Pharmaceutical Pellets

Dr. Beena Gidwani
Associate Professor
CIP, Raipur
Email – beenagidwani@gmail.com

Pellets - Definition

What is pellet?

Small free flowing spherical units ranging in size, prepared by agglomeration of fine powders called pellets.

- Their size and shape allow their administration as injections and also for oral drug delivery.
- Pellets range in size, typically, between 0.5 – 1.5 mm, though other sizes could be prepared.

Introduction:

- Pelletization can be defined as an **agglomeration** process (**size-enlargement process**) that converts fine powders or particles of bulk drugs and excipients of bulk drug into small, free flowing, more or less spherical units, called pellets.
- This technique enables the formation of spherical beads or pellets with a mean diameter usually ranging from 0.5 to 2.0 mm.
- Pellets have free-flowing properties

Pelletization vs. granulation.

- The general terms "granulation" and "Pelletization" are sometimes used synonymously and no clear distinction is made between them.
- generally if agglomerates size distribution within the range of 0.1 to 2.0 mm and a high porosity (about 20-50%), this process may be called **granulation**.

•But if the agglomerates have a narrow size range, usually with mean size from 0.5 to 2.0mm and have a low porosity (about 10%) with free flowing properties then it is called **Pelletization**.

Advantages/Applications of Pellets

- **Improved aesthetic appearance of the product.**
- **Coating of drug pellets with different polymers to achieve controlled release rate of drugs.**
- **For immediate release products large surface area of the pellets enables better distribution, dissolution and absorption.**
- **Chemically incompatible products can be formulated into pellets and delivered into single dosage form by encapsulating them.**
- **Pellets ensures improved flow properties and flexibility in formulation, development , and manufacture.**
- **Bitter taste masking**
- **Suitable for delivery of Chemically incompatible products**
- **Prevention of segregation of co-agglomerated**
- **Improvement of the process safety, as fine powders can cause dust explosions and the respiration of fines can cause health problems**
- **The defined shape and weight improves the appearance of the product**

Disadvantages of pellets

- Often pellets can not be pressed into tablets because they are too rigid. In that case, pellets have to be encapsulated into capsules.
- The production of pellets is often an expensive process and / or requires highly specialized equipment.
- The control of the production process is difficult (e.g. the amount of water to be added is critical for the quality of the pellets and overwetting can occur very easily).

Route of administration

Pellets either filled in hard gelatin capsules or compressed into disintegrating tablets. When pellets are intended for oral use, they quickly liberate their contents in the stomach and gets distributed throughout the gastrointestinal tract and produce maximal drug absorption and also minimize local irritation.

Formulation Aids for Pellets

1. **FILLERS :** add bulk to the product
   are water soluble/insoluble substances
   selection depends on physical property of drug, desired dose and method of preparation.

Examples – MCC, starch, sucrose, lactose.

2. **BINDERS :** used to bind
   provide integrity to product
   selection depends on solubility and physical property of drug .

Examples – HPMC, Gelatin, Methyl cellulose, starch, sucrose, lactose.

3. **LUBRICANT :** used to reduce friction between particles and surface of equipment
   maintain consistency of pellets

Examples – Glycerin, PEG, magnesium stearate, calcium stearate.

4. **SEPERATING AGENT :** to prevent attraction between particles of pellets
   prevent charge development in particles

Examples – Talc, Silicon dioxide, kaolin

Formulation Aids for Pellets

5. DISINTEGRATING AGENT : to promote disintegration in g.i.t.
required in small quantity
Examples – Alginate.

6. SURFACTANT: improve wettability
lowers the interfacial tension between solvent and drug particles .
Examples – SLS, polysorbate.

