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AN ANCIENT DOSAGE FORM "GUTIKA": A REVIEW

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ABSTRACT

Gutika is an ancient and ayurvedic dosage form and it is a result of kalkakalpana among the five key of ayurvedic sciences. They are very minute in size as compared to vati. According to Acharya Sharangdhargutika is a synonym of vatikalpana which called as pills in modern dosage form Gutika plays a very important role in the ayurvedic pharmacy. There are enumerable advantages of this dosage form like easy to administer, transportable, palatable, convenient for dispensing, consume less time in preparation. In the ancient text two types are mentioned Agnisadya and anagnisadya. Method of preparation is classified as per usage of ingredients. In modern, gutika is called as pills and spheroids means spheroids are agglomerates of fine powder or granules of mass medications and additionally excipients. They consist of little, free streaming, circular or semispherical strong units, commonly from 0.5 to 1.5 mm in measurement, and are proposed usually for oral organization. In ancient time gutika is made by hands but as time goes on the methods are also changed. In the place of hands so many modern equipment's are come in the market like ball mill, spheronizers are there. In this study, the development in the pharmaceutical procedures to formulate gutika/pills/spheroids is done.

Keywords: Gutika, spheroids, vati, Ayurveda

Introduction

Gutika is very good and important dosage form of ayurveda which is known as pills, spheroids in the modern era. So many ancient references are available in the context of gutika. These are made of at least one medication from plant, creature, mineral or metal birthplace. Gutika is described as vatikalpana. Because the procedures are same for the both but size variation is there so, gutika describes as vati. In the preparation of vatikalpana, plants or minerals are crushed with specific liquid medias prescribed in ancient literature and molded in the shape of pills or tablets. In ancient books called as Brhatrayi different vati plans are referred to in different setting. Regardless, Acharya

Sarngadhara was the chief person who referred to the point-by-point portrayal with respect to vatikalpana in a different chapter (Srikantamurty, 2001). Spheroids are more agreeable to film covering, because of their smooth, mathematically characterized surface. Spheroids containing various medications can be mixed and planned in a solitary measurement structure including those that display differential delivery rates for a similar medication. Spheroids can scatter in the gastrointestinal lot as discrete subunits, which guarantee a consistent pace of medication assimilation subsequently limiting pinnacle plasma variances. Bothering delivered by a high nearby convergence of a medication from a solitary unit measurement structure can be evaded.

Synonyms

The equivalent words of gutikais portrayed by Acharya Sharangdhara are:

Gutika	After the process of pounding or crushing material is molded into rounded shape is called as gutik. These are smaller than vati.
Vati	Vati is made looking like level roundabout mass and it is like tablet.
Varti	Varti is in the oval shape, long, and strong structure. It is made for the purpose to introduced into vagina, anal, eyes or penis.
Vataka	Tablet made into the large size rather than vati or varti is known as vataka.
Panda or Pindi	All the mixture is pounded with sarkara and made in the shape of large circular mass is known as panda/pindi.
Modaka	This is large in size rather than gutika, vati, vataka, varti or pindi. It is having weight of 20gm or 50gm.

Types of Gutika

AgnisandhyaVati	AnagnisandhyaVati
By its name the process of making gutika is define that fire is used to make this kind of gutika. In this guda or sugar or guggul is made lie leha (concentrated) on the fire then all the powders of drugs are added which become thick like glue. After that gutika are made into roundabout alive and well (Ambika data shastri, 1987).	By its name the process of making gutika is defined that no fire is used to make this kind of gutika. In this the powders of drugs are pounded with guggul or guda or with any prescribed liquid media to give suitable shape (Ambika data shastri, 1987).

