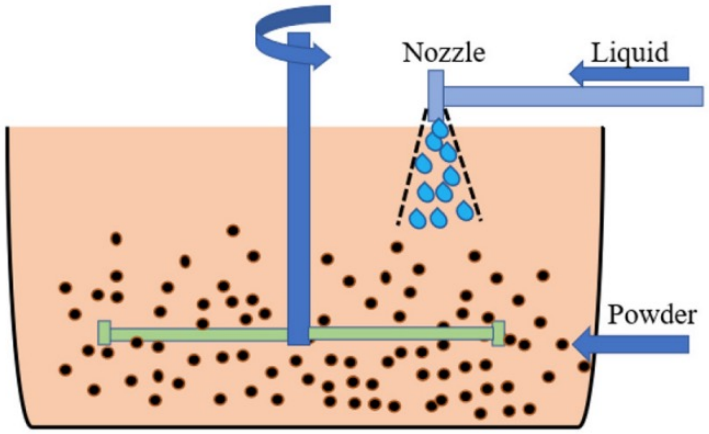
Wet Granulation

2023-2024

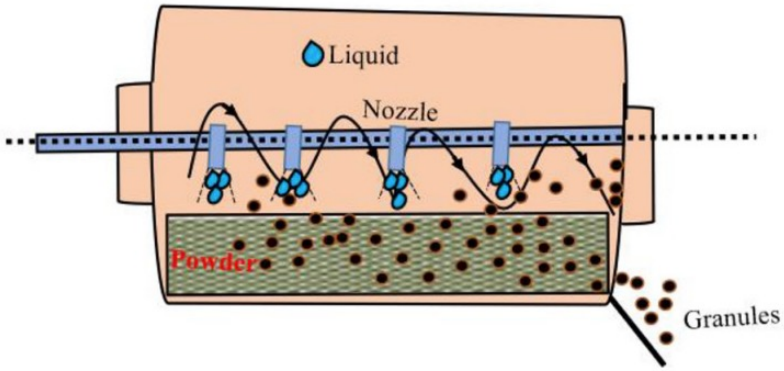
WET GRANULATION

Wet granulation is the widely used technique in manufacturing solid-dosage forms and the granules are produced by wet massing of the excipients and API with granulation liquid with or without binder

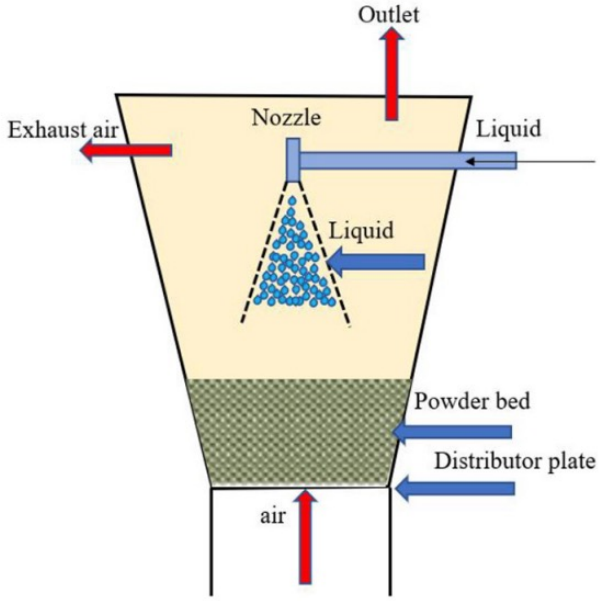
Wet Granulation Technologies ;



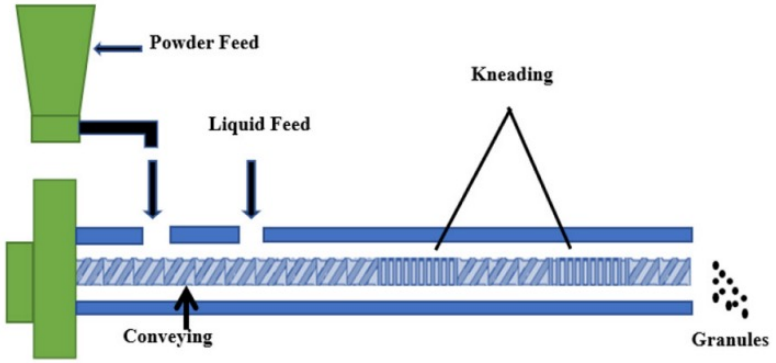
a) High shear Granulation



b) Rotating Drum Granulation



c) Sprayed Fluidized Bed Granulation



d) Wet Twin Screw Granulation

Steps of Wet Granulation

1. **Mixing (blending)** of the drug, diluent and disintegrant

2. **Wet massing** by addition of binder or adhesive or called granulation agent.