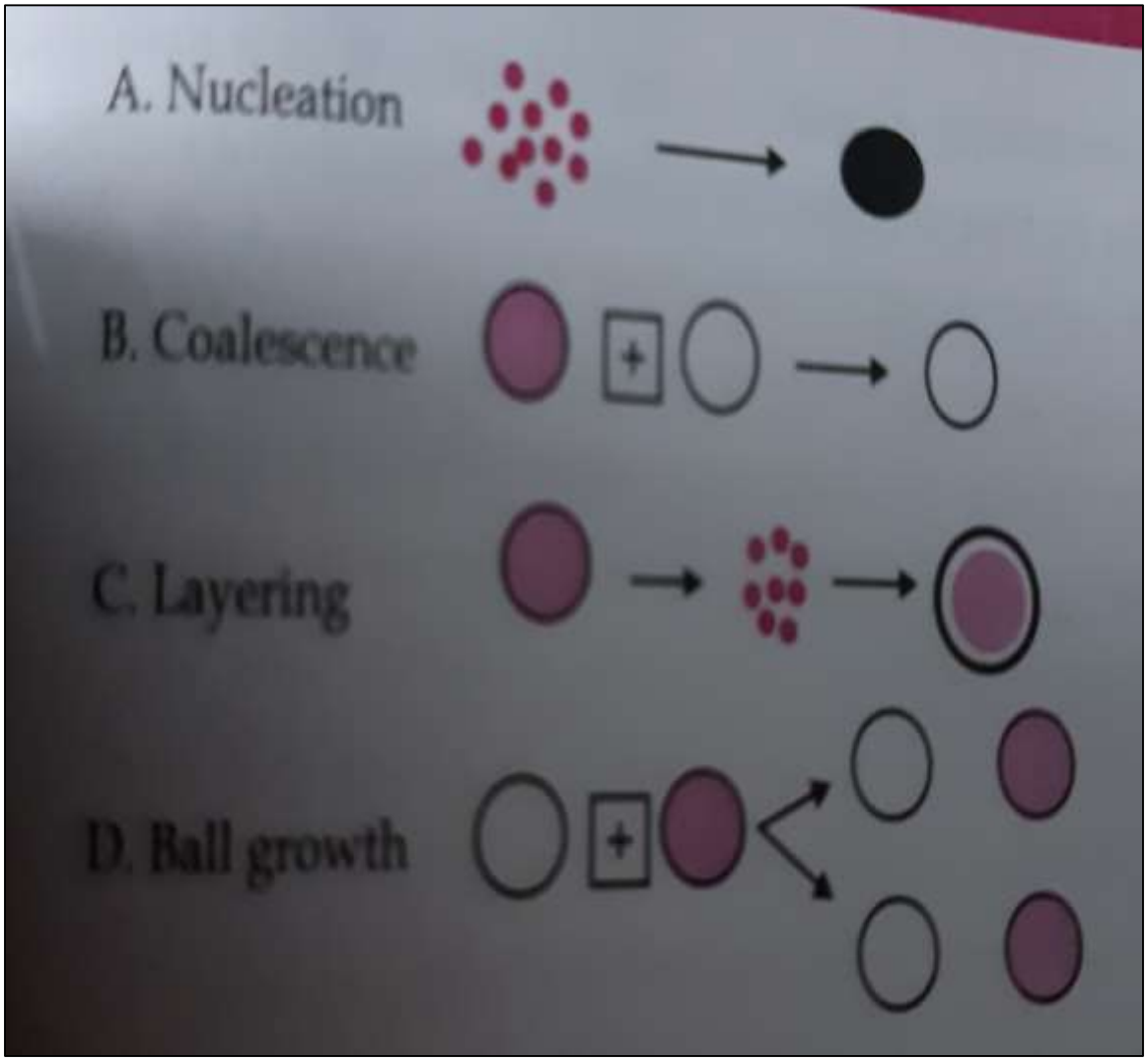
7. pH Adjuster : maintain pH for absorption in g.i.t
Examples – citrate , phosphate .

8. SPHERONIZATION ENHANCER : impart plasticity to pellets
provide strength
Maintain integrity
Examples – MCC (Micro crystalline cellulose), sodium carboxy methyl cellulose.

9. GLIDANT : reduce friction between die wall and material matrix during compression or ejection
Examples – Talc, starch, Magnesium stearate .

10. Miscellaneous agents : coloring, flavoring, sweetning, preservatives, release modifier (Ethyl cellulose, shellac, carnuba Wax).

Mechanism of pellet formation and growth



DRUG RELEASE FROM PELLETS

- Diffusion
- Erosion
- Osmosis

Types of pellets

Implant (pellets)

Example contraceptive

Orally Multiple-Unit Pellet System (MUPS)

Methods of preparation (pelletization)

