

**Multi unit drug delivery system – A brief review of pelletization technique**

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**\*Corresponding author e-mail:** [anwarkhanphar1@gmail.com](mailto:anwarkhanphar1@gmail.com)**ABSTRACT**

At present time pharmaceutical research and development showing its interest on drug delivery. Which enhances therapeutic action while minimizing side effect. Use of multi-particulate is the gift of that research which achieve delayed or controlled release with low risk of dose dumping, flexibility of blending to attain different release pattern as well as reproducible and short gastric residence time. Pelletization is a novel approach for the formation of spherical beads or pellets from fine powder or blend in order to develop site specific drug delivery system. Different techniques of pelletization such as suspension/solution layering, extrusion and spheronisation, cryopelletization etc. can be used for the formation of multi particulate drug delivery system. In order to provide extended or delayed release formulation, thus extending the frontier of future pharmaceutical development.

**Keywords:** Multi particulate drug delivery system, pelletization, and dose dumping.**INTRODUCTION**

Multunit drug delivery system (mudds)- the evolution of concept of multi-unit dosage form was introduced in early 1950s these are mainly oral solid dosage form that consist of multiplicity of small discrete subunit of diameter (0.5-2 mm ) and each exhibit some desired characteristic if necessary . they offers numerous advantages over single unit dosage form ex- reduce chances of dose dumping, greater bioavailability as the surface area increases and size decreases, less dependency on gastric emptying resulting in less inter and intra- subject variability in gastro intestinal transit time and less likely to cause local irritation that's why more emphasis is being laid on the development of multiparticulate drug delivery system<sup>1</sup>.

Multiparticulate drug delivery system may increases drug safety as the film of enteric coating on single unit or monolithic is damaged it will release whole drug in stomach and will cause ulceration or irritation and will cause loss of complete dose or dose dumping but equally if the damage of film coating of multi-unit dosage form occur it will release drug of that

small subunit and affect the release behaviour of that specific sub unit which represent small part of total dose<sup>2</sup>.

**PELLETIZATION:**<sup>3,4</sup>

Pelletization is a novel drug delivery system; a technique which converts fine powder particles into pellets. These oral multiparticulate drug-delivery systems offer biopharmaceutical advantages with respect to predictable and even distribution and transportation in the gastro-intestinal tract. Pelletization can be referred as the conversion of fine powder, granules of drug and excipient by the means of agglomeration to small, free flowing spherical subunit referred as pellets. Which are smaller in size (0.5-1.5mm) and intended mostly for oral administration. It has been used to describe a variety of systematically produced, geometrically defined agglomerate obtained from different starting material utilizing different processing condition.

**Requirements of pellets:**

- Pellets should be of spherical shape and the surface should be smooth so that desired uniform film coating can be done.

- Particle size of pellets should be in range 0.5-1.5 mm.

#### **Advantages of multiparticulate drug delivery system:**

1. Gastric emptying is faster as the particles small in size and passes even if pylorus is closed.
2. Avoidance of dose dumping.
3. Better distributed and less likely to cause local irritation.
4. Increased bioavailability as the surface area increases.
5. Pellets are recommended for paediatrics and geriatric patient with difficulty in swallowing and dysphagia problem.
6. Increased in flow property (smooth surface).
7. Disperse freely in GIT and increase absorption of active drug.
8. Incompatible drug and drugs with different property can be processed individually and later combined to form a modified drug delivery.

**BALLING:** Also known as spherical agglomeration is apelletisation technique in which finely divided particle or powder upon addition of an appropriate quantity of liquid are converted to spherical particle by continuous rolling or tumbling action. They can be done either by adding an appropriate amount of liquid into powder called liquid induced agglomeration or subjecting it to high temperature called melt induced agglomeration. Round curvature pans, horizontal drum mixer, and rotatory fluid – bed granulator can be used for the production of spherical pellets by balling.

**COMPACTION:** Compaction is a form of pressure agglomeration in which mixture or blends of drug and excipient are forced together under pressure to generate pellets of defined shape and size. Interparticle contact increases as the particle approaches close enough and the bonding forces like Vander-wall forces, electrostatic forces is applied to make adsorption layer effective.

**EXTRUSION AND SPHERONISATION:** <sup>6, 8</sup> it is a most commonly used technique in pharmaceutical industry to make uniform sized spheroids. Development of this pelletization technique was started in 1960s.

It is a multi-step compaction process comprising of following step-

- **DRY MIXING:** formation of blend by mixing ingredient to get homogeneous powder
- **WET MASSING:** In this process powder are sufficiently wet to form a plastic mass (

commonly used granulator are planetary mixer ,sigma blade mixer or high shear mixer)

- **EXTRUSION:** it is a compaction process where pressure is applied to wet mass until it passes through the calibrated openings of extruder to form rod shaped particle of uniform diameter spaghetti-like extrudate.
- **SPHERONISATION STAGE:** This process is used to give a proper spheroid shape with narrow size distribution to the extrude (rod shaped particle) formed previously instrument called spheronizer.
- **DRYING:** Drying of spheroid is an important step to achieve desired final moisture content (tray dryer or fluidised bed dryer )
- **SCREENING:** To achieve desired size distribution.

