

# Wet Granulation

Industrial pharmacy •

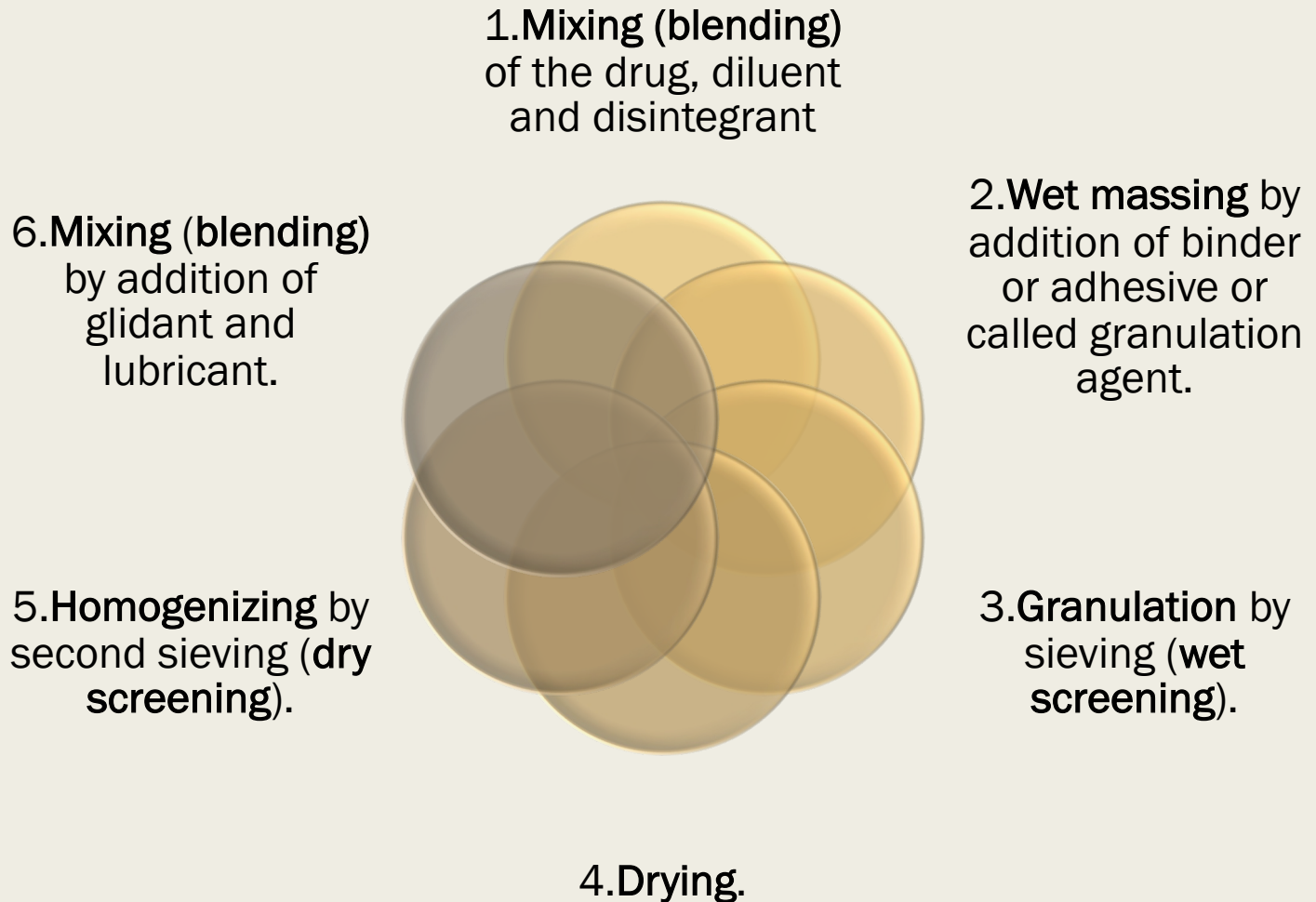
Lec. Ashti M.H. Saeed

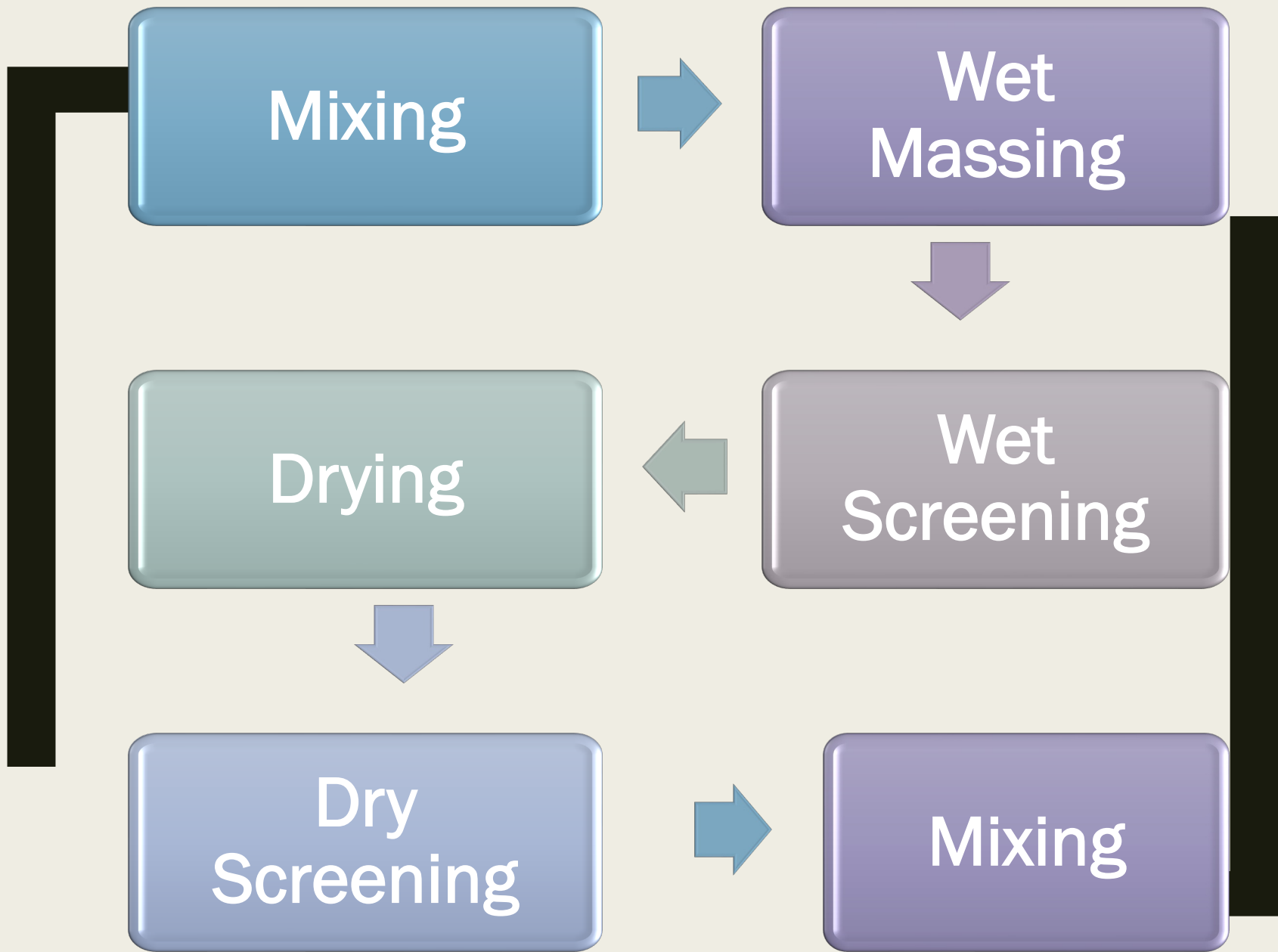
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# WET GRANULATION

The wet granulation technique uses the same preparatory and finishing steps of direct compression and dry granulation (dry screening and mixing); it also involves additional steps of wet massing, wet screening and drying.

# Steps of Wet Granulation





## 1- Mixing

- Mixing starts with adding drug then excipients. The mixing process depends on the properties of the drug and excipients.
  - *If the drug is soluble in water and excipients are little; so we start to add binder solution to the drug to be distributed uniformly then excipients that have little solubility in water (e.g. starch), it is possible to be added extragranularly [as a whole] or [divided and added as one half intragranular and the other extragranular to avoid getting friable tablets].*



Total amount of disintegrant is not always added completely to the powder–diluent mixture (intragranularly), some other portion might be added with lubricants (extragranularly) 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.