Agitation

balling

Drug layering

I. Powder

II. Liquid

Suspension \solution

Globulation

I. Spray drying

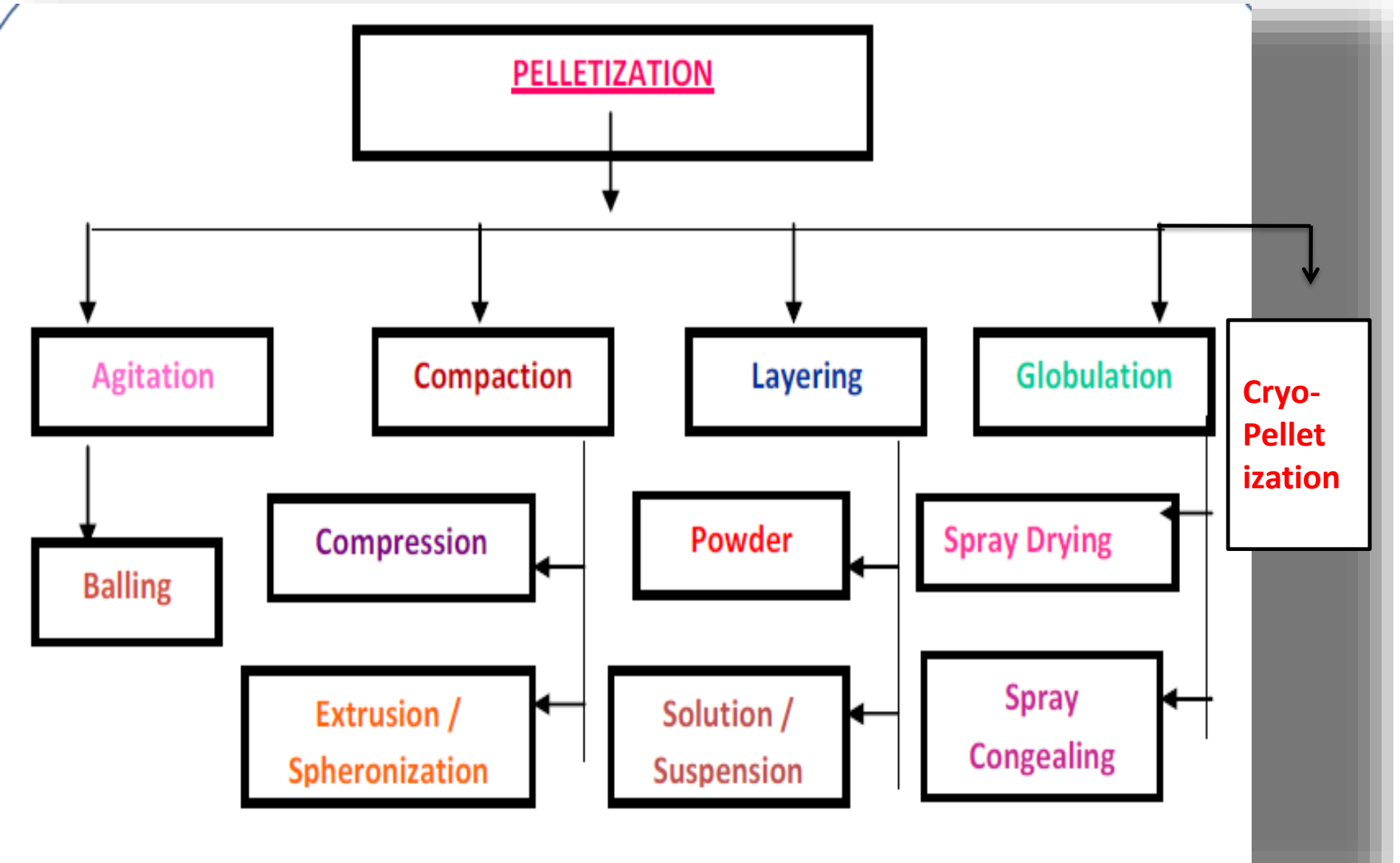
II. Spray congealing

Compaction

I. Extrusion-spheronization

II. Compression

Methods of pelletization



1.Agitation (balling)

It is known as spherical agglomeration .In this method, particles are converted to spherical pellets by continuous rolling or tumbling blender using a rotating drum or pan.

Now this method is limited.

Types

- **Liquid- induced agglomeration**
- **Melt -induced agglomeration**

Compaction

Compression

- In this process mixtures of active ingredients and excipients are compacted under pressure to generate pellets of defined shape and size. During compression at high pressure, particles of a packed mass are forced against each other so that elastic and plastic deformation can take place and create strong interparticle contact.

