INTRODUCTION TO QUALITY CONTROL AND STANDARDIZATION OF HERBALS

Abstract

The use of herbal medicines in modern medicine is becoming more well-known and accepted. Although the majority of these uses are unconventional, it is a known fact that more than 75% of the world's population relies on herbal products and medications to maintain a healthy lifestyle. The difficulties are many and significant, which makes the herbal market risky on a global scale. In order to ensure the security of the global herbal market, this review aims to educate those involved in herbal medicine about the necessity to create quality standards for the collection, handling, processing, and manufacture of herbal medicine. The procedures for effective quality control and standardization of herbal medications and goods were covered. Moreover, it uncover the quality aspects of pharmaceuticals derived from natural sources and gives a outlay understanding for better their regulatory control.

Keywords: Herbal drug, standardization, quality control, WHO Guidelines for quality.

Authors

Iram Jahan
IIMT College of Medical Sciences
IIMT University
Meerut, Uttar Pradesh.
iramjhan1@gmail.com

Jiyaul Hak
IIMT College of Medical Sciences
IIMT University
Meerut, Uttar Pradesh.

Anshu
IIMT College of Medical Sciences
IIMT University
Meerut, Uttar Pradesh.

Standardization and quality assurance are crucial steps in the creation and application of herbal medicines. Since they have been utilized for therapeutic purposes for so long, herbs and herbal products are still widely employed in both conventional and complementary medical practices. However, the consistency and quality of the commodities greatly influence the effectiveness and safety of natural medications. In affluent nations, there has been a huge increase in the demand for items made from plants in recent years. These goods are rising in demand as pharmaceuticals, nutraceuticals, and cosmetics..(M. Shinde et al., 2023)

1. **Quality Control of Herbals:** Herbal medicine quality control is the methodical process of ensuring that the products fulfill strict requirements for quality. To evaluate and maintain the consistency, potency, and safety of herbal products, numerous procedures are used. Generally speaking, one or two markers or pharmacologically active ingredients in herbs and/or herbal mixtures are currently used to assess the efficacy and legitimacy of herbal medicines, to identify single herbs or HM preparations, and to determine the quantitative herbal composition of a herbal product..(Liang et al., 2004)

   Quality control encompasses several steps, including:

   - **Identification and Authentication**To preserve the validity and safety of herbal medicines, proper botanical identification is essential. To establish the existence of particular plant elements, botanical and chemical analysis is required.

   - **Raw Material Inspection:** The Herbal medicines' raw ingredients should be examined for purity, the absence of impurities, and conformance with recognized quality standards.

   - **GACP:** GACP involves guidelines for the cultivation and harvesting of medicinal plants to ensure they are of the highest quality.

   - **Good Manufacturing Practices (GMP):** GMP provides a framework for the manufacturing processes, ensuring cleanliness, proper storage, handling, and labeling of herbal products.

   - **Testing for Contaminants**: Herbal medicines should be tested for heavy metals, pesticides, microbial contamination, and other potential harmful substances to ensure their safety.

   - **Bioactive Compound Quantification**: The concentration of bioactive compounds responsible for medicinal effects should be quantified to determine the potency of the herbal product.

   - **Stability Testing:** Herbal products should undergo stability testing to assess their shelf life and how they might degrade over time.

2. **Standardization of Herbals:** Standardization is the process of ensuring uniformity and an unchanging level of competence and composition of natural medicines. This involves establishing specific criteria for the concentration of active compounds or markers that determine the identity and potency of the herbal product.(Kunle, 2012)

- **Marker Compounds:** Standardization often involves identifying and quantifying specific chemical compounds, known as marker compounds that are characteristic of the herb and responsible for its therapeutic effects.

- **Active Ingredient Concentration**: Standardization ensures that the herbal product contains a specific amount of the active ingredient(s) to ensure its potency and efficacy.

- **Batch-to-Batch Consistency**: By standardizing herbal products, manufacturers aim to achieve consistent quality and therapeutic effects from one batch to another.

- **Regulatory Compliance**: Standardization helps herbal medicines meet the regulatory requirements of various health authorities, ensuring consumer safety and confidence.

