Tablet Granulation
Part 3

Industrial pharmacy

5th class

1st semester

Basic Characteristics

The characteristic of a tablet that make it a popular dosage form:

- **Compactness**
- **Physical stability**
- **Rapid production capability**
- **Chemical stability**
- **Efficacy**

Properties required by compression machine design:

Materials intended for compaction into a tablet must posses two characteristics: Fluidity and Compressibility

1. Fluidity:

A good flow properties are essential for the transport of the material through the hopper, into and through the feed frame, and into the dies.

(i.e: Tablet materials should be in a physical form that flows smoothly and uniformly).

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The ideal physical form for this purpose is spheres (these offer minimum contact surfaces between themselves and with the walls of machine parts).

Note: Unfortunately, most materials do not easily form spheres; however, shapes that approach spheres improve flowability.

The purpose of granulation:

Attempts to improve the flow of powdered materials by forming sphere like or regularly shaped aggregates called granules.

2. Compressibility

Is the property of forming a stable, compact mass when pressure is applied.

The consideration of compressibility is limited to stating that granulation is also the pharmaceutical process that **converts a mixture of powders, which have poor cohesion, into aggregates capable of compaction.**

Granulation properties

Formulation and process variables involved in the granulation step can affect the characteristics of the granulations produced.

The methods used to measure granulation characteristics to monitor granulation suitability for tabletting:

1. Particle size and shape.

P.S. of a granulation is known to affect:

a. Average tablet weight
b. Tablet weight variation
c. Disintegration time
d. Granule friability
e. Granulation flowability
f. Drying rate kinetics of wet granulations.

The exact effect of granule size and size distribution on processing requirements, bulk granulation characteristics, and final tablet characteristics depends upon:

1. **Formulation ingredients and their concentrations**
2. **Type of granulation equipment**
3. **processing conditions**

Methods used for measuring and interpreting P.S. and P.S. distribution:

Microscopy, Sieving, Sedimentation, Adsorption, Electrical-conductivity, Light scatring X-ray

2. Surface area (S.A.)

The determination of S.A. of finely milled drug powders may be of value for drugs that have only limited water solubility.

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In these cases, particle size (P.S.), and especially the surface area of the drug, can have a significant effect upon dissolution rate.

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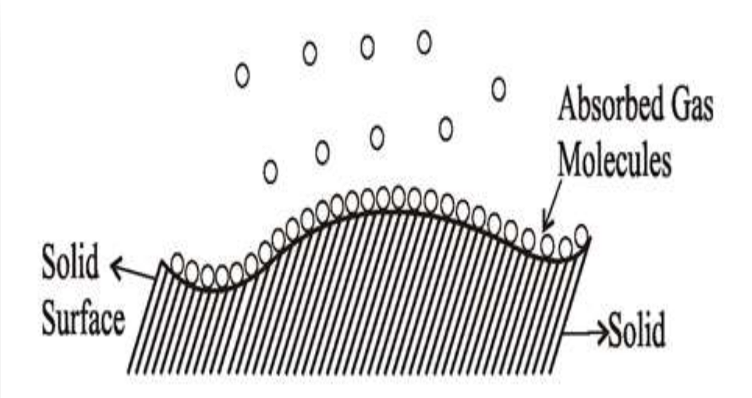
An inverse relationship normally exists between P.S. and S.A.; however, granulations can have convoluted structures with considerable internal surface.

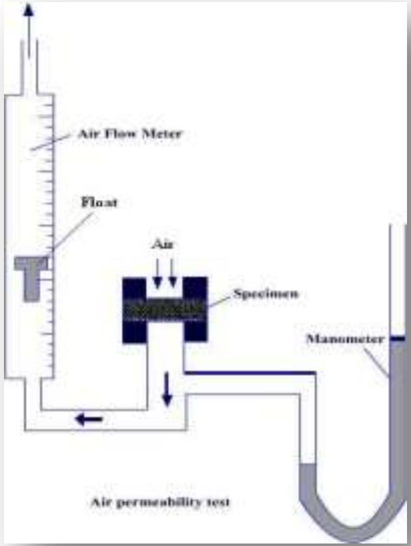
The two most common methods for determining S.A. of solid particles are:

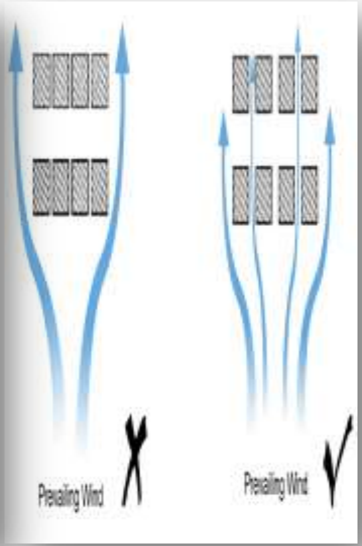
Gas adsorption and Air permeability.