Leads to formation of capsules
Compacted by pressure

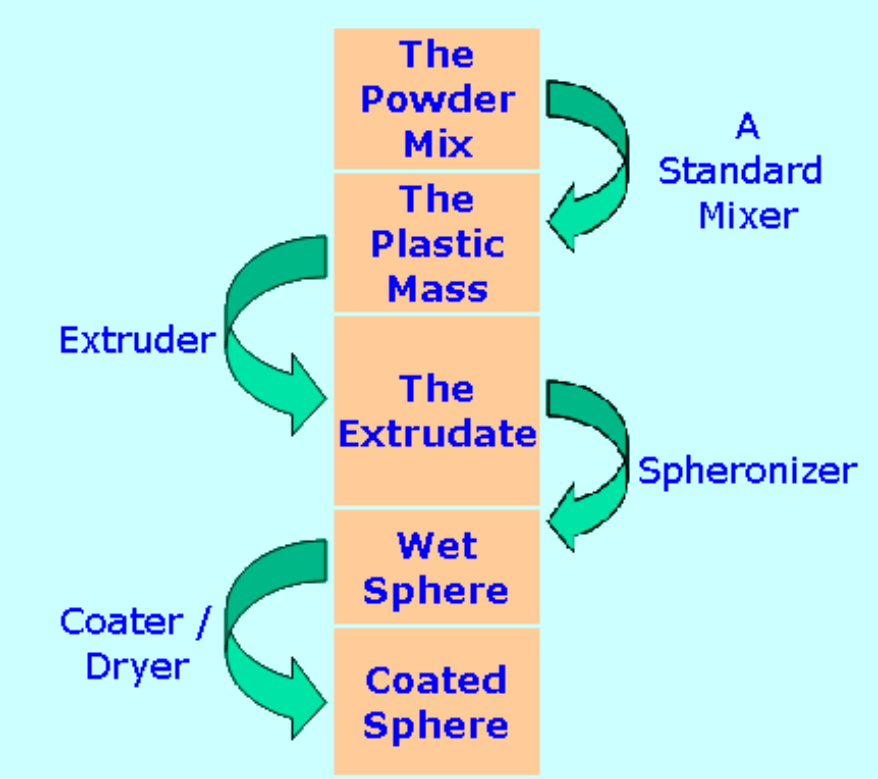
Extrusion-spheronization

In this process, the powder is formed into a wet mass, which is forced through restricted area (extrusion) to form strands of extrudate that are broken into short lengths and rounded by placement on a rotating plate with in a cylinder. The resulting spherical granules or pellets are of uniform shape, size and density.