General method of preparation for gutika

- To make good and effect gutika, firstly we have to dry and make fine powders individually.
- If, minerals are used, we have to convert into bhasam or sindur form, beside if notwithstanding referred to. In the case of parad and gandhak, we have to make kajjli first and all drugs are used as per the conditions maintained in literature. All the matrial placed into khalaw yantra and pounded or grounded with guggul or any prescribed liquid media as per the literature. In the condition where more than one liquid media is used for it, they are mainly utilized in the development.
- After that, when material is pounded properly and molded easily, prakshepdravyas are added and again placed for grounding process (CharakaSamhita, 1989).
- The way to decide the last step of the definition before making the gutika is that it should not to adhere to the fingers when rolled in the middle of two fingers. Tablets can be dried in the shade (CharakaSamhita, 1989).
- In the case where guda or sugar is alluded to, their paka should be made over a smooth fire and dropped from the stove. The powder of these decorations is added to that paka and energetically blended. Right when in all actuality warm, Vatakas should be mold and dried under the shade.
- For arrangement of the gutika, Acharya Sharngadhara has referred to the extent of trimmings that Sita should be taken on various occasions, Guda should be taken on different occasions, Guggulu and Madhu should taken identical sum and various liquids taken on different occasions more than that of churna used for gutika (CharakaSamhita, 1989).
- This method of preparation is given in the ancient literatures but as time goes method of preparation, synonyms, quality control parameters are developed in modern era. In modern gutika is known as pills, spheroids.
- Spheroids are agglomerates of fine powder or granules of mass medications as well as excipients. They comprise of little, free streaming, circular or semispherical strong units, ordinarily from 0.5 to 1.5 mm in width, and are proposed typically for oral organization (Gajdos, 1984, Kristensen and Schaefer, 1987).

Method of Preparation

- Numerous strategies have been accounted for the planning of spheroids, for example, compaction, drug layering, soften spherization, globulation, ball processing, pressure and expulsion spherization (Kader and Jalil, 1998, Zimm *et al.*, 1996).
- Among these, expulsion spherization is the most generally detailed (Reynolds, 1970).

- The primary goal of the spherization measures is to produce round medication centers that are thusly covered so as to adjust the medication discharge. It is additionally conceivable to plan spheroid centers that inalienably have explicit delivery profiles (Reynolds, 1970).
- This is accomplished by the joining of delivery modifiers into the centers that alter the medication discharge (Kader and Jalil, 1998, Zimm *et al.*, 1996).
- Polymers, for example, shellac and waxes are frequently used to impede the arrival of the medication (Reynolds, 1970).

Techniques to formulate spheroids

1. Pellet culture

- In this composition, cells are determined at the bottom of the cell by diffusion force (Achilli *et al.*, 2012, Maritan *et al.*, 2017).
- Cell-cell relationship is enhanced by the area of solitary cells at the bottom of the cell (Achilli *et al.*, 2012, Maritan *et al.*, 2017).
- To assemble the cell pellets, the supernatants dissected together, and the cell pellets are re-suspended in spherical reforming cell culture medium. In the wake of evaluating cell probes, cells in the medium are allocated to each well of a 96-well U support plate with cell disgusting surface (Achilli *et al.*, 2012, Maritan *et al.*, 2017).
- Pellet culture can be used to initiate the division of mesenchymal undivided alive organism. In exacting, a pellet culture system is appropriate for undifferentiated animal division by chondrogenesis because the relationship among nearest cells in a pellet culture look like the correspondence in pre-tendon development that occurs during microenvironment early-stage improvement (Zhang *et al.*, 2010, Bosnakovski *et al.*, 2004).
- In pellet culture, mesenchymal inducible organisms can change their morphological form in chondrocytes from fibroblastic to polygonal (Zhang *et al.*, 2010, Bosnakovski *et al.*, 2004).
- Thus, the pellet culture arrangement can be used to investigate the sine path of chondrogenesis and to assess the chondrogenic chance of inducible animals (Zhang *et al.*, 2010, Bosnakovski *et al.*, 2004).

2. Liquid overlay

- Fluid overlay culture strategy, besides static suspension culture, is called arrangements by intrusive with the grab of cells on non-deviant culture plates (Achilli *et al.*, 2012, Carlsson and Yuhua 1984, Costa *et al.*, 2018).
- A non-adhered culture layer is frequently made from agar or agarose gel. Agarose is an extremely competent material for inhibiting cell relationship and is Better than agar with respect to its non-adherent properties

(Achilli *et al.*, 2012, Carlsson and Yuhas, 1984, Costa *et al.*, 2018).

- As cell associations are discarded, cell-bound solid particles disperse and cover cells on the non-adherent surface (Achilli *et al.*, 2012, Carlsson and Yuhas, 1984, Costa *et al.*, 2018).
- Nevertheless, this biometric does not have the noted non-heritable qualities of agarose, disservices with respect to refined infection cells (Carvalho *et al.*, 2016, Carvalho *et al.*, 2017).
- Agarose has trouble in speaking with tumor cells and may not approve specific treatment lane related to the response of tumor cells to treatment measure (Carvalho *et al.*, 2016, Carvalho *et al.*, 2017).
- As of late, hyaluronic unhelpful may be a fitting substitute biometric that can override agarose. It has the aptitude to interface with exterior receptors of damaging growth cells during diseasemovement (Carvalho *et al.*, 2016, Carvalho *et al.*, 2017).
- It corrects the abduction of cell signals related to association growth, angiogenesis, persistence, and division, similarly as medical insurance (Carvalho *et al.*, 2016, Carvalho *et al.*, 2017).

