University of Tikrit
College of Pharmacy
Department of Pharmaceutics

Practical Industrial Pharmacy II

Lab 1

Preformulation study

Flowability Measurement

Assist. Lec. Ahmad Abdullah Essa

Course Outcomes

- A detail study involving machinery and theory of **pharmaceutical unit operations like solid orals:** Direct compression, Dry granulation, Wet granulation and Capsule filling.
- **Advances in pharmaceutical excipients:** Excipients selection for tablet and capsule dosage forms.
- **Formulation and evaluation of tablets and capsules and their advantages over other dosage forms.**
- **Parenteral Dosage Forms:** Steps for their preparation, container selection and quality control studies.

Preformulation

- **Preformulation** is the investigation of the physical and chemical properties of the drug substance (alone or with the additives or excipients) in order to formulate a stable, safe, effective and bioavailable dosage form and avoid the interaction that may occur between active and non active ingredients.

❖ Preformulation Steps, Stages or Factors:

1. Organoleptic Properties
2. Purity
3. Particle Size and Surface area
4. Solubility

Pre-compression Study

Powder flow

The largest use of powders pharmaceutically is to produce tablets and capsules. Together with mixing and compression properties, the flowability of a powder is of critical importance in the production of pharmaceutical dosage forms.

Flowability

- **Some of the reasons for producing free flowing pharmaceutical powders include :**

1. Uniform feed from bulk storage containers or hoppers into the feed mechanisms of tableting or capsule-filling equipment, allowing uniform particle packing and a constant volume-to-mass ratio which maintains tablet weight uniformity.
2. Reproducible filling of tablet dies and capsule dosators, which improves weight uniformity and allows tablets to be produced with more consistent physicomechanical properties.
3. Uneven powder flow can result in excess entrapped air within powders, which in some high-speed tableting conditions may promote capping or lamination.
4. Uneven powder flow can result from excess fine particles in a powder, which increase particle-die-wall friction, causing lubrication problems, and increase dust contamination risks during powder transfer.

Flowability Measurement

The methods which are frequently used for characterising powder flow are:

- **Angle of repose**
- **Carr´s Compressibility index or**
- **Hausner's ratio**

- Numerous variations of each of these basic methods are available. Hence, an appropriate strategy may well be the use of multiple standarised test methods to characterise the various aspects of powder flow as needed by the pharmaceutical scientist.

Angle of repose

- **Angle of repose** (θ) is a characteristic related to interparticulate friction, or resistance to movement between particles.

- **Process of measuring angle of repose:**

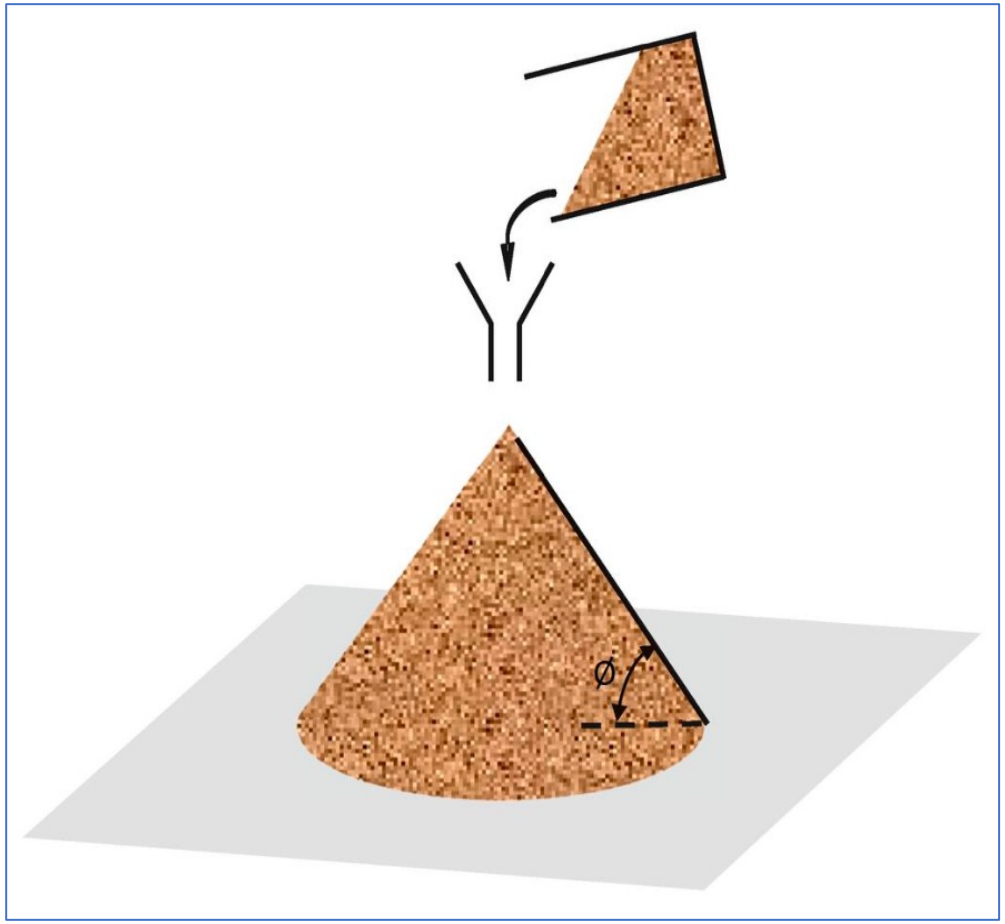
1) Weight 100 g of powdered material (sieve if necessary).
2) Place a funnel at fixed height from a stable base.
3) Pour the powder in the funnel (a pile will be formed on the horizontal plane).
4) Calculate the height and the radius of the pile.

