

*Wet Granulation
practical
industrial pharmacy*

Fifth Stage

2024-2025

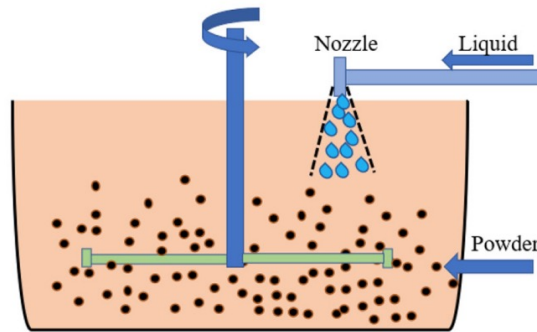
Lec. Zeina Dawood

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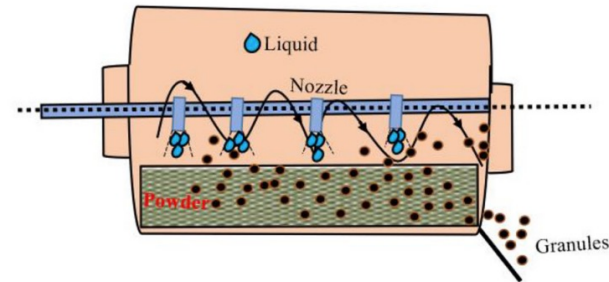
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Wet Granulation

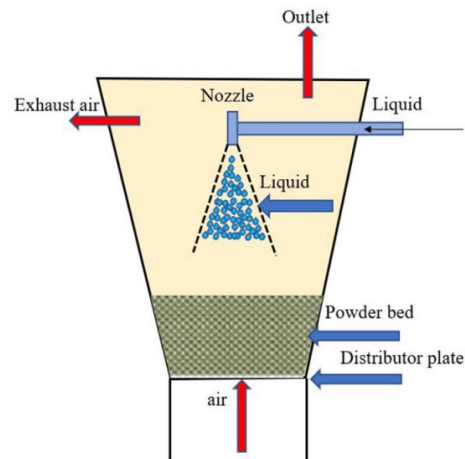
Or moist granulation is a process used to produce granules from a powder mixture. The powder mixture is wetted with a liquid binder, and then the mixture is agitated to form granules. The granules are then dried and milled to the desired size.