STEPS

1. **DRY MIXING**
2. **WET MASSING**
3. **EXTRUSION**
4. **SPHERONIZATION**
5. **DRYING**
6. **SCREENING**

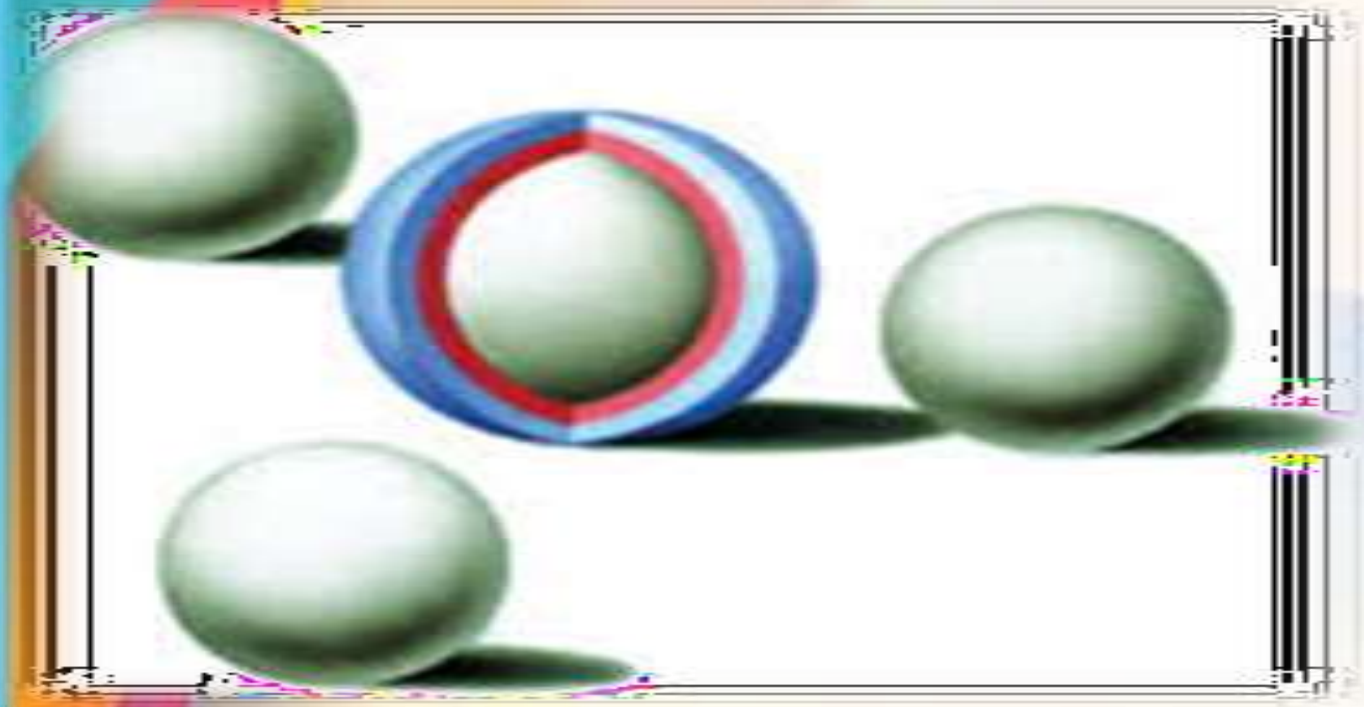
Extrusion – spheronization



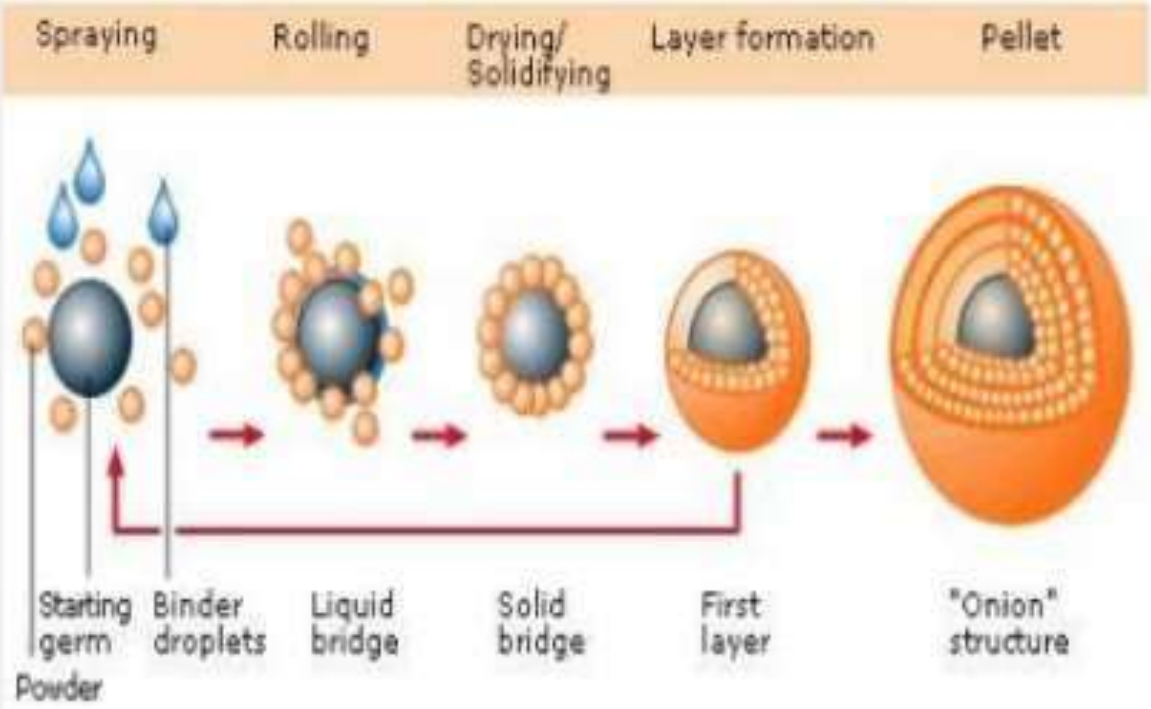
Spheronization is a process of forming a spherical particles from different rod shapes , by extrusion , that has a diameter ranging from 0.5 to 1 mm .

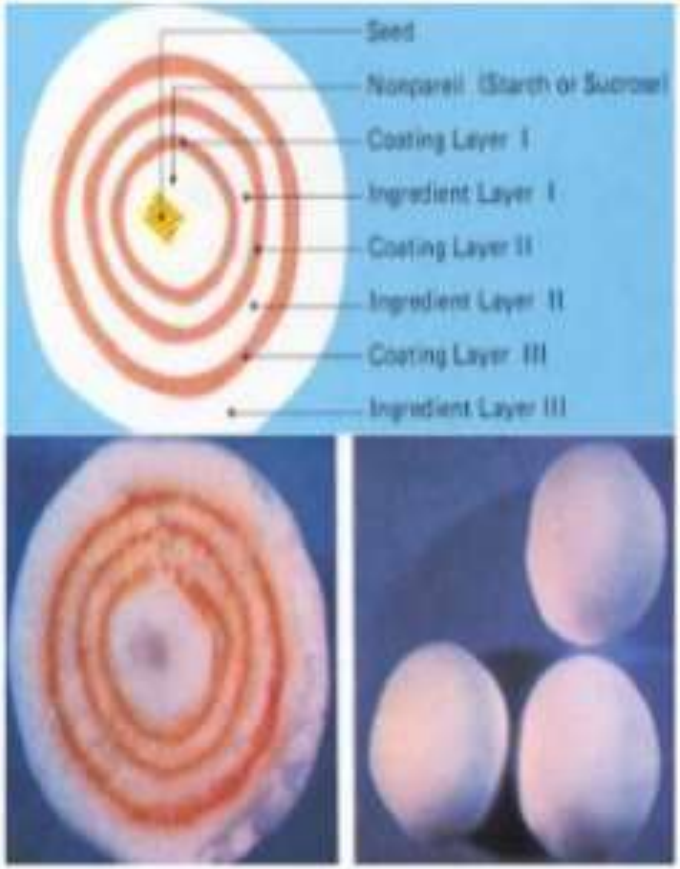
Layering

Layering involves the deposition of successive layers of dry powder or liquid droplets of drug and binding into inert seed.

