC) approach is extensively used in the pharmaceutical sector for the creation of procedures, contaminants detection and recognition in botanical goods, pesticide component verification, mycotoxin recognition, and quality control of medicines and nutritious meals.[30] The most widely employed fingerprint in analyzing substances with slight or medium polarization is HPTLC. It has already been widely documented that using a less mobile phase than in HPLC allows various specimens to be processed concurrently.[31] Additionally, it has been stated that HPTLC can be performed with mobile phases that are pH 8 or higher. The ability to repeatedly identify (scan) the chromatogram under either identical or various circumstances is another plus of HPTLC. As a result, research has been done on using HPTLC to test numerous elements in a multi-component composition simultaneously. This method makes it feasible to independently verify different kinds of plants and assess the uniformity and stability of formulations made by diverse producers. The concurrent testing of multiple elements in a multi-component composition has been studied using HPTLC.[32]

High-performance liquid chromatography

As it is simple to understand & apply, high-performance liquid chromatography (HPLC) is a widely used technology for the examination of medicinal plants. Furthermore, it is not constrained by the sample compound's volatility or durability. Generally speaking, nearly every component of herbal remedies may be examined using HPLC. Compared to GC, HPLC has a far larger range of applications. With its various mobile phases and detectors, HPLC can also identify the most natural compounds. The pharmaceutical sector uses empirical and preparative HPLC extensively to extract and refine plant elements. Preparative HPLC can be broadly divided into two categories: high-pressure HPLC (pressure >20 bar) and low-pressure HPLC (usually < 5 bar).In preparative HPLC, the total quantity of chemicals that might be generated per unit of time, productivity, and the level of solute clarity are key characteristics to take into account. In analytical HPLC, these are resolution, sensitivity, and rapid evaluation duration. Greater stainless steel columns and packing materials with particle sizes between 10 and 30 μm are required for preparative HPLC (pressures greater than 20 bar).[33] Reversed-phase columns are the most widely utilized columns for the analytical differentiation of medicinal products. Liquid chromatography research has produced innovative methods such as reversed phase ion-pairing HPLC, strong anion swapping HPLC, low-pressure size exclusion chromatography, ultra-fast counter-current chromatography, and micellar electrokinetic capillary chromatography to achieve a greater degree of separation. A primary benefit of HPLC is its ability to perform hyphenation using various detection devices, including ultraviolet for substances that consume UV light,[34] diode array detection devices for medicinal fingerprinting,[35] evaporative light scattering detectors,[36] and chemo-luminescence detection devices for substances that cannot absorb UV light. Additionally, NMR can be used for metabolomic profiling,[37] and mass spectrometry can be used to identify distinct substances.[38]

Gas chromatography

Gas chromatography (GC) is a highly regarded analytical method for detecting, quantifying, and analyzing volatile chemicals. GC is an invaluable tool for the evaluation of essential oils due to its strong separation effectiveness and sensitive identification.[39, 40] Notwithstanding its benefits, GC analysis of medicinal goods is typically restricted to essential oils due to the potential for thermolabile chemical breakdown and the need for volatile molecules, which renders GC inappropriate for numerous natural elements.[41, 42] Several varieties of fast-scan mass spectrometers can immediately linked with GC equipment. Because of their outstanding effectiveness, stability, and sensitivity, GC and GC-MS are widely used techniques for analyzing the volatile components of medicinal herbs. In particular, the hyphenation process using MS yields trustworthy data for the qualitative examination of the intricate components.[43, 44]

Ultra-performance liquid chromatography

Decocting-induced alterations in chemical makeup and chemical uniformity among conventional and distributed granule tinctures were assessed utilizing it.[45, 46]

Spectroscopic techniques

Spectroscopic techniques used as follows:

- *Infrared spectroscopy*

Fourier-transform infrared spectroscopy (FTIR) was implemented in conjunction with the statistical approach known as principal component analysis (PCA) to separate and recognize medicinal products in the 400 to 2000 cm^{-1} fingerprint range for quality control purposes. A further approach for differentiating natural remedies is the proportion between the regions of any two designated distinctive peaks, which has been discovered to be almost constant for identical plants across various locations. PCA classifies medicinal products into distinct categories, demonstrating unequivocally that the IR approach can effectively distinguish between various natural remedies employing FTIR spectra.[47] The quick identification of chemically active components, creatures, geographic location, distinctive pharmaceutical formula, digital quality control, detection of counterfeit products, and differentiation of geographical roots of Chinese herbal medicines have all been accomplished through the application of the NIR spectroscopy approach.[48, 49] *Fructus lycii*, a conventional Chinese medicinal herb, was identified as cut off in various geographic zones utilizing a two-dimensional NIR correlation spectroscopy.[50, 51]

Biological evaluation

Some medications' pharmacological effects are being utilized to assess and standardize them. The potency of the medication or its formulations can be determined by testing performed on living organisms and their separated or entire body parts.[1, 2, 8]

Microbial contamination

The material produced by plants typically contains aerobic fungal and bacterial species, which can proliferate as a result of improper cultivation, collection, preservation, or preparation. The development of bacteria might be accelerated by medicinal substances, especially ones that are rich in starch. Medicinal components were found to be infiltrated by infectious bacteria such as *Enterobacter, Enterococcus, Clostridium, Pseudomonas, Shigella,* and *Streptococcus*. Determining thresholds for contamination by microorganisms is crucial, and the European Pharmacopoeia now provides non-obligatory recommendations for appropriate levels.[1]

Botanical evaluation

- *Macroscopic*

This technique refers to the medication's shape, dimension, external surface, and overall state. Color, taste, and texture are all described by a sensory or organoleptic feature.[52]

- *Organoleptic evaluation*

An organoleptic examination of a nutritional item is crucial in determining whether it should be approved for sale or rejected. Impact on the color, taste, and consistency ratings of medium humidity apricots of multiple procedures (The process of blanching, puncturing, and lye preparation), the amount of sugar (50, 60, and 70%), and preservation. In 70% of sugar syrup cases, the items' general acceptance was noticeably greater, but as their preservation duration went on, these ratings declined.

- *Microscopic*

The structure of the tissue lacks the components of lignin and cellulose, and the interior pseudo parenchyma cells are oblong or spherical, including fixed oil and polypeptide. In the field of micros, several variables are considered.[52, 53]

- Content of leaves
- Trichome,
- Stomata

- *Investigations on toxicology*

This aids in figuring out pesticide residue levels, possibly dangerous substances, animal risk assessments like LD_{50}, and bacterial screenings to identify whether or not theoretically dangerous bacteria are found.[2]

CONCLUSION

The Indian Ayurvedic market is expanding astronomically. The development of methodologies for analysis will provide a quick and targeted means of conducting a medicinal investigation, enabling producers to establish superior requirements and guidelines as well as apply for regulatory agencies' endorsement for the distribution of their products to ensure the safeguarding, effectiveness in therapy and duration of storage of herbal remedies.

Bibliographies, which are collected in standard books such as the Indian Pharmacopoeia, the Ayurvedic Pharmacopoeia of India, Wealth of India, and the Ayurvedic formulary, offer comprehensive information for conducting different assessments to ascertain whether a crude or developed medicinal product complies alongside established guidelines. It is imperative to investigate the impact of several elements, such as atmosphere, development circumstances, and how they are stored, upon the therapeutic value of unprocessed medications or formulations, including them in their entirety, as extracts, or as separated constituents. Everything must be standardized, not just the manufacturing process. It's been said correctly: "Precaution is better than cure." When considering the patient's health, standardization is an essential component. One needs to go by the regulations set forth by national and international governing bodies to obtain pharmaceuticals of a higher caliber. Even in the modern day, standardization is a significant issue. It is important to make sure that the pharmaceuticals grown abide by the laws of both national and international agencies. The drug's standardization ensures that the dosage form meant for usage by humans is prepared safely not just the various excipients and ingredients added, but also the medication's component.

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