3. Hanging Drop

- Hanging drop culture strategy grants single cells to add up to and make spheroids as dabs. By controlling the amount of degradation or thickness of the cell suspension, it is possible to control the spheroid size (Bartosh and Ylostalo, 2014).
- The story hanging drop group stage is set up to do viably outlining unequivocal size spheroids (Tung *et al.*, 2011).
- This process can shape a scattering round spheroids with a 10% to 15% classification coefficient, while the spheroid correction in non-adherent surface culture strategies has a 40% to 60% classification coefficient (Kelm *et al.*, 2003).
- An in general technique incorporates starting with a monolayer cell culture, after which the cells are set up as suspensions and diluted with the culture medium to attain best cell thickness (Achilli *et al.*, 2012, Timmins and Nielsen, 2007)
- In this way, the cell suspension is directed into wells of a more modest than typical plate with the help of a reasonable multi-step or multi-channel pipette (Achilli *et al.*, 2012, Timmins and Nielsen, 2007).
- A cover is attached to the little scope plate and entire small plate is exchanged topsy turvy (Achilli *et al.*, 2012, Timmins and Nielsen, 2007).
- Cell suspension drops connected at greater restraint then the normal palte will remain on the surface exchanged by the surface tension. In this method, spheroids are referred to as dabs due to the coordinated action of surface weight and gravitational force (Achilli *et al.*, 2012, Timmins and Nielsen, 2007).
- In addition to the flexible shape of a spheroid, the droplet drop structure has distinctive central focus. Expensive and master equipments is not required to outline spheroids for low degree tests. A monstrous remedy of spheroids can be rapidly created by multichannel piping and purchased by scratching fronts of culture dishes (Bartosh and Ylostalo, 2014).

- Likewise, mesenchymal youthful microorganisms refined by methods for hanging drop structure can release great measures of serious alleviating similarly as against tumorigenic factors (Bartosh *et al.*, 2010).

4. Spinner culture

- The spinner culture strategy reflects the technique in which telephone suspension are continuously mixed in spinner carafe bioreactor compartments. The resulting spheroid bioreactor is responsible for the compartment gauge (Lin and Chang, 2008, Kim, 2005).
- The position of the fluids and the mass in the compartments are influenced by the convection strength of the mixing strip, which is basic to draw round the spheroid. High mixing rates cause damage to spheroid cells (Achilli *et al.*, 2012).
- In any case, an extraordinary moderate progress of licensed spheroid cells to submerge the lower part of the compartment, while achieving the constraint of spheroid correction in the holder (Achilli *et al.*, 2012).
- In spite of adipogenesis, osteogenic detachment of mesenchymal deficient cells is additionally aided by the correction of osteogenic markers, for example, osteopen and osteocalcin in spinner framework (Frith *et al.*, 2010).

5. Rotating wall vessel

- Rotating divider vessel reproduces microgravity by consistent traffic circle revolution (Carpenedo, 2007)
- Because of reliable turn, cells are continually in a suspended state in the vessel (Manley and Lelkes, 2006)
- This microgravity may affects the interpretation of the quality mesenchymal undifferentiated living beings. In microgravity conditions, cells are deficient due to lack of chondrogenic and osteogenic quality, although adipogenic quality is subjected to verbalization (Sheyn *et al.*, 2016)
- This is in light of the fact that microgravity controls explanation intergin/Collagen I shaking pathway during Collagen I and osteoblastic ablation of osteoblastic marker quality (Meyers *et al.*, 2004).
- In addition, microgravity covers the development of force fibers and improves intracellular lipid aggregation (Meyers *et al.*, 2005).
- Nevertheless, degradation of osteogenic quality by microgravity can be observed. Validation of the RhoA protein alters these micro-gravitational effects and improves the elucidation of markers of osteoblastic division of mesenchymal non specificcells (Meyers *et al.*, 2005).
- Communication of chondrogenic characteristics is enhanced by the rule of p38 MAPK activation pathways (Zhao *et al.*, 2011).