**EXTRUSION:** is a process comprising of applying pressure to a wet metered mass until it passes through a calibrated openings of a screen or die plate of extruder and further shaped into small extrudate segment. Amount of granulating fluid and uniform dispersion of fluid plays an important role in preparation of wet mass because optimum cohesiveness and plasticity is required which affect the final mass because excessive plasticity may lead to extrudate which stick to each other .final size of spheroid depend on the diameter of opening in the extruder screen.

**SPHERONISATION:** refers to formation of spherical particle from the small rod produced by extrusion .it is rotated at higher speed by friction plate that break the rod shaped particle into smaller particle and round them to form sphere.

#### **SOLUTION/ SUSPENSION LAYERING:** <sup>9, 10</sup>

Drug particles and excipient are suspended or disperse in liquid medium. And a growth of pellets involve deposition of successive layer of solution and/ or suspension of drug and binder on existing nuclei which may be either (inert seed or non pariel seeds, crystal or granules) this process can be done for controlled release, extended release or delayed release .Equipment employed for this kind of coating consist of modified conventional coating pans (perforated pans) and fluid bed granulator wrester technique is widely used. During drying liquid evaporates and the dissolved substance crystallizes out in suspension layering, particles have low solubility and are bounded by solid bridges (higher concentration of binder is required).

**POWDER LAYERING:**<sup>11</sup> The process is similar to the solution/suspension layering which involves the successive layering of dry powder of drug or excipient or both on solid nuclei or inert cores with the help of binding liquid. Most commonly used equipment is conventional coating pans. Initially nonpareil seeds or inert core is charged in the rotating coating pans they are wetted by spraying an adhesive solution as the wet tacky seeds reach the front end of the pan the powder added in the vortex adheres to them and proceed until it is dried.

**GLOBULATION:** Globules or droplet include two techniques of pelletization:

- **SPRAY CONGEALING** ( Spray chilling process ) in this technique the drug is allowed to melt , suspend or dissolve in hot melt of gum , fatty acid ,waxes and other solid then sprayed into air or steam chamber with temperature below the melting point of formulation components under appropriate processing condition to obtain spherical congealed pellets.
- **SPRAY DRYING:** Technique involves solution and/or suspension of drug with or without excipient into hot air stream to generate dry and highly spheroid shaped particle. This technique is used for development of delayed or extended release

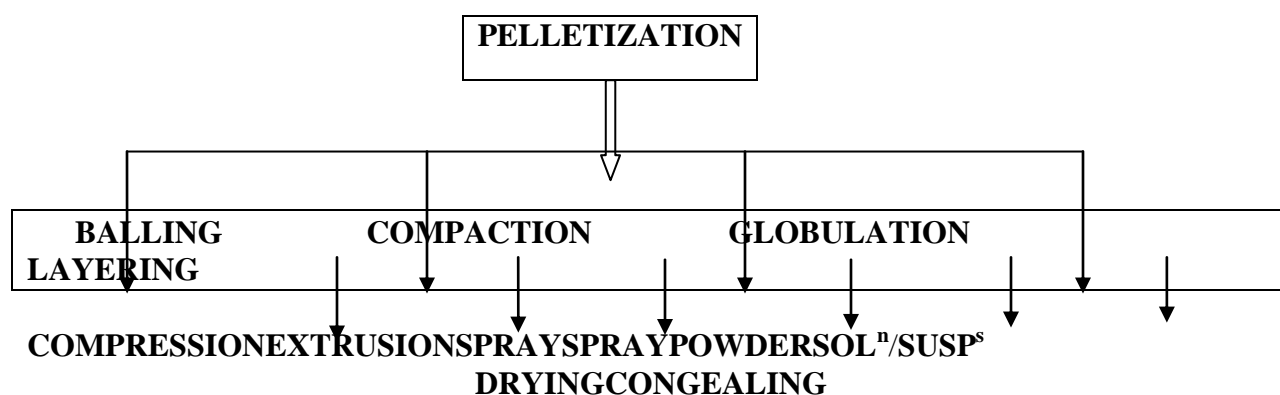
to improve dissolution rate and hence bioavailability of poorly soluble drug of BCS class IV<sup>th</sup>.

**CRYOPELLETIZATION:**<sup>12</sup> Cryopelletization is a process where the conversion of liquid droplet into solid spherical particle or pellets occur using liquid nitrogen as the fixing medium. The process involves sudden and uniform freezing of the processed material owing to the rapid heat transfer that occurs between the droplets and liquid nitrogen. The quantity of liquid nitrogen required for manufacturing a given quantity depends on the solid content and temperature of the solution or suspension being processed.

## CONCLUSION

Development of pelletization has acquired the market of novel drug delivery involving both the controlled as well as immediate release. Due to its simple design, high efficiency of producing spherical pellets, flexibility and robustness. It has acquired a special place in pharmaceutical industry. It can be concluded that due to their good technological and biopharmaceutical advantages, pelletization has gained an importance in modern pharmaceutical science.

**FIG NO: 1 SCHEMATIC PRESENTATION OF VARIOUS TECHNIQUES OF PELLETTIZATION<sup>5</sup>**



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