In conclusion, quality control and standardization are crucial steps in the production of herbal medicines. They aim to ensure the safety, efficacy, and consistency of herbal products, thereby promoting their acceptance and integration into modern healthcare systems.

I. BASIC TESTS FOR DRUG – PHARMACEUTICALS SUBSTANCES

The main ingredient in a medicine that cause the desire effect of the medicine. Some medicine contain more than one pharmacologic substance that act in different way in the body. The extent to which stress testing should be performed, i.e., how much stress should be imposed or how much deterioration should be sought after, is likewise not specified in the guideline materials that are currently accessible(Klick et al., 2005).

1. Amikacin Sulphate:

- Tests of identity
- Almost odorless, white to yellowish-white, crystalline powder.
- Melting Point: 204 °C or such.

Procedure:

- 1 ml of water should be added after dissolving 10 milligrams in it.
- 0.05 gramme should be dissolved in 3 ml of water before 2 ml of cobalt (II nitrate) (10 gm/l) is added.
- Violet colour is generated.
- Test for degradation: The test material turns discolored.
- Slowly add 4 ml of anthrone • Bluish violet colour appears.

2. Captopril

- Tests of identity
- A white or nearly white, crystalline powder with a distinctive odour. Melting Point: 108°C or such.

Procedure:

- 10 mg should be dissolved in 2 ml of HCL, 1 ml of iodine should be added, and then a white, turbid solution should be generated.
- Red colour is generated after dissolving 10 mg in 5 ml of ethanol, adding 0.5 ml of tetramethylammonium hydroxide/ethanol, and 0.5 ml of triphenyl tetrazolium chloride/ethanol.

3. Cisplatin:

- Tests of identity
- Description: A golden powder or white to yellowish crystals. Melting Point: around 270 °C

Procedure:

- Remaining solution from test 1
- Dissolve 5mg in 5 ml of HCL
- Take half of the solution & add few crystal of iodide
- Add few crystal of Tin(ii) chloride
- Brownish colour is generated; reddish-brown colour changes to reddish-brown when standing; reddish-orange colour changes to reddish-brown when standing.

4. Ketamine Hydrochloride:

- Tests of identity
- A white, hygroscopic, crystalline powder with a distinctive smell. About 260°C is the melting point.

Procedure:

- 10 mg should be dissolved in 4 ml of sulfuric acid (-5 gm./L). One drop of potassium iodobismuthate/acetic acid should also be added.
- Precipitate that is reddish-brown is created.

5. Levamisole:

- Tests of identity
- A white, hygroscopic, crystalline powder with a distinctive smell. Melting Point: 59 °C or such.

Procedure:

- 0.05 grammes are dissolved in 20 milliliters of water. One milliliter of sodium hydroxide is added.
- The mixture is boiled for 10 minutes, cooled, and sodium nitroprusside is added.
- The result is a red colour that gradually fades.

6. Magnesium Sulfate

- Tests of identity
- White, crystalline powder or brilliant, colorless crystals that are odorlessAbout 1124 °C is the melting point.

Procedure:

- A white precipitate is created when 10 mg are dissolved in 2 ml of water and 1 ml of ammonia is included.
- The Precipitate disintegrates when one ml of ammonium chloride is added.
- The precipitate also dissolves when 1 ml of disodium hydrogen phosphate is added.

7. Magnesium Sulfate:

- Identity Tests:
- Description: Brilliant, colorless crystals or a white, crystalline powder, odorless Melting Point: About 1124°C.

Procedure:

- Dissolve 10 mg in 2 ml of water
- Add 3 drops of titan yellow
- And add 2 ml of sodium hydroxide
- Distinct pink color is produced

II. WHO GUIDELINES FOR QUALITY CONTROL OF HERBAL DRUGS

As of my last update in September 2021, the World Health Organization (WHO) had not published specific guidelines for regulation of herbal medicine as a single comprehensive document. However, WHO has developed general guidelines and suggestions for controlling natural drugs, including aspects related to quality control. Quality control is an essential operation of the pharmaceutical industry. Drugs must be marketed as safe and therapeutically active formulations whose performance is consistent and predictable (V. M. Shinde et al., 2009).