6. Microfluidic culture

- This microfluid culture technique, in addition to lab-on-a-chip system, is used for applications, for example, single cell testing, innate measures, and prescription toxicity thinking (Ziolkowska *et al.*, 2010).
- This culture technique has microscopic projections as opposed to the in vivo microstructures. In addition, microfluidic devices enable microscopic control of the atmosphere reflecting the three-dimensional

environment in vivo. A features of the microfluidic functioning is that it facilitates various cycles including cell receiving, mixing, acknowledgment, and cell refining (Ziolkowska *et al.*, 2010).

- Another component is a massively high cell throughput for cell examination. Microfluidic controls use oxygen-using materials and correction factors that affect expansion (Ziolkowska *et al.*, 2010).
- This product name characteristic of microfluidics progress can reduce hypoxia, which is the inevitable burden of spheroid culture (Ziolkowska *et al.*, 2010).
- As of late made fluidic structures beat the limitations introduced by customary fluid system and, for example, models and cell reagents offer inclination for planning and cost degradation through more urgent requirement for reagents (Nie *et al.*, 2007)
- By and by, fluidic structure can express a specific assembly of the analysis mixes and supports stable viewing of living cells (Chung *et al.*, 2005, Gao *et al.*, 2008, Truong *et al.*, 2017).
- In addition, this arrangement can enhanced cell culture conditions for the repetition and division of young microorganisms, and can be used for tissue planning cycles, for instance, organ substitution and tissue recurrence, and prospect clinical preferences (Chung *et al.*, 2005, Gao *et al.*, 2008, Truong *et al.*, 2017).
- The presently used micro fluidics structure can be used to develop a time related co-refined system of microvascular networks using mesenchymal elements microorganisms. Co-culture system can similarly prompt course of action of a human microvascular network (Jeon *et al.*, 2014).

7. Magnetic levitation

- Attractive levitation-based refined uses alluring particles and fuse with hydrogels as demonstrated by the given conditions. In the appealing levitation structure, cells are mixed in with attractive atoms and

presented to interesting force during cell culture (Anil-Inevi *et al.*, 2018).

- This arrangement uses unfavorable magnetophoresis, which can simulate a weightlessness condition, as positive magnetophoresismay prevent weightlessness satisfaction (Anil-Inevi *et al.*, 2018).
- Because of alluring force, phones combined with attractive particles stay suspended beside gravity. This situationinitiates an approximate change of cell mass and increases the contact between cells, leading to cell accumulation (Kim *et al.*, 2013, Lewis *et al.*, 2017)
- In addition, this system can support multi-cell co-refined with stacks of different cell types (Kim *et al.*, 2013, Lewis *et al.*, 2017).
- When mesenchymal necessary microorganisms and attractive atoms are refined with collagen gel, nuclear camouflage occurs. Spheroid growth can be reproducible and reduce decay in spheroid community, in this way keeping up its stemness as a spheroid (Lewis *et al.*, 2017).
- In any case, a couple of social occasions have indicated that misleadingly controlled gravity can incite changes in cell structures and can achieve apoptosis (Meng, 2011, Sytkowski and Davis, 2001)

➤ Quality control parameters for gutika

In ancient time quality control parameters of gutika are very simple and few in numbers like organoleptic characterstaste, odour, size, shape color, texture, weight. But in modern there are so many quality control parameters like organoleptic characters, physical evaluation and physicochemical evaluation and heavy metal examination.

1. Organoleptic characters

Sr.No.	Characters	Characteristic
1	Color	Color of gutika is determined and match to the standards or match to the ancient literatures (Siddiqui A and Hakim MA, 1995).
2	Size	Size of gutika generally smaller thanvati. In this evaluation size is determined and matches to the standards (Siddiqui A and Hakim MA, 1995).
3	Shape	General shape of gutika is circular or spherical (Siddiqui A and Hakim MA, 1995).
4	Odour	Odour is determined and match to the standards or match to the ancient literatures (Siddiqui A and Hakim MA, 1995).
5	Texture	Texture should be hard solid so patient can store it for longer period (Siddiqui A and Hakim MA, 1995).
6	Weight	Weight should accurate. To check accuracy in weight, weight variation test is performed. Normal weight per tablet was determined from the aggregate weight. At that point the loads of individual tablets were contrasted with the normal load with decide weight variety (Siddiqui A and Hakim MA, 1995).