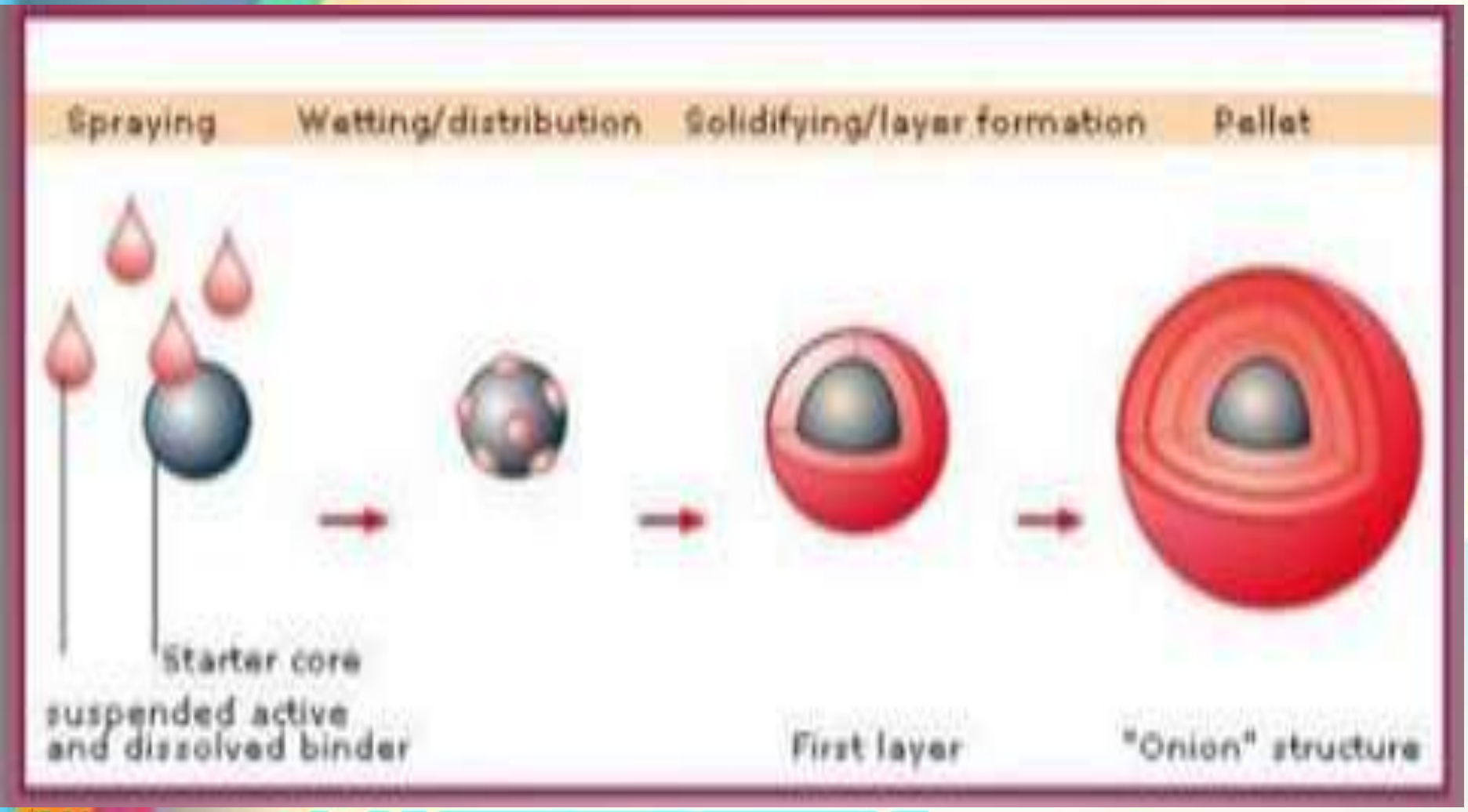


Powder layering





Liquid layering



Globulation or Droplet formation

Spray drying

- A drug solution or suspension is sprayed, with or without excipients, into a hot-air stream, generating dry and highly spherical particles.