The following are some key principles and aspects that WHO emphasize for ensuring the quality control of herbal drugs:

1. **Adopting Good Agricultural and Collection Techniques:** In order to maintain the safety and high quality of herbal raw materials, these rules emphasize the right growth methods, harvesting, and storage of medicinal plants.

2. **GMPs: Good Manufacturing Practices:** These regulations lay forth the requirements for the production of herbal medicines and goods. Herbal goods are routinely produced and inspected in accordance with set quality standards thanks to GMP.

3. **Quality Control Testing:** WHO supports the use of suitable testing procedures to determine the source, quality, potency, and safety of herbal medications. In order to confirm the existence and concentration of active ingredients as well as to look for possible contaminants, established analytical methods are used.

4. **Contaminant Control:** Drugs made from plants should be examined for the presence of heavy metals, pesticides, microbes, and other potentially dangerous elements. To guarantee the safety of the products, strict limitations are imposed for these pollutants. In order to ensure constant quantities of active ingredients in each batch of the product,

herbal medications must be standardized. This may be done by identifying acceptable limits for the active chemicals and using approved analytical techniques.

5. **Documentation and Record Keeping:** Proper documentation of all stages of production, quality control testing, and distribution is essential to maintain product traceability and facilitate regulatory compliance.

6. **Stability Testing:** Herbal drugs should undergo stability testing to determine their shelf life and appropriate storage conditions to ensure that they remain effective and safe during their intended use.

7. **Regulatory Compliance**: To assure the quality, safety, and effectiveness of herbal medicines, WHO encourages nations to create and put into place laws and standards. It is significant to note that many nations may have their own unique laws and standards for the quality control of herbal medicines. These can be based on WHO standards and might include further specifications to fit local conditions. As the landscape of herbal medicine regulation and guidelines might have evolved since my last update, I recommend referring to the official WHO website or contacting the relevant authorities for the most up-to-date and comprehensive guidelines on the quality control of herbal drugs. To establish a system to check the caliber, effectiveness, and security of conventional medicine and its products, the WHO will offer technical assistance. Herbal medicines are substances and preparations derived from plants that have therapeutic or other advantages for human health and comprise either unprocessed or processed compounds from one or more plants, inorganic substances, or substances with animal origin. The contemporary pharmaceutical business develops and manufactures herbal medicinal formulations(Choi et al., 2002) to promote the use of herbal medications, to raise the standard of such medications, and to reduce the likelihood of adverse effects brought on by inferior herbal drugs. To ensure the quality of pharmaceutical products, including herbal medicines, quality control is required at one of the key points in the production process. Because of poverty and a lack of access to modern medicine, the World Health Organization (WHO) (5) believes that between 65 and 80 percent of the world's population, who live in developing nations, rely mostly on plants for basic healthcare.(Calixto, 2000).

   One of the most crucial instruments for this measurement is cGMP.

   - Qualification & Validation for sanitation and hygiene
   - Device recalls
   - Self-inspections,
   - Instruction
   - Property examinations
   - Production Areas
   - Material
   - Good Production Practice
   - Good Practice in Quality Practice
   - Complaints
   - Contract Production & Analysis Personnel
   - Personal Hygiene
   - Storage areas Equipment's Documentations

To characterize herbal medications, current analytical methods, in particular HPTLC, GC, HPLC, CE, MS, and AA, are applied. Controlling raw materials, storing them, and processing them is also necessary for quality assurance. Because of this, the production of herbal medications should use a suitable quality assurance method.

1. **Sanitation and Hygiene during:** the production process, a high standard of cleanliness and hygiene is required to prevent changes and minimize contamination. To maintain consistency of quality, the production facility's water supply should be examined, and if necessary, properly treated. At least once each day, trash cans must be cleaned, emptied, and made accessible.

2. **Qualification & Validation:** The number of process runs, the type of validation to be carried out, the acceptance criteria, as well as the process steps and parameters (such as extraction time, temperature, and solvent purity), should all be included in the written protocol.

3. **Objections:** Issues with product quality, such as poor manufacturing, product flaws, degradation of herbal medications, and adulteration of the herbal ingredient, may result in complaints. These concerns ought to be thoroughly documented, along with their origins, using reference samples saved from the same batch as a guide.