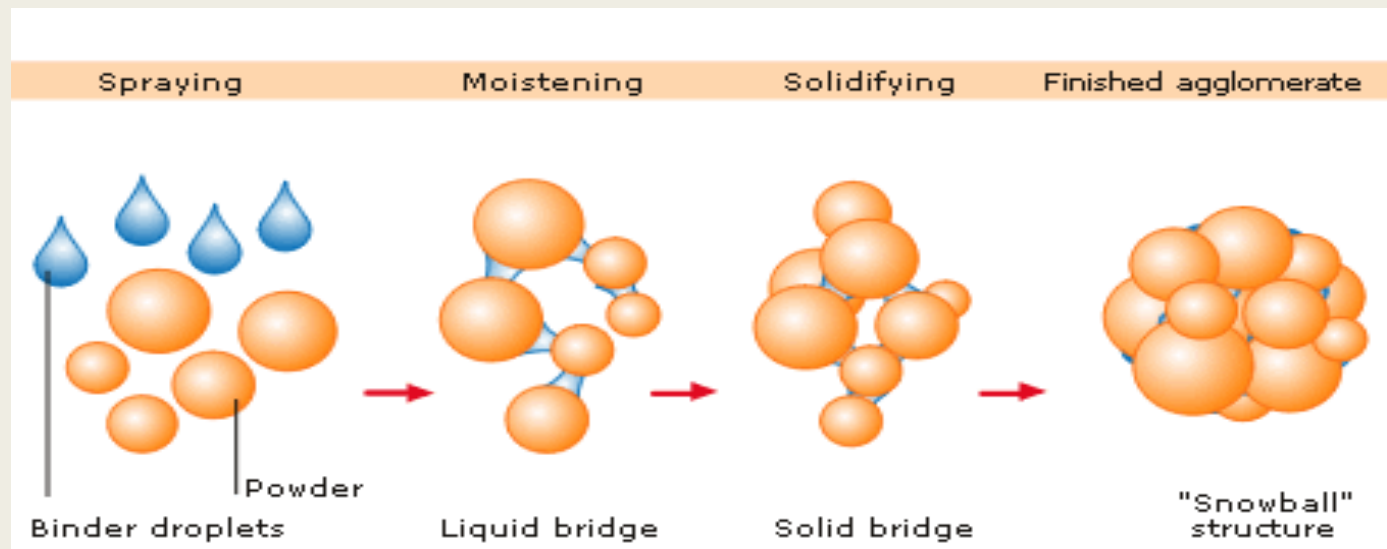
- Once the liquid is added, mixing is continued until we get a uniform dispersion of the adhesive within the whole system.
- The length off wetting time depends on the wetting property of the powder mix. and the granulating fluid, and on the efficiency of the mixer.
- The end point can be determined 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**.
- The **final cohesive force** obtained after **drying stage** when evaporation of solvent occurs as a result of **fusion, recrystallization and curing of the binding agent** with **Van der Waals forces** playing a significant role.





## 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).

## Advantages of wet granulation method:

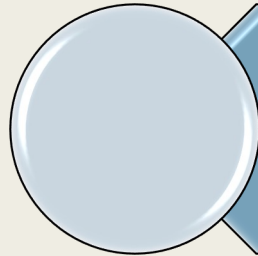
1. Improve flowability, cohesiveness and compressibility of the powder, so the powder is easily compressed with lower binder concentration (due to the stick of powder particles together and surrounded by layer of a binder) in addition to the low pressure and low energy comparing to dry granulation (prolong machine age).
2. Can be used for high dose drug with weak compressibility that is not affected by heat and moisture.
3. Maintaining uniform distribution for low dose drug and water soluble dyes (coloring agent).

4. Improve the dissolution rate of hydrophobic drug because of the presence of moisture of the already used water.

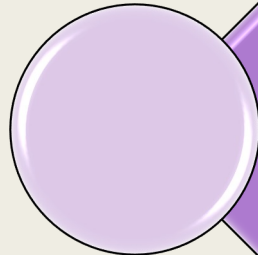
5. Maintaining good content uniformity due to prevent of particle segregation since all the granules will have the same density (same constituent of the powder mixture).

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

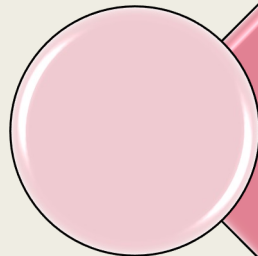
# Disadvantages of wet granulation method



**1.cost-time consumer.**



**2. Personal and environmental hazards upon using organic solvents represented by the flammability and toxicity of these solvents after evaporation during drying, handling or storage.**



**3. Stability problem because of the presence of moisture speeds up the reaction between active ingredients and the additives and the additives itself.**

## 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:

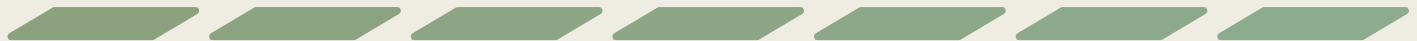
**1.They are not affected by moisture and heat.**



**2.Large doses**



**3.Present in powder form as fine crystals.**



- 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

$1\text{gm}/50 * 1000 = 20 \text{ mg of acacia per tab.}$

- 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.**

$$=33200 / 820$$

$$=40.4 \text{ tablets}$$

- 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 <sub>2</sub> CO <sub>3</sub>	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!