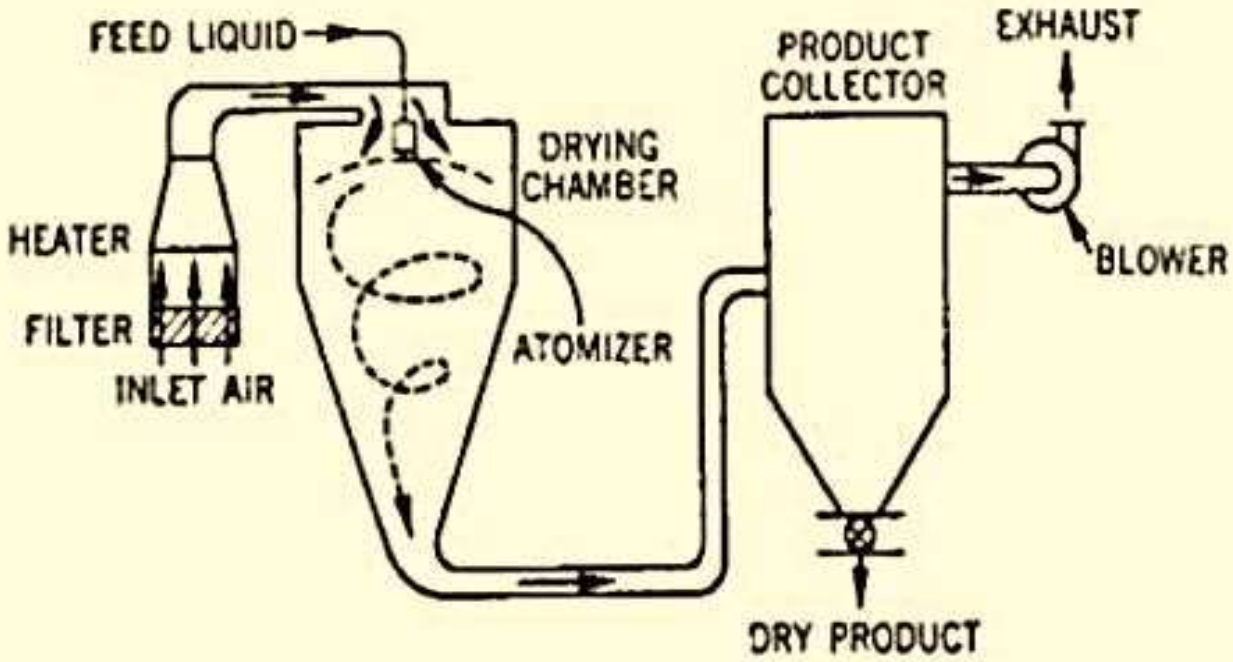


Figure: Typical Spray-Drying System.

- Vitamin A and D can be coated by this process to prevent their deterioration

Advantages:

The spray-dried powder particles are homogenous, approximately spherical, nearly uniform in size.

- This technique is suitable for development of controlled-released pellets.
- It is generally employed to improve dissolution rates and bioavailability of poor soluble drugs.
- This method is applied for heat sensitive pharmaceuticals: amino acids, antibiotics, ascorbic acid, liver extracts, pepsin and similar enzymes, protein hydrosylate and thiamine.
- Particle size and size distribution, bulk density, porosity, moisture content, flowability and friability can be easily controlled by the design and operation of the spray drier.

Globulation or Droplet formation

Spray congealing / spray chilling

- Also called Spray-Chilling, a technique similar to Spray-Drying but no source of heat is required
- Drugs can be suspended in molten wax and can give sustain release effect
- Monoglycerides and similar components are spray-congealed

