Pelletization technology in pharmaceutical formulation

K. Shyam Sundar Rao* V.V Mishra [1] ,Monalisha Nayak[2]
*** Research Scholar, 1,2-Asst Professor, Dept of Pharmaceutical Technology, Jeypore College of Pharmacy, Jeypore, Odisha, India**

An open access journal

Supporting Information:

Received: 19 November 2018
Accepted: 16 December 2018
Published: 16 January 2019

Competing Interests:
The authors have declared that no competing interests exist.

Corresponding author address

K. Shyam Sundar Rao*
* Research Scholar, Dept of Pharmaceutical Technology, Jeypore College of Pharmacy, Jeypore, Odisha, India

ABSTRACT

The present time is taken into account as an era of advancements in drug delivery systems.. Pelletization is one among the novel drug delivery technique that gives an efficient way to deliver the drug in modified pattern. These pelletized dosage forms have gained popularity significantly from then owing to their distinct benefits, like easy capsule filling due to higher flow properties of the superbly spherical pellets; enhancement of drug dissolution; ease of coating; sustained, controlled, or site-specific delivery of the drug from coated pellets; uniform packing; even distribution within the GI tract; and fewer GI irritation. Pelletization may be a novel drug delivery system; a method that converts fine powder particles into pellets.It is advantageous in providing site specific delivery of the drug. medication with unpleasant taste, poor bioavailability and short biological half-life is delivered with efficiency through pellets. different techniques are used to fabricate the pellets. the aim of this review is to discuss pellets, their characterizations, different techniques of pelletization and also the polymers with potential of being appropriate for pellets formulation.

Keywords: Pelletization,GI tract, potential

Introduction

Traditionally, pellets are represented as agglomerates that are created from different types of raw materials. Specifically, with regard to pharmaceutical sector, pellets is outlined as agglomerates of fine powders or granules made of drugs and pharmaceutical Excipients. Pellets range in size generally between 0.5 to 1.5mm and are largely preferred for oral route of drug delivery [1, 2].Pellets is defined as small, free flowing, spherical or semi-spherical solid units, typically from regarding 0.5 mm to 1.5 mm, and meant usually for oral administration, manufactured by the agglomerates of fine powders or granules of bulk medication and excipients using acceptable processing instrumentation. Pellets is prepared by several ways, the compaction and drug-layering being the most widely used today[3].

Pellets supply larger degree of flexibility throughout the look and development of oral indefinite quantity forms. they'll be divided into totally different dose strengths with none method changes and may be wont to deliver incompatible biologically active agents all at once or particles with different unleash profiles at same site} or at different site of gastrointestinal tract. Pellets are the multiple unit dosage forms which may be developed within the type of suspensions, capsules or disintegrating tablets.Multiple unit systems hold important benefits over single unit systems. they're less dependent on viscus evacuation when put next to single unit indefinite quantity forms. thanks to their, they withstand the pyloric sphincter simply that minimizes the put down and intra-subject variability in channel transit time. Pellets exhibit high loading capability of active ingredients while not manufacturing intensive massive particles. Pellets area unit less liable to dose dumping when put next to single unit systems. Pellets is coated simply due to their spherical form and low surface to volume ratio and thence no additional coating material is needed to fill the irregularities on the surface [1, 4.]

Criteria for Pellets

Regardless of that manufacturing method is used, pellets have to meet the subsequent requirements.

•They should be close to spherical and have a smooth surface; both considered optimum characteristics for ensuing film coating.

•The particle size range should be as narrow as possible. The optimum size of pellets for pharmaceutical use is considered to be between 600 and 1000mm.

•The pellets should contain as much as attainable of the active ingredient to keep the scale of the final dosage kind among reasonable limits. they must be close to spherical and have a smooth surface; each considered optimum characteristics for subsequent film coating.

•The particle size range ought to be as narrow as attainable. The optimum size of pellets for pharmaceutical use is taken into account to be between 600 and 1000mm.

•Regardless of that producing method is employed, pellets need to meet the subsequent necessities. they must be close to spherical and have a sleek surface; each thought of optimum characteristics for ensuant film coating.

•The particle size vary ought to be as slender as attainable. The optimum size of pellets for pharmaceutical use is taken into account to be between 600 and 1000mm.

•The pellets ought to contain the maximum amount as potential of the active ingredient to keep the size of the ultimate dosage kind inside reasonable limits. they should be close to spherical and have a smooth surface; each considered optimum characteristics for subsequent film coating.

Significance of Pellets

Pellets may have varied applications in varied industries. It just needs an innovative bend to use it to derive maximum gain. the smooth surface & the uniform size of the pellets enable uniform coating not just for every pellet however also from batch to batch.

Highlighted below are a number of the few instances wherever smooth surfaced uniform pellets are being with success used:

1. Improved look of the merchandise. Coating of pellets is through with different drugs to alter a controlled unleash rate.

