WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Standardization of Herbal Gutika Review Article

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ABSTRACT

According to an ancient and historical approach on medicine mainly performed in the Indian origin is Ayurveda. Ayurveda is one of the oldest medicinal system which show the plants, herbs and various shrubs used as the ingredient in medicine formulation to show pharmacological and harmonizing physiological doshas to ensure full recovery. Medicines which are prepared in this medicinal system are in the form of tablet known as vati and gutika. Gutika (tablet) is an efficient ayurvedic formulation that maintain the balance of vata and kapha doshas in the body. In the present era, changing trends towards the Ayurvedic drugs & formulations and development of reliable quality control protocols are important so the various standardization parameters like physical parameters includes Hardness, Friability, Disintegration time, Dissolution time, Weight variation test, and HPLC fingerprinting, Quantification of markers, physiochemical parameters which includes Ash value, Total Ash value, Water soluble Ash value, Acid Insoluble Ash value, Extractive value, Loss of drying, pH are used to be within the norms specified in Indian Pharmacopoeia with respect to a Gutika(tablet). These parameters can determine the quality of the product as Gutika. All these standardization and evaluation parameters methodology for gutika is given in these review.

Keywords: Ash value, Disintegration time, Dissolution time, Extractive value, Friability, HPLC fingerprinting, Physiochemical parameters, Standardization of Gutika.

INTRODUCTION

Ayurveda is the one of the ancient and oldest system of medicine originated mainly from India also known as Indian system of medicine as compared to other systems of medicine like Unani, Homeopathy, and Allopathy. Ayurveda has the very long history of rich heritage in India which deals with the natural origin products are used to prepare or formulate the medicine for recovery, treatment, or prevention of Diseases. The word Ayurveda is the combination of word “Ayur” means Life and “Veda” means knowledge or science which means “the science of life”. The Ayurveda system is based on the theory of Tridosha and diseases causing because of Vata, Pita and Kapha and can be treated by substances obtained from nature i.e. plant, minerals and metal, etc. as compared to synthetic drugs. Maintaining the proper quality of the product is a result of the development of traditional medical systems. India is rich in its flora and fauna.[1]

According to WHO report, approximately 70% of population using ancient medicinal system in India and the demand for this system is gradually amplified day by day.[2] The plants used for curing various diseases used in raw condition rather than formulation the standardization parameters are essential for development of standardization protocol to avoid variation arising in batch to batch.[3] Plant active constituent efficiency based on the right time and atmospheric condition for the collection and processing.[4] According to a recent current issue in many journals, most of the researchers have an enormous curiosity in a herbal medicinal system for a healthy life because it contains most of the natural element with no side effect for preventing the cause of the disease.[5]

In Ayurveda formulation of drug are single drug or combination of drug formulation are prepared, polyherbal formulation is a combination formulation prepared by combination of more than one herb to attain desired therapeutic effects. [6] The different types of formulations which includes Gutikas [7] (tablets), Bhasma [8], Churnas [9] (fine powders), Kashayam [10] (aqueous extracts) and Taila [11] (lipid extracts) etc. Standardization of Ayurvedic formulations deals with quality and purity of it various standardization methods of protocol based in new changing trends necessitated establishment of standards for Ayurvedic drugs and formulations using modern techniques of analysis is extremely important.[12] Gutika, Vati, Varti, Vataka, Panda, or Pindi, Mordaka, are the same words that Acharya Sharangdhargutika uses to describe Gutikais.[13] The CCRAS and WHO has introduced certain standards and guidelines to maintain uniformity between the production batches. Good manufacturing practices and quality control of the ingredients and products can result in ensuring quality assurance of the formulation. [14]

Gutika traditional ayurvedic dose form, gutika is a product of kalkakalpana, one of the five fundamental principles of Ayurvedic sciences. They are extremely small in comparison to vati. The term vatikalpana, which is commonly referred to as pills in the modern dosage form, was attributed to Acharya Sharangdhar Gutika. Gutika is a key ingredient of the ayurvedic pharmacy. Modern terminology refers to gutika as pills, and spheroids as agglomerates of fine powder or granules of bulk pharmaceuticals as well as excipients. [15] mainly the Gutika are of two types Agnisandhya vati and Anagnisandhya vati.

Gutika formulation advantages are Easy to administer, Consume less time in preparation, More stable dosage form, Maintain the accuracy of dosage, Easy to transportable, Economical dosage form, Convenient for dispensing, Palatable, Easy to administer.