3. **Granulation** by sieving (**wet screening**).

4. **Drying.**

5. **Homogenizing** by second sieving (**dry screening**).

6. **Mixing** (**blending**) by addition of glidant and lubricant.

1- Mixing

- Mixing starts with adding drug then excipients. Total amount of disintegrant is not always added completely to the powder–diluent mixture (intragranulary), some other portion might be added with lubricants (extragranulary) in the final step prior to compression **(double disintegration)**

2- Wet Massing

- Adhesive (binder) is most commonly employed as solution, suspension, slurry, or used as a dry powder.
- Method of introducing the binder depends on its solubility and on the components of the mixture (wettability). In the wet massing step the binder solution will distribute and filling the spaces between particles
- The primary force of granulation acts as a bridge and is obtained from surface tension (cohesive force) and capillary force (adhesive and cohesive force) or pressure of the liquid (binder solution) between particles.

- Once the liquid is added, mixing is continued until we get a uniform dispersion of the adhesive within the whole system.

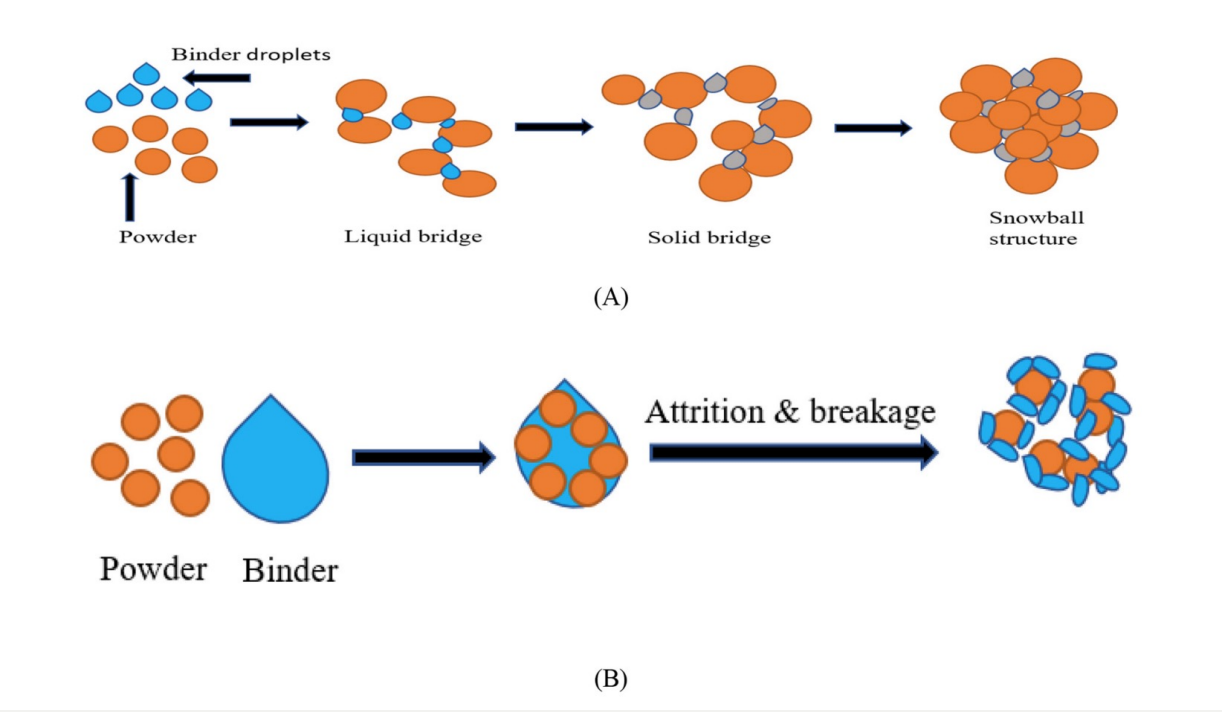
- The **end point** can be determined **by the press mass test** (ball test) as the mass must be moisten rather than pasty or wet, it is done **by pressing a portion of the mass in the palm if the ball crumbles under a moderate pressure, the mixture is ready for the next step (wet screening).**

3- Wet Screening (granulation)

- **Granulation** are performed **to further consolidate the granules by increasing the particles contact points,** and to **increase surface area to facilitate the drying process.**

4- Drying

- After **drying** step the granules should contain **some degree of humidity** to act as a **binder** (not be 100% free of humidity) as **over drying** may leads to weak force and **friable granules.**
- When the liquid binder is sprayed into the powder mass, particles start aggregating and form some clusters (nucleation). The liquid binder acts as a bridge between clusters and forms granules. The granules further undergo compaction to form solid particles (consolidation).



