Introduction to Quality Control and Standardization of Herbals

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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 .

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 goods have a significant impact on the efficacy and safety of herbal 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)

1.1Quality 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:

a) **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.
b) **Raw Material Inspection:** The Herbal medicines' raw ingredients should be examined for purity, the absence of impurities, and conformance with recognized quality standards.
c) **Good Agricultural and Collection Practices (GACP):** GACP involves guidelines for the cultivation and harvesting of medicinal plants to ensure they are of the highest quality.
d) **Good Manufacturing Practices (GMP):** GMP provides a framework for the manufacturing processes, ensuring cleanliness, proper storage, handling, and labeling of herbal products.
e) **Testing for Contaminants**: Herbal medicines should be tested for heavy metals, pesticides, microbial contamination, and other potential harmful substances to ensure their safety.

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

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

1.2 Standardization of Herbals:

Standardization is the process of ensuring uniformity and consistency in the quality and composition of herbal 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)

a. **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.
b. **Active Ingredient Concentration**: Standardization ensures that the herbal product contains a specific amount of the active ingredient(s) to ensure its potency and efficacy.
c. **Batch-to-Batch Consistency**: By standardizing herbal products, manufacturers aim to achieve consistent quality and therapeutic effects from one batch to another.
d. **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.

2.1 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).

2.2 Amikacin Sulphate

a. Tests of identity
b. Almost odorless, white to yellowish-white, crystalline powder.
c. 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.

2.3 Captopril

a. Tests of identity
b. 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.

2.4 Cisplatin

a. Tests of identity

b. 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 .

2.5 Ketamine Hydrochloride

a. Tests of identity
b. 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.

2.6 Levamisole

a. Tests of identity
b. 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.

2.7 Magnesium Sulfate

a. Tests of identity
b. White, crystalline powder or brilliant, colorless crystals that are odorless About 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 added.
- The precipitate dissolves when 1 ml of ammonium chloride is added.
- The precipitate also dissolves when 1 ml of disodium hydrogen phosphate is added.

2.8 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

3.1 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 quality control of herbal drugs as a single comprehensive document. However, WHO has developed general guidelines and recommendations for the regulation of herbal medicines, 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. **Good Agricultural and Collection Practices (GACP)**: These guidelines focus on the cultivation and collection of medicinal plants, emphasizing proper cultivation techniques, harvesting, and storage to ensure the safety and quality of herbal raw materials.
2. **Good Manufacturing Practices (GMP):** These guidelines outline the standards for the manufacturing process of herbal drugs and products. GMP ensures that herbal products are consistently produced and controlled according to established quality standards.
3. **Quality Control Testing**: WHO encourages the implementation of appropriate testing methods to evaluate the identity, purity, strength, and safety of herbal drugs. This involves using validated analytical techniques to verify the presence and levels of active constituents and to detect potential contaminants.
4. **Contaminant Control:** Herbal drugs should be tested for possible contamination with heavy metals, pesticides, microorganisms, and other potential harmful substances. Strict limits are set for these contaminants to ensure the safety of the products. Standardization: Standardization of herbal drugs involves ensuring consistent levels of active constituents in each batch of the product. This can be achieved through the use of validated analytical methods and by specifying acceptable ranges for the active compounds.
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**: WHO encourages countries to develop and implement regulations and guidelines for herbal medicines to ensure their quality, safety, and efficacy. It is important to note that different countries may have their own specific regulations and guidelines for quality control of herbal drugs. These can be based on WHO recommendations and may incorporate additional requirements to suit their local contexts. 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 encourage the use of herbal medicines, to enhance their quality, and to lessen the incidence of side effects brought on by subpar herbal medication. One of the crucial stages in the production process is where quality control is necessary to guarantee the quality of pharmaceutical goods, including herbal medicines. The World Health Organization (WHO) (5) estimates that between 65 and 80 percent of the world's population, who reside in underdeveloped countries, rely mostly on plants for basic healthcare due to poverty and a lack of access to modern medication(Calixto, 2000).

cGMP is one of the most important tools for this measure.