2. Physical and physicochemical evaluation

- **Hardness:** Hardness demonstrates the elasticity of a tablet. It was estimated utilizing a Monsanto hardness analyzer (Pharmacopeial standards for Aurvedic formulations, 1987).
- **Friability:** Twenty tablets were taken in a Roche Friabilator pivoting at a speed of 100 rpm for 10 min and rechecked after the treatment. Friability was communicated as % misfortune in weight. Twenty tablets were weighed independently and by and large. Normal weight per tablet was determined from the

aggregate weight. At that point the loads of individual tablets were contrasted with the normal load with decide weight variety (The Ayurvedic Pharmacopeia of India, 1999)

- **Disintegration:** Breaking down test is acted in a crate rack gathering supporting six glass containers of 3 inches in length, open at the top and held against a 10-work screen at the base finish of the bushel rack get together. One tablet was set in each cylinder and the get together is gone here and there at a recurrence of 28 to 30 cycles for every min at a temperature of 38°. For fluorescence test, 1 mg of powdered medications of every detailing were presented to bright light at frequency of 366 nm and sunshine while wet, in the wake of being treated with various reagents (The Ayurvedic Pharmacopeia of India, 1999).
- **Alcohol soluble extractive:** Five grams of air-dried and coarsely powdered medication is macerated with 100 ml of 70% ethanol in a shut funnel shaped flagon for 24 hours, shaken regularly during the initial 6 hours, and permitted to represent 18 hours. This was sifted quickly avoiding potential risk against loss of ethanol. 25 milliliters of the filtrate is vanished to dryness in a petri dish, dried at 105° C, and gauged. Level of liquor dissolvable extractive was determined regarding air-dried medication (The Ayurvedic Pharmacopeia of India, 1999).
- **Water soluble Extractive:** Five grams of broadly powdered air-dried medicine is macerated with 100 ml of water in shut tapered jar for 24 hours, shaken much of the time for the initial 6 hours and permitted to represent 18 hours. This is sifted through Whatman channel paper grade no.100. 25 milliliters of the filtrate is vanished to dryness in petri dish, dried at 105°C, and gauged. Level of water dissolvable extractive regarding air-dried material is determined (Mukharjee, 2008, Indian Herbal Pharmacopeia, 2002).
- **Ash Value:** Absolute debris Two grams of grounded air-dried material is precisely said something a formerly touched off and tared silica cauldron. The medication is steadily lighted by raising the temperature to 450°C until it was white. The example is cooled in a desiccator and gauged. The level of all out debris is determined regarding air-dried medication (Indian Herbal Pharmacopoeia, 2002, Mukharjee, 2008).
- **Moisture content:** The shade-dried medication was grounded in a blender processor. The powder went through #40 and held on #120. Precisely gauged 10 g of # 40/120 medication powder was kept in a tared dissipating dish. This was dried at 105°C for 5 hours in plate drier and gauged. The drying was proceeded and weighing was done at one-hour span until distinction between two progressive weighings relates to not more than 0.25 percent. Drying was proceeded until a steady weight was reached with two progressive weighings subsequent to drying for 30 minutes and cooling for 30 minutes in a desiccator was demonstrating not more than 0.01 g distinction (The Ayurvedic Pharmacopoeia of India, 1999).
- **Acid Insoluble Ash:** The debris was overflowed with 25 ml of 2 M hydrochloric corrosive for 5 minutes, the insoluble issue was gathered on a debris less channel

paper, washed with boiling water, lighted, cooled in a desiccator, and gauged. The level of corrosive insoluble debris was determined concerning the air-dried medication (Saurabh Singh *et al.*)

- **Heavy metal determination:** In this respective evaluation heavy metals like lead, chromium, copper, cadmium, nickel, zinc, cobalt, bismuth are evaluated with standard procedures and results are matched with standard values which are suitable for health (Singh *et al.*, 2019, Singh *et al.*, 2020).

➤ Some marketed gutika

1. Eladigutika
2. Nembadigutika
3. Bilwadigutika
4. Khadiradigutika
5. Makardhwajgutika
6. Shiva gutika
7. Prandagutika
8. Chitrakadigutika

Conclusion

Gutika is very important dosage form came from ancient era. Almost every ancient scholar of ayurveda gives the information regarding gutika and some describes gutika as a vati. In modern it is known as spheroids. From ancient time to days time so many developments are occur like development in the name, in ancient it is known as gutika and now spheroids, pills etc. in olden period methods are very easy like gutika made with hands but in modern spheroids, pills are made in different equipment's. And the big development is the procedures to make gutika/pills/spheroids. Evaluating parameters are also developing as per the studies. So, there are so many developments are occurring in the context of ancient formulation and modern formulations. Present review highlights the developmental stages and existences and importance of gutika along with comparison of existing modern dosage form like spheroids.

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