Various examples of marketed gutikas are Trivutadi gutika, Marichadi Gutika, Khadiradi gutika, Shiva gutika, Bhagottar gutika, Komla gutika, Arogyavardhini gutika, Pranda gutika.

Standardization is an important aspect in maintaining the quality and safety of any polyherbal formulation as these are combinations of more than herb to attain the desired therapeutic effect and it also helps minimize batch to batch variation. [16]

STANDARDIZATION

Standardization:

Standardization is the confirmation and evaluation of the drug for the means of its identity and determination of its quality and purity and detection of its nature of adulteration [17] by various parameters like morphological, physical, chemical and biological observations.

All measures implemented in the manufacturing process and quality control resulting in a consistent quality shall be described by means of standardization. It also encompasses the entire field of study from the selection of sample and raw materials to its clinical application. Standardization shall be the first step in establishing a consistent biological activity, chemical profile or simply a quality assurance programme for production and manufacturing.

- **Need for standardization of Gutika:**

Standardization is the process by which standards are established for a specific or medicinal product. Ensuring that the medicine is given to consumers which guarantees purity, safety, potency and efficacy is a cardinal responsibility of the regulatory authorities. Regulatory authorities fulfil this responsibility by enforcing strict adherence to quality standards for both raw materials and finished products as outlined in pharmacopoeias. They oversee manufacturing processes by implementing formularies and ensuring compliance with statutory "Good manufacturing practices."

- **Enlist the standardization parameters of Gutika[18-19]:**

A. Organoleptic parameters:

1. Description.
2. Colour: Uniform, no mottling.
3. Odour: Characterisation of the formulation; no disagreeable odour.
4. Taste: if sweet.
5. Determination of total sugar (if added).
6. Determination of reducing sugar/Non reducing sugar (if added).

B. Phytochemical assessment:

1. Particle size.
2. Identification: Microscopic characters (if vegetable parts are used as ingredients; HPLC/TLC/HPTLC/LC-MS (any one of all).
3. Test for heavy/toxic metals – Lead, Cadmium, Arsenic, mercury.
4. Microbial contamination test – Total bacterial count and total fungal count.
5. Test for specific Pathogen – E.coli, Salmonella spp., S.aureus, Pseudomonas aeruginosa.
6. Pesticide residue test – Organochlorine pesticides, Organophosphorus pesticides and Pyrethroids.
7. Test for Aflatoxins – B1, B2, G1 and G2.

C. Physical evaluation:

1. Total ash.
2. Acid insoluble ash.

3. Water soluble ash.
4. Water soluble extractive.
5. Alcohol soluble extractive.
6. pH of 5% aqueous solution.
7. Volatile oil determination.
8. Loss of drying at 105°C.

D. Pharmaceutical parameters:

1. Hardness.
2. Friability.
3. Thickness.
4. Weight variation.
5. Drug content.
6. Content uniformity.
7. Disintegration time.
8. Dissolution test.

EVALUATION OF GUTIKA

ORGANOLEPTIC EVALUATION:

Organoleptic evaluation refers to the study of drugs that use organs of senses. It covers the methods of analysis, for example like colour, odour, taste, size, shape and special features, such as touch, texture or other characteristics. The initial observation of the plant or extract is often distinctive enough to enable its identification. Perhaps the plant or extract has a characteristics smell or taste if this is not enough. Morphology means the study of form of a crude drug while description of its form is morphography.

All the details for organoleptic evaluation and methods are given in the table 1.

CHARACTERS	CHARACTERISTICS
Description	Provide a small description about the Gutika.
Colour	Identify the colour and matches the standard.
Odour	Identify the odour and matches the standard.
Taste	Check if the any odour.
Size and shape	Check for the shape and size and matches the standard.
Microscopic characters	If any vegetable part is used as ingredients.

[Table 1]: Parameters for Organoleptic evaluation.[19-20]

PHYTOCHEMICAL ASSESSMENT:

- **Heavy metal determination:**

Heavy metal determination test is conducted to detect the presence of the heavy metals in the Gutika. In this assessment, heavy metals like lead, chromium, copper, cadmium, nickel, zinc, cobalt, and bismuth are examined using standardised techniques, and the outcomes are compared to standardized values that are appropriate for health. [21] The safety values which are given by the authorities like WHO and FDA, so the concentration of the heavy metal presence should be not more than the given standardised value which are safe and appropriate for health of the individual.

The standardised value is given in the table 2.