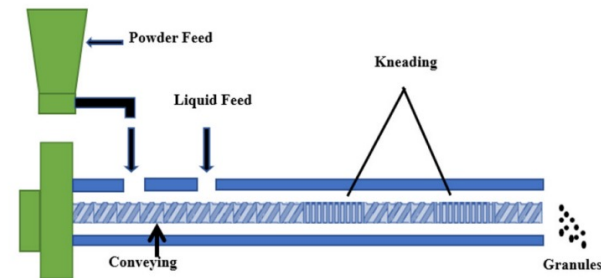
a) High shear Granulation



b) Rotating Drum Granulation



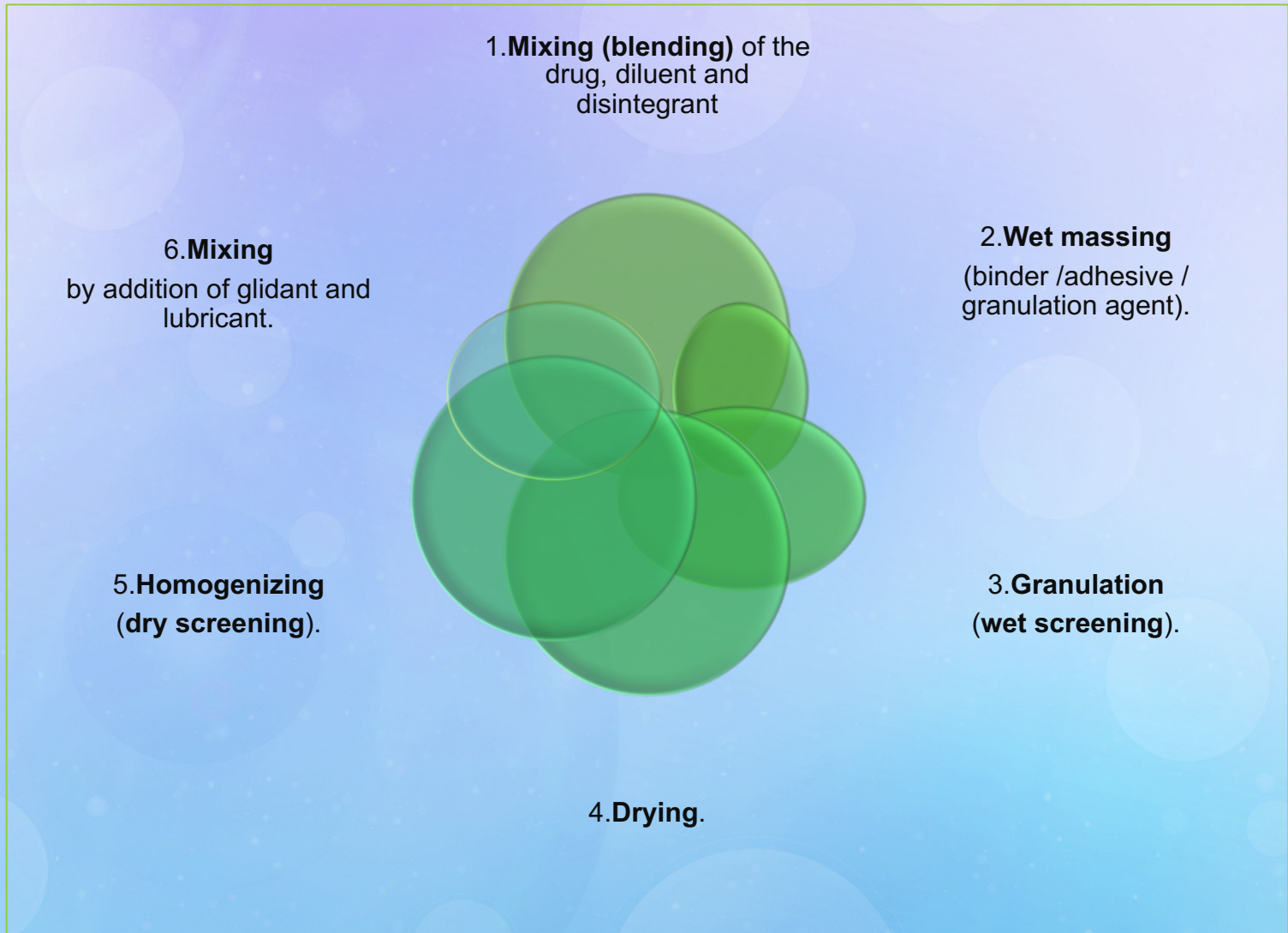
c) Sprayed Fluidized Bed Granulation



d) Wet Twin Screw Granulation

Wet Granulation Technologies

Steps of Wet Granulation



1 - Mixing

By adding drug then excipients.

Note: disintegrant is not always added completely to the powder–diluent mixture (intragranular), some might be added (extragranular) with lubricants in the final step prior to compression (**called !**)

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 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 and capillary 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.