- Sanitation and hygiene Qualification & Validation
- Product Recalls
- Self-Inspection
- Training
- Premises
- Production Areas
- Material
- Good Practice in Productions
- 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 water supply to the

production facility should be checked and, if necessary, treated correctly. Waste containers must to be accessible, emptied, and cleaned at least once each day.

2. **Qualification & Validation: The** written procedure should specify process steps and factors (such as extraction time, temperature and solvent purity), acceptance criteria and the type of validation to be conducted and the number of process runs.
3. **Complaints:** Product quality complaints may be caused by problems such as faulty manufacture, product defects or deterioration of herbal medicines and adulteration of the herbal material. These complaints should be recorded in detail and their causes by comparing with the reference samples kept from the same batch.
4. **Product Recalls :**There should be a standard operating procedure (SOP) for the storage of recalled herbal medicines in a secure isolated area, complying with the requirements specified.
5. **Contract Production & Analysis Contract:** should be drawn up by experienced people suitably knowledgeable on the specific characteristics of herbal medicines including their production and quality control testing.
6. **Self-Inspection:** One member of the self-inspection should have a thorough knowledge of herbal medicine.
7. **Personnel:** All responsible staff should have their duties recorded in written descriptions and adequate authority to carry out their responsibilities. Their duties may be given to designated deputies of a satisfactory qualification level.
8. **Training:** The staff should be well trained in relevant disciplines including pharmaceutical technology, taxonomy botany, photochemistry, pharmacognosy, hygiene, microbiology, and related topics.
9. **Personal Hygiene:** Personnel must be protected from contact with toxic irritants and allergenic plant materials using suitable protective clothing. They should wear suitable gloves, caps, masks, work suits and shoes throughout the whole procedure from plant processing to product manufacture.
10. **Premises: The** premises should be designed, located, constructed, adapted and maintained to suit the operations to be carried out according to WHO guidelines.

11. **Storage areas:** The areas should be well labeled and materials stored in such a way as to avoid any risk of cross-contamination. An area should be identified for the quarantine of all incoming herbal materials. Different herbal materials should be stored in separate areas.
12. **Production Areas:** To facilitate cleaning and to avoid cross contamination, adequate precautions should be taken during the sampling, weighing, mixing and processing of medicinal plant
13. **Equipment's:** Effective cleaning of the equipment is therefore necessary. Vacuum or wet-cleaning methods are preferred. If wet-cleaning is done, the equipment should be dried immediately after cleaning to prevent the growth of micro-organisms.
14. **Material's: All** incoming herbal materials should be quarantined and stored under appropriate conditions. Only permitted substances should be used for fumigation and allowable limits for their residues together with specifications for the apparatus used should be set according to the national regulations.
15. **Documentations**

a. Good Practice in Productions
b. Good Practice in Quality Practice

4.1 Evaluation of commercial crude drugs intended for use

The evaluation of commercial crude drugs intended for use involves a series of tests and assessments to determine their quality, safety, and efficacy. Crude drugs are natural substances derived from plant, animal, or mineral sources, and they form the basis of many traditional and modern medicines. Traditional herbal medicines are rapidly gaining popularity throughout the world as food supplements and sales of these products have increased exponentially.(Ali et al., 2005)

According to WHO (1996a and b, 1992), standardization and quality control of herbals is the process involved in the physicochemical evaluation of crude drug covering aspects, such as selection and handling of crude material, safety, efficacy and stability assessment of finished

product, documentation of safety and risk based on experience, provision of product information to consumer and product promotion.(Kunle, 2012)