TEST FOR HEAVY (PERMISSIBLE LIMIT)	AS PER WHO/FDA
Mercury	0.30ppm
Arsenic	10.0ppm
Lead	10.0ppm
Cadmium	0.30ppm

[Table 2]: List of heavy metal with permitted limit [21]

Method: Detection of heavy metals done by various methods like:

A. Common method:

1. **Limit tests:** limit tests are performed for Arsenic, Mercury, Lead, and Cadmium.
2. **Flame photometry method:** The photoelectric flame photometer are used to determine the concentration of heavy metals the reading is noted in the unit ppm.

B. Advanced method:

1. X-Ray diffraction method.
2. X-Ray fluorescence spectrometer method.
3. Atomic absorption spectroscopy method.
4. Inductively coupled plasma mass spectroscopy method.

Side effects of heavy metals: the following side effects on individual are:

METAL	ACUTE	CHRONIC
Arsenic	Nausea, Vomiting, Diarrhoea, Painful neuropathy.	Cancer: Lung, Bladder, Skin, Encephalopathy.
Lead	Nausea, vomiting, encephalopathy (headache, seizures)	Encephalopathy, Anaemia, Abdominal pain, Nephropathy, Foot-drop/wrist-drop.
Chromium	GI haemorrhage, Haemolysis, Acute renal failure.	Pulmonary fibrosis, Lung cancer (inhalation).
Mercury	Elemental(inhaled): Fever, Vomiting, Diarrhoea, Inorganic salts (ingestion): Caustic gastroenteritis.	Nausea, Nephritic syndrome; Hypersensitivity (Pink disease).

[Table 3]: Side effects of heavy metals.

- **Microbial contamination:**

Microbial contamination test is performed for the determination to check whether the Gutika is contaminated with the microorganisms. There are limit for the microbial contamination according to WHO. The total count of microbial colony is done on the nutritional culture media like agar plate, sabouraud plate, dextrose plate, sabouraud dextrose plate. Various techniques like spread plate and pour plate method are used for microbial contamination determination.

WHO's most widely recognised method for counting all microorganisms in plant materials and herbal preparations is total viable count [22]. The overall viable count ranges in every pharmacopoeia from 105 to 107cfu/g. Spread plate techniques [23] is used to count all aerobic and anaerobic bacteria, which is followed by a 24- hours incubation period at 30-35°. Spread plate technique is utilised in sabouraud and dextrose agar [24] is incubated at 30-

35ºC for 24 hours to count yeast and mould. The WHO has set a limit of 107cfu/g for total aerobic microorganisms and 104cfu/g for fungus and mould in plant materials. [25]

- **Chromatographic evaluation:**

HPTLC conditions Chromatographic separation was achieved on HPTLC plates precoated with silica gel 60 F254 (E. Merck) of 0.2 mm thickness with aluminium sheet support. Samples were spotted using CAMAG Linomat IV Automatic Sample Spotter (Camag Muttenz, Switzerland) equipped with syringe (Hamilton, 100 µL). Plates were developed in a glass twin trough chamber (CAMAG) and presaturated with mobile phase. The one scanning device used with CATS 3 software is the CAMAG Scanner II. The experimental condition was maintained at 20 ± 2ºC. After derivatizing the plates with anisaldehyde sulphuric acid reagent and photo documentation using CAMAG Reprostar 3 at 550 nm, detection of piperine was possible. [26]

- **Test for Pesticide residue:**

Organochlorine pesticides, Organophosphorus pesticides, Pyrethroids are the pesticides which are harmful for the consumption and any amount more than permitted limit is detected in Gutika then that batch should be discarded for prevention of side effects and toxic effects of pesticide in Gutika. WHO/FDA has standardised the permitted limit of these residue of pesticides in herbal Gutika is further given in the table 4.

PESTICIDE RESIDUE – ORGANOCHLORINE PESTICIDE	PERMISSIBLE LIMIT
DDT	1.0mg/kg
HCH	0.3mg/kg
Endosulfan	3.0mg/kg
Alderin	0.05mg/kg
Organophosphorus	Permissible limit
Malathion	1.0mg/kg
Parathion	0.5mg/kg

[Table 4]: List of pesticide residue with permitted limit. [27]

- **Test for Aflatoxins:**

TEST FOR AFLATOXINS	PERMISSIBLE LIMIT
B1	0.5ppm
B2	0.1ppm
G1	0.5ppm
G2	0.1ppm

[Table 5]: List of Aflatoxins with permitted limit. [28]

PHYSICAL EVALUATION:

- **Determination of Total ash:**

Total ash method is used to measure the total amount of material remaining after incineration is called total ash. Determination of total Ash value is determined for identity and purity of gutika. A high ash value is indicative of contamination, substitution, adulteration, presence of silica, rice husk or careless in preparing the drug.