2. just in case of immediate release product larger surface area of pellets allows higher distribution.

3. chemically incompatible product is formed into pellets & delivered in a single dose by encapsulating them.

4. in the chemical industries it's used to avoid powder dusting.

5. Varied applications are possible within the pellet kind. Eg: sustained release.

6. Pellets guarantee improved flow properties, and adaptability in formulation development and manufacture.

7. The coating material could also be coloured with a dye material so the beads of various coating thickness are darker in color and distinguishable from those having fewer coats.

8. The beads or granules of various thickness of coatings are blended within the desired proportions to convey the specified impact.

9. The thickness of the coat on the pellets dictates the rate at that the drug/ contents are discharged from the coated particles .A smooth surface of the pellets & uniform coating thickness for every pellet.

10. By choosing the correct formulation, process conditions and process equipment it's possible to achieve smooth surfaced & uniform pellets.

Advantages of Pellatization[5]:

Multiple unit systems hold significant advantages over single unit systems.

- They are less dependent on gastric emptying when put next to single unit dosage forms. thanks to their, they withstand the pyloric sphincter simply that minimizes the put down and intra-subject variability in gastrointestinal transit time.
- Pellets exhibit high loading capacity of active ingredients without producing extensive large particles.
- Pellets is coated simply thanks to their spherical form and low surface to volume quantitative relation and thence no further coating material is needed to fill the irregularities on the surface.
- Improved look of the merchandise and therefore the core is pharmaceutically elegant.
- Pellatization offers flexibility in indefinite quantity kind style and development.
- Pellets are less liable to dose selling.
- It reduces localized concentration of irritating medication.
- It improves safety and effectuality of a drug.
- Pellets supply reduced variation in gastric emptying rate and transit time.
- Pellets disperse freely in G.I.T. and invariably maximize drug absorption and additionally reduce peak plasma fluctuation.
- Pellets guarantee improved flow properties in formulation development

Theory of Pellet Formation

It's necessary to understand the basic mechanisms of granule formation and growth. different theories are postulated associated with the mechanism of formation and growth of pellets. as the typical granulation, the foremost completely studied, most classified Pellatization method, that involves a rotating drum, a pan or a disc, has been divided into 3 consecutive regions: nucleation, transition and ball growth. However, supported the experiments on the mechanism of pellet formation and growth, the subsequent steps were proposed: nucleation, coalescence, layering and abrasion transfer.

Methods of Preparing Pellets

Compaction and drug layering are the foremost wide used Pellatization techniques in pharmaceutical business. Of the compaction techniques, extrusion and Spheronization is that the hottest methodology. Recently, however, soften Pellatization has been used oftentimes in creating compaction pellets employing a totally different style of instrumentation, e.g. a high-shear mixer. different Pellatization ways like globulation, balling and Compression also are employed in development of pharmaceutical pellets though in an exceedingly restricted scale.

Powder layering:

Powder layering involves the deposition of ordered layers of dry powders of medication and excipients on preformed nuclei or cores with the assistance of binding liquids. As powder layering involves cooccurring application of binding agents and dry powders, thence it needs specialised equipments like spheronizer. the first demand during this method is that the product container ought to be solid walls with no perforation to avoid powder lose at a lower place the product chute before the powder is picked off by the wet mass of pellets that's being layered.

Solution / suspension layering:

Solution/suspension layering involves the deposition of ordered layers of answer or suspensions of drug substances and binder over the starter/non-pareil seeds, that is associate inert material or crystals/granules of an equivalent drug. actually the coating method involved generally is applicable to answer or suspension layering technology. Consequently typical coating pans, fluidized beds, centrifugal granulators, wurster coaters are used in turn to manufacture pellets by this methodology. The potency of the method and therefore the quality of the pellets produced are partially associated with the kind of equipment used.

Pelletization by extrusion and spheronization:

The process involves first making extrudes from the powder material and then converting the extrudes into beads using the spheronizer. The powder material could be any kind of powder (drug powder, ayurvedic powder, food ingredient powder, detergent powder, nuclear powder etc). Beads as fine as 0.6mm can also be made.

Table: 1.Excipients used in Pellatization

Filler	MCC, starch, sucrose, lactose, mannitol
Binder	Gelatin, HPC, HPMC, MC, PVP, sucrose, starch
Lubricant	Calcium stearate, glycerin, PEG, Mg. Stearate
Separating agent	Kaolin, talc, silicon dioxide
Disintegrant	Alginates, Croscarmellose sodium
pH adjuster	Citrate, phosphate, meglumine.
Surfactant	Polysorbate, SLS
Spheronization enhancer	MCC , sodium CMC
Glidants	Talc, starch, Mg stearate.
Release modifier	Ethyl cellulose, carnauba wax, shellac.