Angle of repose

5) Angle of repose (could be calculated from the following equation:

$$\tan(\theta) = h/r$$

* Where θ is the angle of repose obtained by calculating the tan -1
h is the distance from the lower tip of the funnel to a surface.
r is the radius of the resulted cone.



Angle of repose

- As explained in Table 1 below, powders with angle of repose greater than 50° have unsatisfactory flow properties, while minimum angle close to 25° correspond to very good flow properties.

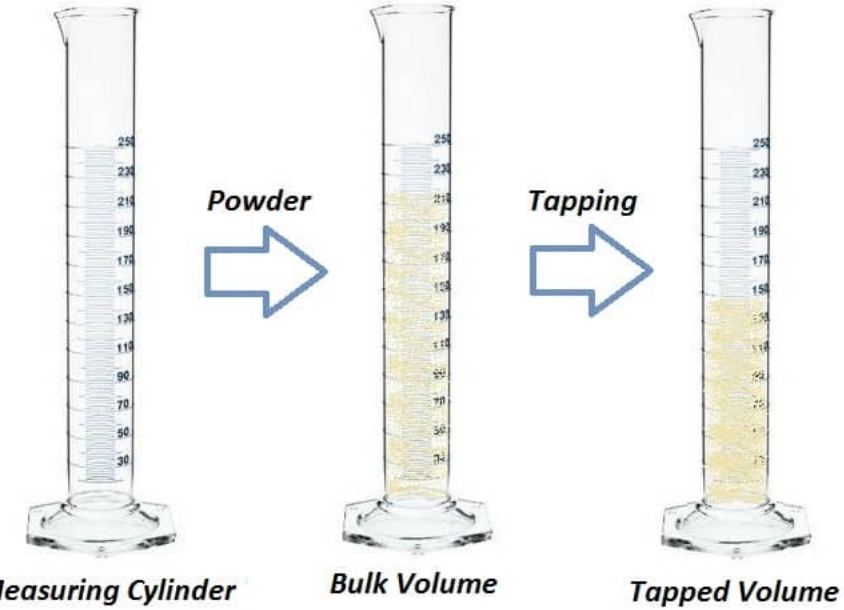
Angle of repose (°)	Type of flow
25 – 30	Excellent
31 – 35	Good
36 – 40	Fair (flow aid not needed)
41 – 45	Passable (many hang up, flow aid might be needed)
46 – 55	Poor (agitation or vibration needed)
56 – 65	Very poor
> 65	Very, very poor

Carr´s index and Hausner's ratio

- In recent years the compressibility index and the closely related Hausner ratio have become the simple, fast, and popular methods of predicting powder flow characteristics.

- The compressibility index and the Hausner ratio are determined by measuring both the bulk volume (V_0) and tapped volume (V_f) of a powder.

Tapped Density Apparatus



Measuring Cylinder *Bulk Volume* *Tapped Volume*

Density

- **Bulk density**
- It is the ratio of the powder mass to bulk volume and it is dependent on the particle packing. It is measured by pouring a certain weight of powder into a graduated cylinder and record the initial volume and then the density can be calculated by the following equation:
- **Bulk Density = Powder mass / Bulk volume**

Tapped density

It is the ratio of the powder mass to tapped volume. It is measured by pouring certain weight of powder into a graduated cylinder and manually tapping the cylinder until no further change in powder volume is observed and recording the final volume and then the density can be calculated by the following equation:

Tapped Density = Powder mass / Tapped volume

Compressibility Index (Carr´s index)

- **Process of measuring Carr´s compressibility index:**

1) Use a 250 ml cylinder.

2) Add 100 g of the powder in the cylinder.

3) Determine the bulk density of the powder.

4) The cylinder is tapped vertically until the volume of the powder retained at a certain volume (which is the tapped density).

5) Carr´s compressibility index can be calculated by applying the following equation:

$$\text{Carr's index} = \frac{\text{Tapped density} - \text{Bulk dnsity}}{\text{Tapped dnsity}} \times 100$$

Hausner’s ratio

Hausner's ratio is an indicator of powder flow ease.

1) Use a 250 ml cylinder.
2) Add 100 g of the powder in the cylinder.
3) Determine the bulk density of the powder.
4) The cylinder is tapped vertically until the volume of the powder retained at a certain volume (which is the tapped density).

The following equation is used to calculate it:

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk dnsity}}$$

Carr´s index and Hausner's ratio

Compressibility index (%) (Carr's index)	Type of flow	Hausner ratio
1 – 10	**Excellent**	1.00 – 1.11
11 – 15	**Good**	1.12 – 1.18
16 – 20	**Fair**	1.19 – 1.25
21 – 25	**Passable**	1.26 – 1.34
26 – 31	**Poor**	1.35 – 1.45
32 – 37	**Very poor**	1.46 – 1.59
> 38	**Very, very poor**	> 1.60

Experimental Part

Procedure:

- Weight 100 gm of sugar and 100 gm of glucose powder
- Use cylinder and measure the bulk density and tap density
- Measure the **angle of repose** using fennel
- Calculate **carr's index** and **hausner's ratio**

Pre-compression studies

- The two most useful and best methods for powder flow properties determination are Hausner's ratio and compressibility index.

- **Powder flow properties of the powder can be improved by:**

1. Formulation additives: flow activators = Glidant : reduce adhesion or cohesion
2. Granulation (particle size)

Experimental Part

Group 1	Group 2	Group 3	Group 4	Group 5

Thank You