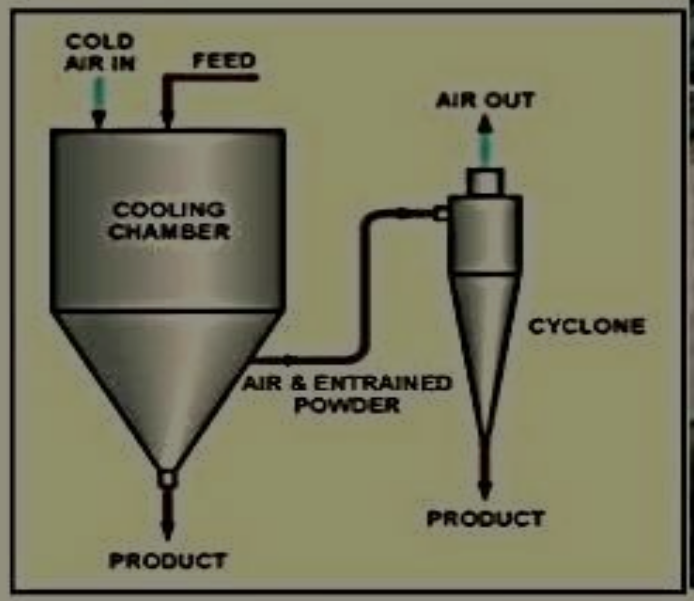
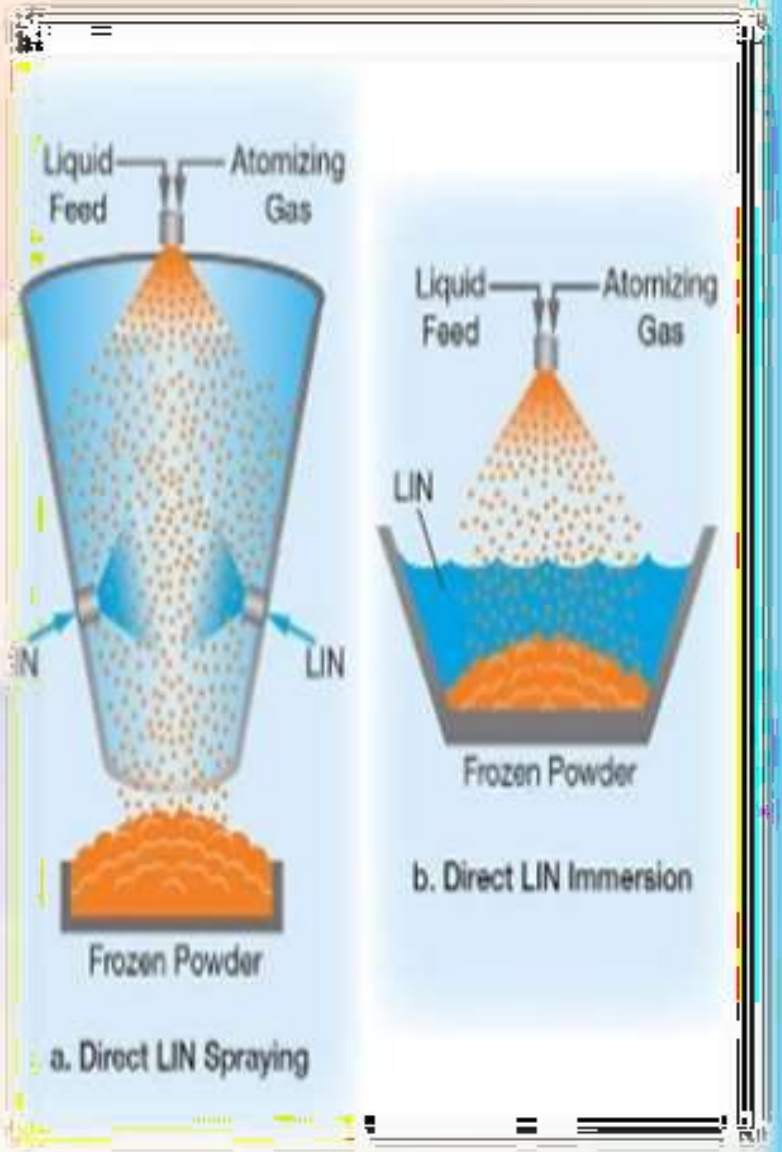


Figure: Spray-Congealing.

Cryopelletization

A process whereby droplet of a liquid formulation are converted into solid spherical pellet by using liquid nitrogen as fixing medium at - 160 ^{0}C



Cryopelletization

Application:

- It is used as an intermediate holding step
- It is used for long-term storage
- It enables ultra-fast freeze drying
- It is used to halt a fermentation reaction

Advantages of cryopelletization:

It is very easy to handle.

It produces free-flowing pellet forms.

It offers ultra-fast thawing for consistent and fast reconstitution eliminating the need tofreeze in block form which is difficult to handle.

CHARACTERIZATION OF PELLETS

1. Pellets size distribution
2. Pellets shape
3. Surface morphology (SEM)
4. Specific surface area
5. Friability
6. Disintegration Time
7. Dissolution
8. Density
9. Porosity
10. Tensile strength

Marketed product

DRUG	THERAPUTIC CATEGORY	FORMULATION TYPE
Omeprazole magnesium	Antiulcer	Antiulcer
Esomeprazole magnesium	Antiulcer	Antiulcer
Metoprolol tartrate	Antihypertensive	Extended release
Lansoprazole	Antiulcer	Delayed release orodispersible tablet
Theophylline	Antihistaminic	Extended release

Example of Tablets & Capsules:

Amoxicillin
Pseudoephedrine
Propranolol HCL
Esomeprazole
Omeprazole
Lansoprazole
Niacin
Duloxetine HCL
Prochlorperazine
Phendimetrazine tartrate