5- Dry screening

- After drying; then **dry screening** is performed to get a **homogenized granules with uniform size and shape.**

6- Mixing

- By addition of lubricants, glidants and disintegrant. Therefore, the granules will possess **good compressibility** (good cohesive forces once applying punch forming solid impact tab.), **good flowability** (spherical shape that is the ideal physical form in providing smoothness and size uniformity to the particles which is easily flow).

Note: we have **double sieving** in wet granulation, the 1st for sizing aggregates to give granules and the 2nd for homogenizing the already formed granules to regular shape (spherical particles).

Advantages of wet granulation method:

1.Improve flowability, cohesiveness and compressibility of the powder

2. Reduces the Risk of Air Entrapment

One of the enemies of tablet compressibility is air entrapment. Once air is trapped between the particles of the powder form of the drug, it becomes difficult to compress..

3. Maintaining good content uniformity due to prevent of particle segregation since all the granules will have the same density (same constituent of the powder mixture).

4. Limits the Level of Dust

Disadvantage of wet granulation method

- 1. The Process is Complex Without Machines
- 2. It is More Expensive
- 3. It Requires More Effort And Energy Consumption
- 4. Not Suitable For Moisture Control

Preparation of Sulfadiazine (sulfa drug) by wet granulation

- **Organoleptic properties:** White crystalline or white yellowish **fine crystals** or powder form, tasteless or slightly bitter taste.
- **Solubility:** Practically insoluble in water, chloroform, and ether; very slightly soluble in ethanol; soluble 1 in 300 of acetone; soluble in dilute mineral acids and in solutions of alkali hydroxides and carbonates.
- **Absorption:** it is weak acid (pKa=6.36), so they are well absorbed from GIT, mainly in stomach because are present in undissociated form.

- **Stability:** **Stable in dry air and not affected by moisture and heat**, slowly darken and decompose, so should be protected from light should be kept in dark closed container (opaque containers).

Sulfadiazine is prepared by wet granulation method for the following reasons:

1. They are **not affected by moisture and heat.**
2. **Large doses**
3. Present in powder form as **fine crystals.**

- Sulfa drug are not prepared by direct compression because:

1.They had bad flowability because they present as fine powder or fine crystals

2.They are used in large doses and direct compression is only used for intermediate doses.

Example

Sulfadiazine 500 mg (active ingredient)

Ca carbonate 250 mg (diluent)

Explotab 50 mg (disintegrant)

Zn stearate 10 mg (lubricant)

Acacia mucilage 20%(w/v) q.s. (binder)

prepare 50 tablets

Answer

- Mix all ingredients except lubricant and binder.
- Add the binder drop by drop (ball test).
- Calculate the weight of acacia in each tablet

(If we use for example 5 ml of (20%w/v) acacia mucilage for 50 tab.)

20 gm 100 ml

x 5ml

= 1 gm of acacia for 50 tab

1gm/50 *1000= 20 mg of acacia per tab.

- Calculate the **theoretical wt.** of one tablet (without lubricant)

500 mg+250 mg+50 mg+20 mg =820 mg wt. of one tablet without lubricant

- Weigh the prepared granules (**actual wt.** of tablets without lubricant)

for example it was found to be 33200 mg

- Find the real no. of tablets

Real no. of tab. = actual wt./theoretical wt.

=33200 / 820

=40.4 tablets

- Calculate the actual amount of lubricant to be added:

amount of lubricant =10 mg * Real no. of tab.

=10 * 40

=400mg of lubricant added

- **Question**

Na_2CO_3		125mg
Lactose		100mg
Starch		10mg
Acacia mucilage	Q.S.	20%(w/v)
Zn stearate		0.5mg

Prepare 20 tablet

- If you know that the weight for 20 tablet is 6.8 g and the volume of acacia mucilage is 2 ml.. Calculate the real no. of tablet and the amount of lubricant that should be added


THANK YOU!