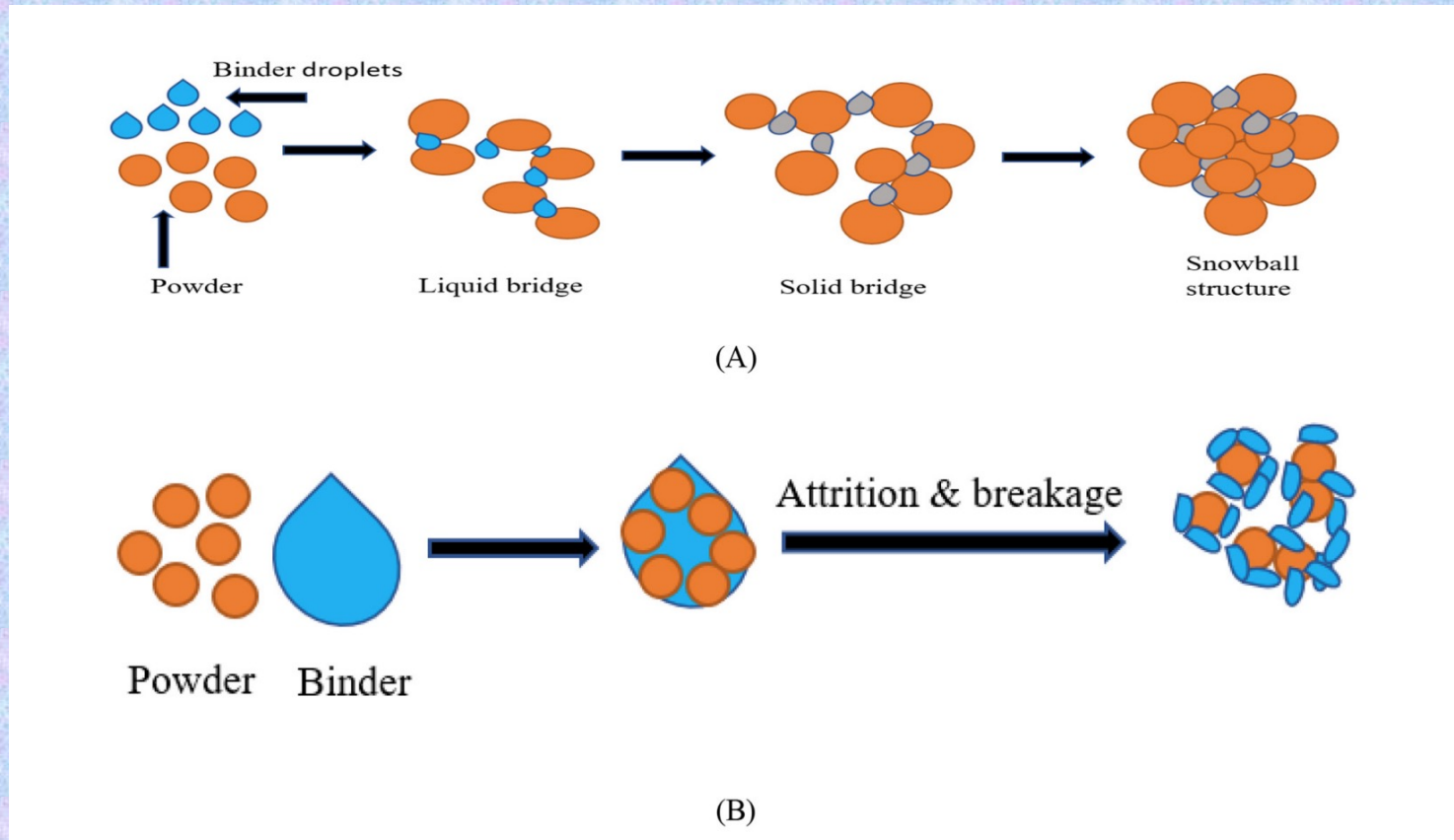
The **end point** can be determined **by the press mass test (ball test)** as the mass must be moisten rather than pasty or wet, it is done **by pressing a portion of the mass in the palm** if **the ball crumbles under a moderate pressure**, the mixture is ready for the next step

3- Wet Screening (granulation)

The mass is screened (sieved) to form pellets or granules

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

- it is performed to get a **homogenized granules with uniform size and shape** , can it reduce the size ?

6- Mixing

- By addition of lubricants, glidants and disintegrant. Therefore, the granules will possess **good compressibility, good flowability**

Note: **double sieving** in wet granulation,
the 1st for sizing aggregates to give granules
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
3. Maintaining good content uniformity due to prevent of particle segregation since all the granules will have the same density.

Disadvantage of wet granulation method

- 1. The Process is Complex Without Machines
- 3. It Requires More Effort And Energy Consumption ; hence, it is expensive
- 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 ($pK_a=6.36$), 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.**



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 one tablet (check the acacia weight , how ?!)

Calculate the weight of acacia in each tablet

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

$$\begin{array}{r} 20 \text{ gm} \quad 100 \text{ ml} \\ \times \quad \quad 5 \text{ ml} \\ \hline = 1 \text{ gm (1000mg) of acacia for 50 tab} \\ 1000/50 = 20 \text{ mg of acacia per tab.} \end{array}$$

- Find the real number of tablet by firstly, 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

Then, Weigh the prepared granules (**actual wt.** of tablets without lubricant) for example it was found to be 33200 mg

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

$$=33200 / 820$$

$$=40.4 \text{ tablets}$$

- Calculate the actual amount of lubricant to be added:

$$=\text{amount of lubricant} * \text{Real no. of tab.}$$

$$=10\text{mg} * 40 \text{ tablet}$$

$$=400\text{mg of lubricant added}$$



Home work for next lab

Na ₂ CO 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