Formula: Percentage of total ash = $\frac{\text{Weight of ash}}{\text{Weight of sample}} \times 100$

Method [29-30]:

Weight accurately about 2-3gm of the powdered drug in a tared silica crucible.

↓

Heat at 450°C until free from carbon.

↓

Cool and weigh determine the amount of ash in relation to the air-dried medication (percentage of total ash calculated).

- **Determination of Acid insoluble ash:**

Acid insoluble ash is the residue obtained after boiling the total ash with dilute HCl and igniting the remaining insoluble matter is called as acid insoluble ash. Determination of acid insoluble Ash value is determined for identity and purity of gutika. A low acid insoluble ash value affects in the gastrointestinal canal when taken orally.

Formula: Acid-insoluble ash = Total ash – solid matter

Percentage acid insoluble ash = $\frac{\text{Weight of acid insoluble ash}}{\text{Weight of sample}} \times 100$

Method [29-31]:

Boiled the ash with 25 ml of conc. hydrochloric acid for 5 min.

↓

Filter it and the solid matter was collected on an ashless filter media.

↓

Solid matter was washed with hot water and ignited in Gooch crucible at 450°C.

↓

Allowed to cool in desiccator and weighed.

↓

Determine the amount of acid insoluble ash in the drug's air-dried form (percentage of acid insoluble ash).

↓

Acid-insoluble ash = Total ash – solid matter.

- **Determination of Water soluble ash:**

Water soluble ash is the difference in weight between total and residue after treatment of total ash with water. Determination of water soluble Ash value is determined for identity and purity of gutika.

Formula: Water-soluble ash = Total ash – insoluble solid

Percentage of water soluble ash = $\frac{\text{Weight of water soluble ash}}{\text{Weight of sample}} \times 100$

Method [29-32]:

In 25 ml water, total ash was boiled for 5 min.

↓

Insoluble matter was filtered and collected on ashless filter media.

↓

Insoluble matter washed with hot water and ignited in Gooch crucible at 450°C.

↓

Allowed to cool in desiccator and weighed.

↓

Determine the amount of water-soluble ash in relation to the air-dried medication (percentage of water soluble ash).

↓

Water-soluble ash = Total ash – insoluble solid.

- **Determination of Alcohol soluble extractive:**

Extractives are the natural chemical products of biomass that are capable of being extracted by some solvents. It comes under physical parameters of the drug evaluation of Gutika. It helps to indicate the nature of chemical constituents present in Gutika. Alcohol soluble extractive is one of the type of extractive.

Formula: Percentage of Alcohol soluble extractive = $\frac{\text{Weight of residue}}{\text{Weight of drug}} \times 100$

Method [29-33]:

Macerate about 5gm of the accurately weighed coarse powder (air dried drug) with 100ml of 90% alcohol in a 100ml closed volumetric flask for 24 hours.

↓

Shake frequently for first 6 hours and then letting that stand for the last 18 hours.

↓

Filter rapidly to prevent the loss of solvent, through filter paper and evaporate 25ml of alcohol extract (steam bath0 to dryness in a tarred flat bottomed shallow dish.

↓

Dry the residue at 105°C (muffle furnace) and weigh. Keep in a desiccator.

Dry the extract to constant weight.

↓

Determine the amount of extractive that is alcohol-soluble in relation to the air-dried substance (percentage of alcohol soluble extractive).

- **Determination of Water soluble extractive:**

Extractives are the natural chemical products of biomass that are capable of being extracted by some solvents. It comes under physical parameters of the drug evaluation of Gutika. It helps to indicate the nature of chemical constituents present in Gutika. Water soluble extractive is one of the type of extractive.

Formula: Percentage of Water soluble extractive = $\frac{\text{Weight of residue}}{\text{Weight of drug}} \times 100$

Method [29-34]:

The method for determining the water soluble extractive follow the instructions of determination of alcohol soluble extractive only the difference and change to use chloroform water rather than ethanol.

- **Loss of drying:**

This procedure determines the amount of volatile matter or water present in the drug. For a stable shelf life, the moisture content should be below 2%. The moisture present in the product is also known as water activity. Higher water activity is directly proportional to microbial growth such as yeast, mould and bacteria. The LOD is determined by moisture balance equipped with an infra-red lamp. [35]

Method [24]:

After precisely weighing the medication (to within 0.01g), put about 10g of it in a tar-coated evaporating plate (without first drying it).