4. **Product Recalls:** A standard operating procedure (SOP) should be in place for the storage of recalled herbal medications in a safe, isolated location that complies with all standards.

5. **Contract Analysis & Production Contract:** Should be drafted by qualified, experienced individuals who are familiar with the unique traits of herbal medicines, including their manufacture and quality control testing.

6. **Self-Inspection:** One self-inspection participant should be well-versed in herbal medicine.

7. **Personnel:** All accountable employees should have formal job descriptions of their obligations and sufficient power to carry them out. Their responsibilities may be delegated to qualified appointed subordinates.

8. **Training:** The employees should have thorough training in all pertinent fields, such as pharmaceutical technology, taxonomy, botany, photochemistry, pharmacognosy, hygiene, microbiology, and associated subjects.

9. **Personal Hygiene:** Personnel must wear appropriate protective clothes to prevent contact with allergic plant materials and harmful irritants. Throughout the whole process, from plant processing to product production, they should be wearing the appropriate gloves, hats, masks, work suits, and shoes.

10. **Premises:** In accordance with WHO recommendations, the premises should be planned, situated, built, modified, and maintained to accommodate the operations to be carried out.

11. **Materials:** Materials should be stored in places that are clearly labeled to reduce the chance of cross-contamination. All entering herbal products should be quarantined in a specific location. Herbal products should be stored in separate locations.

12. **Production Areas:** Adequate care should be taken while sampling, weighing, combining, and processing medicinal plant materials to simplify cleaning and prevent cross-contamination.

13. **Equipment:** Thirteen. Equipment The need for thorough equipment cleaning follows. Wet cleaning techniques like vacuuming are preferable. To stop the growth of microorganisms, equipment that has undergone wet cleaning should be dried right afterwards.

14. **Materials:** All arriving herbal items need to be stored properly and disinfected. In accordance with national legislation, only approved compounds should be used for fumigation, and allowed limits for their residues as well as requirements for the equipment utilized should be defined.

Documentations

- Good Practice in Productions
- Good Practice in Quality Practice

III. ANALYSES OF READILY ACCESSIBLE, CRUDE MEDICINES FOR USAGE

A number of tests and analyses are used to examine the quality, safety, and efficacy of commercial crude medicines intended for use. Crude drugs are natural substances derived from plant, animal, or mineral sources, and they form the basis of many traditional and modern medicines. As dietary supplements, traditional herbal remedies are swiftly becoming more and more popular across the world, and sales of these items have skyrocketed.(Ali et al., 2005)

Standardization and quality control of herbals is, in accordance with WHO (1996a and b, 1992), the process involved in the physicochemical evaluation of crude drugs covering facets such as the choice and handling of crude material, the safety, efficacy, and stability assessment of finished product, the documentation of safety and risk based on experience, the provision of product information to consumers, and product promotion.(Kunle, 2012)

Here's an overview of the key aspects involved in the evaluation process:

- **Identification and Authentication:** The first step in evaluating a crude drug is to accurately identify the botanical, animal, or mineral source. This involves morphological, microscopic, and chemical characterization to ensure the authenticity of the material. Authentication is crucial to avoid adulteration and misidentification.

- **Quality Control Testing**: Various tests are conducted to assess the quality of the crude drug. These tests might include extractive values, total ash content, acid-insoluble ash content, and organoleptic assessment (sensory properties including colour, odour, and taste). These evaluations aid in determining the material's quality and purity.

- **Phytochemical Screening**: Phytochemical screening is done on plant-based crude pharmaceuticals to find and measure the presence of different bioactive chemicals such alkaloids, glycosides, flavonoids, tannins, etc. These substances support the drug's therapeutic effects.

- **Microbiological Testing**: To ensure the safety of the crude drug, microbiological tests are carried out to detect the presence of harmful microorganisms like bacteria, yeast, and molds. This is especially important for herbal drugs that are consumed orally or topically.

- **Heavy Metal Analysis**: Heavy metals including lead, arsenic, cadmium, and mercury, which may be dangerous if present in large amounts, are checked for in crude pharmaceuticals. To guarantee the safety of the medicine, certain restrictions are established.