Other Pelletization Methods

Other Pellatization methods like globulation, cryopellatization, balling and compression also are used, though a limited scale within the preparation of pharmaceutical pellets.

Globulation or droplet formation consists 2 related processes, spray drying and spray congealing.

Spray drying: It's the method within which drugs in the suspension or solution without excipients are sprayed in to a hot stream to produce dry and a lot of spherical particles. This method is usually used for improving the dissolution rates; thus bioavailability of poorly soluble drugs.

Spray congealing:

It is the method within which a drug is allowed to soften, disperse or dissolve in hot melts of gums, waxes or fatty acids, associated is sprayed into an air chamber wherever the temperature is kept below the melting point of the formulation components, to produce spherical congealed pellets. both immediate and controlled release pellets is prepared during this process depending on the physiochemical properties of the ingredients and other formulation variables.

Cryopellatization:

It's a method in which the liquid formulation is converted in to solid spherical particles or pellets within the presence of liquid nitrogen as fixing medium. the form depends up on the distance the droplet travel before contacting liquid nitrogen.

Compression:

It's one type of compaction technique for preparing pellets. Compacting mixtures or blends of active ingredients and excipients under pressure prepare pellets of definite sizes and shapes. The formulation and process variables dominant the standard of pellets ready are just like those utilized in tablets manufacturing.

Balling:

It's the pellatization method within which pellets are shaped by

Table 2: Parameters Used in Bottom Spray Equipment

Inlet temperature	38-42ºC
Product temperature	32-36ºC
Exhaust temperature	32-38ºC
Spray rate	8-12mg/min
Peristaltic pump	12-18 rpm

Conclusion:

This temporary review on the pelletization technology herewith concludes with a note that they're thought-about as a most promising drug delivery system nowadays that is catching up with the pace of speed to own a high existence within the pharmaceutical company world. this technique gain additional quality due to their simple movability improved patience compliance and easy administration and adaptability within the fabrication as tablets or capsules or packed merely as one dose packlets. they will be applied by each oral and buccal routes. This technology is growing in fast pace difficult most of the prescribed drugs firms to develop pelletized dosage forms for wide range of active pharmaceuticals ingredients.

References:

1. R., Damle. A.V: Controlled release pellets of nitrofurantoin. Ind. J. Pharm. Sci.; 1996; *5*, 179-85.
2. L., Liew. C.V., Heng. P.W.S: Wet spheronization by rotary processing-a multistage single-pot process for producing spheroids. Drug Dev. Ind. Pharm.; 2004; *30*, 111-9.
3. A., Ashokraj. Y., Panchagnula.R: Multiunit matrix based particulate systems (MUMPS) for controlled delivery of nifedipine. Formulation development using extrusion-spheronization and *in vitro* evaluation. Pharm. Tech.; 2004; *28*, 62-71.
4. H., Nielsen.G: Controlled Release multiple units and single unit doses. Drug. Dev. Ind. Pharm.; 1978; *4*, 53-7.
5. S., Chambliss. W.G., Wyandt. C.M: A novel freeze pelletization technique for preparing matrix pellets. Pharm. Tech.; 2004; *28*, 98-108.

6. Celik, M: In Multiparticulate oral drug delivery, Marcel Dekker.; New York; 1994; pp.181.
7. Celine V. Liew., Siarg Meng Chua., Paul W.S.Heg. : Elucitation of spheroid formation with and without the extrusion step; AAPS pharma. Sci. tech.; (2007); 09.
8. Ghebre-sellassie. I: Pharmaceutical Pelletization Technology marcle dekker inc.; NewYork USA; 1989; 1-13.
9. Paul Wan Sia Heng.: Pelletization and Pelltets coating 15th international symposium on microencapsulation. Parma Italy; Sep 18-21-(2005).
10. Raymond C. Rowe., Peter York., Elizabeth A. Colbourn, Stephen J.Roskilly. Size and distribution on capsule filling- A preliminary evaluation of three-dimensional computer simulation using a Monte –Carlo technique; J. Pharm. 300; (2005); 32-37.
11. Raymond C., Amazon.C. *et al*.: Hand book of pharmaceutical Excipient; (Ed.-4th), 487-488,.
12. Pernilla Navsten., Per Borgquist., Anders Axelson., Wallenberg L. Reine., J. Pharm. 290; (2005); 109-120.
13. Abbaspour M.R., Sadeghi F., Afrasiabi Garekani H.: Preparation and characterization of ibuprofen pellets based on Eudragit RS PO and RL PO or their combination; J.Pharm. 303; (2005); 88-94.
14. Harun A.R, Rashid. J, Heinamaki. O, Antikaiman and J. Yliruusi.: Centrifugal granulating process for preparing Drug layer pellets based on micro cryatalline cellulose Beads; April (2001).
15. MJ. Pellet manufacture for controlled release; Manuf. Chem; June 1985, 56-59.