↓

Drugs are weighed after 5 hours of drying at 105°C in a tarred evaporating plate.

↓

Continue drying and weighing every hour until the difference in weigh between two subsequent measurements is no greater than 0.25 percent.

↓

When two subsequent weighs after drying for 30 minutes and cooling for 30 minutes in a desiccator show a variation of no more than 0.01g, the weight is considered constant.

- **Determination of pH:**

pH is playing the essential role in the standardization of Gutika where the drug can be affected on pH value increased or decreased. It also would show effect in of inconvenience in GIT or with the API or herbal drug. The pH value of a liquid can be determined potentiometrically by means of the glass electrode [36], a reference electrode and a pH meter [37] either of the digital or analogue type. [38]

Method [19-39]:

In a beaker, 5 g of the sample was dissolved with water and covered it with Aluminium foil.

↓

Allow to withstand in room temperature for 24 h.

↓

After 24 h, decanted the supernatant liquid and determined the pH using pH meter.

PHARMACEUTICAL PARAMETERS:

- **Hardness:**

Hardness [40] is the measure of the mechanical integrity of the tablets and Gutika. It is the force required to break the gutikas (tablets) in a specific plan. The tablets must have a specific amount of strength or hardness and resistance in order to be able to withstand mechanical shaking during manufacture, packaging and transport. Pfizer's tablet hardness tester [41] was used to independently test the randomly chosen tablets. The tablet was held vertically between the hardness tester's jaws. By gradually applying more pressure to the tablet's edge while pressing the jaws with the aid of a hand, the tablet eventually broke. The reading was taken, and each group's average hardness was determined independently. The reading is given in Newton's or kg/cm2 (N). [12]

- **Friability:**

One of the often used tests to assess a tablet's ability to withstand mechanical stresses evaluates how resistant it is to surface abrasion and chipping by spinning it in a rotating drum. The friability of the tablets is measured by the amount of weight loss following tumbling. The friability test is conducted in the Roche friability apparatus [42] by taking 20 tablets. This consists of a plastic drum that revolves at 25rpm, dropping the tablets through six inches in the friabilator to undergo shock, which is then operated for 100 revolutions. The tablets are reweighed. The tablet that lose less than 1.0% of the tablet weight are considered as acceptable. [12]

- **Weight variation test:**

The weight variation test performed with the gutika where the desired amount of gutika in numbers are taken and weight variation test is performed to determine whether there is any variation in gutika (tablets) if its variation more than desired limit which is 5% should not cross. Weighed 20 tablets and then its average weight is calculated. Values are compared with the standard. [44-45]

Methods:

20pills were chosen at random and each one was weighed using a Shimadzu electronic analytical balance. [43]

↓

Average weight was determined, and the following formula used to determine the percentage of variance.

↓

Individual weights of two tablets should not deviate from the average weight by more than 5%, and none should deviate by more than 10%, per USP guidelines. [40]

- **Disintegration time:**

Disintegration [46] is defined as that state in which no residue of the tablet remains on the screen of apparatus. This test will determine whether the tablet disintegrates within a specified (prescribed) time when it is placed in liquid medium under the controlled prescribed experimental conditions.

Method:

The tank of the disintegration apparatus [47] was filled with distilled water up to the mark.

↓

750ml of distilled water in each of the 1000ml beaker is taken.

↓

The timer of the instruments was set for 60 minutes.

↓

The temperature of water in beakers to 37°C was maintained.

↓

1 tablet was introduced into each tube added a disk to each tube. The assembly was suspended in the beaker containing water in it after that apparatus is operated.

↓

The time duration at which the tablets disintegrates was noted.

↓

As per set criteria by USP if 6 tablets are tested, all the 6 tablets should be disintegrated. [12]

CONCLUSION

The Standardization of Herbal Gutika involves ensuring consistent quality, safety, and efficacy. Standardization include establishing parameters for Raw materials, Manufacturing processes, and final product characteristics to meet regulatory and quality standards. It aims to provide consumers with reliable herbal products and support their safe use. This process enhances product reliability, regulatory compliance, and consumer confidence in the herbal remedy.

Clear understanding of the Standardization of herbal Gutika and objectives and the potential contributions of the study to the field of herbal medicine and pharmaceuticals of herbal Gutika.

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