- **Pesticide Residue Analysis**: In the case of plant-derived crude drugs, pesticide residues are analyzed to ensure they comply with established safety standards.

- **Determination of Active Constituents**: To determine the potency and therapeutic effectiveness of the crude medication, quantitative analysis of the active ingredients is conducted.

- **Pharmacological Evaluation (if necessary):** In some cases, further pharmacological and toxicological studies might be conducted to assess the potential therapeutic benefits and safety profile of the crude drug.

- **Stability Testing**: In order to preserve the quality and effectiveness of the medicine over time, stability tests are carried out to ascertain the shelf life and storage requirements.It's vital to note that the review procedure may change dependent on the kind of crude medicine (plant-based, animal-based, or mineral-based), the planned application of the medication, and the legal requirements of the nation or area in which the drug will be sold. Overall, the evaluation of commercial crude drugs is a critical step in ensuring the safety, quality, and efficacy of herbal and natural medicines. These assessments contribute to the protection of public health and provide confidence to healthcare providers and consumers in their use.Drug evaluation establishes a drug's identification, as well as its quality and purity. The biochemical variations in the medication, the effects of handling and storing the drug, and adulterations and replacements are the primary drivers of the requirement for examination of crude pharmaceuticals(Bandaranayake, 2006).

  - Organoleptic Assessment
  - Examination under a microscope
  - Chemical Analysis
  - Physical Assessment
  - Biological Assessment

1. **Organoleptic Assessment:** Using the sense organs to evaluate medications is known as organoleptic assessment. It alludes to analytical techniques including colour, smell, taste, size, form, and unique characteristics like touch and texture. Naturally, the plant or extract tends to recognize itself upon first sight since it is so distinct. If this isn't enough, the plant

or extract may also have a distinctive flavor or aroma. Morphology is the description of the shape, whereas morphology is the study of the form of a crude medication.

2. **Microscopic Evaluation:** This method makes it possible to analyze drugs more thoroughly and may be used to identify organized medications based on their recognized histological characteristics. It is mostly used for the qualitative evaluation of organized, unprocessed medications that are entire and in powder form. Every plant has a unique tissue characteristic. The structural characteristics of drugs derived from plants may be examined under a microscope. For instance, glandular trachoma of mint, warty trachoma of senna, wavy medullary rays of cascara bark, etc.

   Trachoma size, fiber length and width, starch grain size, etc. are examples of linear measurements. Leaf constants are influenced by a variety of variables, including stomata number, stomata index, vein islet, veinlet termination number, and palisade ratios.

3. **Quantitative Microscopy (Lycopodium Spore Method):** This is a crucial strategy used to identify unprocessed drugs when chemical and physical approaches are not viable. It is a low-cost approach with formal recognition. Using a microscope allows for detailed examination of the internal structure, content, and inclusions of plant and animal cells as well as other objects.(Alamgir, 2017).

4. **Chemical Evaluation:** Chemical assays, quantitative chemical testing, qualitative chemical tests, and instrumental analysis are all included in the chemical evaluation. In many ways, medicines made from natural sources are essential therapeutic tools that help people improve their health and quality of life. Chemical evaluation methods involve the separation, purification, and recognition of active ingredients. Qualitative chemical assays include identification tests for various phytoconstituents, such as alkaloids, glycosides, tannins, etc. (Rashmi Saxena Pal et al., 2016).For instance, copper acetate is used to identify the presence of colophony in adulterants. Vitali-Morin's reaction for trepan alkaloids Van-Urk's reagent for ergot.

5. **Physical Evaluation:** Physical requirements for the drugs should be specified wherever possible. These parameters, in particular moisture content, specific gravity, density, optical rotation, refractive index, melting point, viscosity, and solubility in various solvents, may be helpful in assessment even though they are seldom constant for crude medications.

6. **Biological Evaluation:** The word "bioassay" describes the method of evaluating a drug's efficacy by observing its effects on live organisms such as bacteria, fungus, animal tissue, or an entire animal. Whenstandardization by chemical or physical methods is insufficient, as well as when the therapeutic activity of the raw material and the finished product must be constant, this method is usually needed. The three basic types of biological assay techniquestoxic, symptomatic, and tissue techniques are only a few.