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

1. **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.
2. **Quality Control Testing**: Various tests are conducted to assess the quality of the crude drug. These tests may include organoleptic evaluation (sensory characteristics like color, odor, and taste), determination of moisture content, total ash content, acid-insoluble ash, and extractive values. These tests help ascertain the purity and quality of the material.
3. **Phytochemical Screening**: For plant-based crude drugs, phytochemical screening is performed to identify and quantify the presence of various bioactive compounds such as alkaloids, glycosides, flavonoids, tannins, etc. These compounds contribute to the therapeutic properties of the drug.
4. **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.
5. **Heavy Metal Analysis**: Crude drugs are tested for the presence of heavy metals such as lead, arsenic, cadmium, and mercury, which may be harmful if present in high quantities. Strict limits are set to ensure the safety of the drug.
6. **Pesticide Residue Analysis**: In the case of plant-derived crude drugs, pesticide residues are analyzed to ensure they comply with established safety standards.
7. **Determination of Active Constituents**: Quantitative analysis of the active constituents is carried out to establish the potency and therapeutic efficacy of the crude drug.
8. **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.
9. **Stability Testing**: Stability studies are performed to determine the shelf life and storage conditions required to maintain the quality and efficacy of the drug over time.It's important to

mention that the evaluation process may vary depending on the type of crude drug (plant, animal, or mineral-based), its intended use, and the regulatory requirements of the country or region where it will be marketed. 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).

1)Organoleptic Evaluation

2)Microscopically Evaluation

3) Chemical Evaluation

4)Physical Evaluation

5)Biological Evaluation

4.2 Organoleptic evaluation; 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.

4.3 Microscopic evaluation -

This technique enables a more thorough analysis of a drug and can be used to recognize organized medicines by their recognized histological characteristics. It is mostly employed for the qualitative assessment of whole and powdered organized crude pharmaceuticals. Every plant has a distinctive tissue feature. Drugs made from plants can have their structural features verified using a microscope. Eg. Lignified trachoma in nux vomica, warty trachoma of senna, wavy medullary rays of cascara bark, glandular trachoma of mint etc.

Linear measures include trachoma size, fiber length and breadth, starch grain size, etc.Stomatal number, stomatal index, vein islet, veinlet termination number, and palisade ratios are all factors in determining leaf constants.

4.4 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. The interior makeup, composition, and inclusions of plant and animal cells or other things can be studied in depth using a microscope(Alamgir, 2017) .

4.5 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 techniques of assessment include the isolation, purification, and identification of active components. Identification tests for different phytoconstituents including alkaloids, glycosides, tannins, etc. are included in qualitative chemical assays..(Rashmi Saxena Pal et al., 2016)

Eg. Copper acetate used in the detection of colophony present as an adulterant. Van Urk’s reagent for ergot Vitali Morin’s reaction for trepan alkaloids.

4.6 Physical evaluation: Wherever feasible, physical requirements for the medications are to be established. Although they are seldom consistent for crude pharmaceuticals, these characteristics, particularly moisture content, specific gravity, density, optical rotation, refractive index, melting point, viscosity, and solubility in various solvents, may be useful in assessment..

4.8 Biological evaluation: The term "bioassay" refers to the process of determining a drug's effectiveness by seeing how it affects living things like bacteria, fungi, animal tissue, or a complete animal. This approach is typically required when standardisation by chemical or physical means is insufficient, as well as when the therapeutic activity of the raw material and the end product must be consistent.

Biological assy methods are mainly of 3 types

1. Toxic
2. Symptomatic
3. Tissue methods

5.CONCLUSIONS

Standardization of herbal drugs comprises total information and controls to essentially guarantee consistent composition of all herbal including analytical operations for identification. In both industrialized and developing countries, plant materials are utilized as over-the-counter medications, as a source of raw materials for the pharmaceutical industry, and as home cures. They also account for a sizeable share of the worldwide drug market. Therefore, it is crucial to create widely accepted standards for evaluating their quality. Even if some herbs have gained popularity throughout time, the general public, healthcare professionals, and the media still have little knowledge about the safe and efficient use of herbal therapy. It is impossible to overstate the importance of using contemporary analytical instruments to assess the many quality factors for an efficient quality control herbal product. Monitoring the quality of the product from collection through processing to the completed packaged product is necessary to ensure the safety and efficacy of a herbal medication. It is advised that different government organizations implement the WHO recommendations and create monographs utilizing the numerous quality criteria mentioned above in order to take a more global approach to herbal quality. The regulatory framework will be strengthened, and quality breaches will be reduced.

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