IV. CONCLUSIONS

In order to essentially assure constant composition of all herbal pharmaceuticals, including analytical processes for identification, standardization of herbal drugs entails all information and controls. Plant materials are used as over-the-counter pharmaceuticals, a source of raw materials for the pharmaceutical industry, and as natural remedies in both

industrialized and developing nations. Additionally, they represent a sizable portion of the global medication industry. Therefore, it is essential to establish generally regarded standards for assessing their quality. Even while some herbs have become more well-known throughout time, the general public, medical experts, and the media still lack a lot of information about how to utilize herbs safely and effectively.It is impossible to stress the importance of using contemporary analytical technologies to assess the many quality indicators for a successful quality control herbal product. To guarantee the safety and effectiveness of a herbal treatment, quality control must be maintained throughout the whole production process, from product collection through processing to finished packaged product. To adopt a more comprehensive approach to herbal quality, it is proposed that various government organizations apply the WHO recommendations and produce monographs using the many quality standards described above. Quality violations will decline when the regulatory framework is tightened.

REFRENCES

[1] Alamgir, A. N. M. (2017). Microscopy in pharmacognosy. In *Progress in Drug Research*. https://doi.org/10.1007/978-3-319-63862-1_11

[2] Ali, N., Hashim, N. H., Saad, B., Safan, K., Nakajima, M., & Yoshizawa, T. (2005). Evaluation of a method to determine the natural occurrence of aflatoxins in commercial traditional herbal medicines from Malaysia and Indonesia. *Food and Chemical Toxicology*. https://doi.org/10.1016/j.fct.2005.05.019

[3] Bandaranayake, W. M. (2006). Quality Control, Screening, Toxicity, and Regulation of Herbal Drugs. In *Modern Phytomedicine: Turning Medicinal Plants into Drugs*. https://doi.org/10.1002/9783527609987.ch2

[4] Calixto, J. B. (2000). Efficacy, safety, quality control, marketing and regulatory guidelines for herbal medicines (phytotherapeutic agents). In *Brazilian Journal of Medical and Biological Research*. https://doi.org/10.1590/S0100-879X2000000200004

[5] Choi, D. W., Kim, J. H., Cho, S. Y., Kim, D. H., & Chang, S. Y. (2002). Regulation and quality control of herbal drugs in Korea. *Toxicology*. https://doi.org/10.1016/S0300-483X(02)00487-0

[6] Klick, S., Muijselaar, P. G., Waterval, J., Eichinger, T., Korn, C., Gerding, T. K., Debets, A. J., Sänger-Van De Griend, C., Van Den Beld, C., Somsen, G. W., & De Jong, G. J. (2005). Toward a generic approach for: Stress testing of drug substances and drug products. In *Pharmaceutical Technology*.

[7] Kunle. (2012). Standardization of herbal medicines - A review. *International Journal of Biodiversity and Conservation*. https://doi.org/10.5897/ijbc11.163

[8] Liang, Y. Z., Xie, P., & Chan, K. (2004). Quality control of herbal medicines. In *Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences*. https://doi.org/10.1016/j.jchromb.2004.08.041

[9] Rashmi Saxena Pal, Wal, P., Pal, Y., Rai, A. K., Wal, A., Srivastava, A., Chandra, S., & Saraswat, N. (2016). Physico-chemical and phytochemical evaluation of crude drug powder (leaves) of Polyalthia longifolia. *~ 212 ~ Journal of Pharmacognosy and Phytochemistry*.

[10] Shinde, M., Bais, S., & Devmare, D. (2023). Review on standardization of herbal drug and formulation. *International Journal of Pharmacognosy and Life Science*. https://doi.org/10.33545/27072827.2023.v4.i1a.69

[11] Shinde, V. M., Dhalwal, K., Potdar, M., & Mahadik, K. R. (2009). Application of Quality Control Principles to Herbal Drugs. *International Journal of Phytomedicine*. https://doi.org/10.5138/ijpm.2009.0975.0185.05786