The amount of gas that is adsorbed onto the powder to form monolayer.

The rate at which air permeates a bed of powder







3. Density.

Granule density may influence:

a. Compressibility
b. Tablet porosity
c. Dissolution.

Note: **Dense, hard granules may require higher compressible loads to produce a cohesive compact**

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Increasing the tablet disintegration and drug dissolution times.

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Even if the tablets disintegrate readily, the harder, denser granules may dissolve less readily.

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At the same time, harder, denser granules are usually less friable.

Two methods are used to determine granule density. Both involve the use of a pycnometer. In one, the intrusion fluid is mercury, and in the other, it is a solvent of low surface tension (e.g., benzene) in which the granules are not soluble.

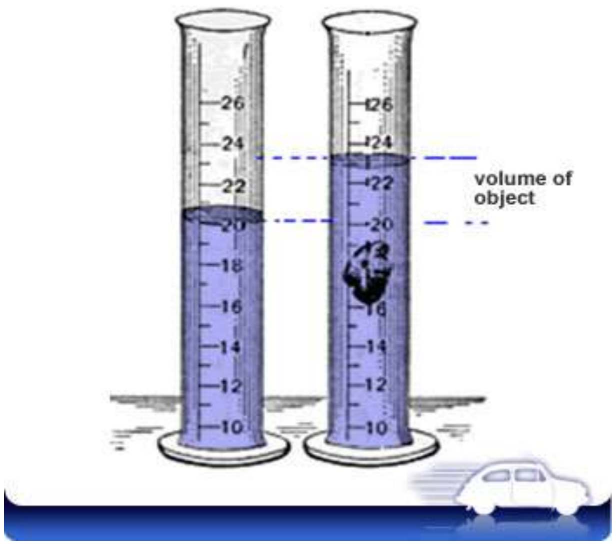
Note: 1- The accuracy of these pycnometer methods depends on: (the ability of the intrusion fluids to penetrate the pores of the granules).

2- Bulk density largely depends on particle shape.

(As the particles became more spherical in shape, bulk density is increased).

3- As the granule size increases, bulk density decreases.

(The smaller granules are able to form a close, more intimate packing than larger granules).



4. Strength and friability.

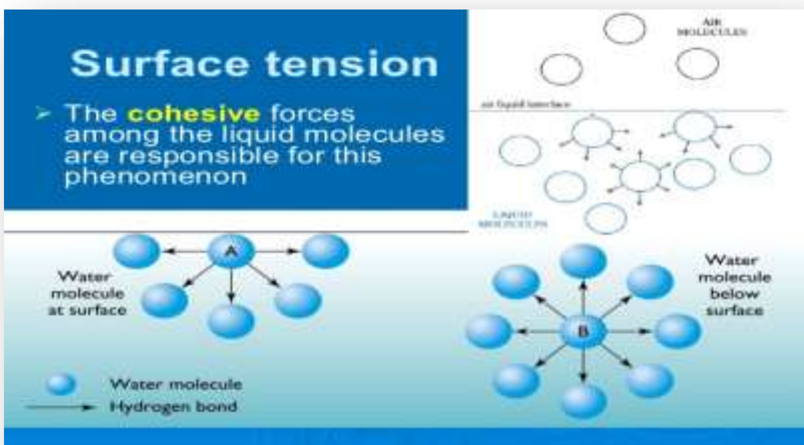
A granule: is an aggregation of component particles that is held together by bonds of finite strength.

- **The strength of a wet granule is due mainly to surface tension of liquid and capillary forces.**

These forces are responsible for initial agglomeration of the wet powder.

Upon drying, the granule has strong bonds resulting from fusion or recrystallization of particles and curing of the adhesive or binder.

Under these conditions, van der Waals forces are of sufficient strength to produce a strong, dry granule.



Aim of measuring granule strength:

Estimating the relative magnitude of attractive forces seeking to hold the granule together.

Granule strength depends on:

1. Base materials
2. Kind and amount of granulating agent used
3. Granulating equipment used.

Granule strength and friability affect:

i. Changes in particle size distribution of granulations
ii. Compressibility into cohesive tablets.

Methods used to measure granule strength:

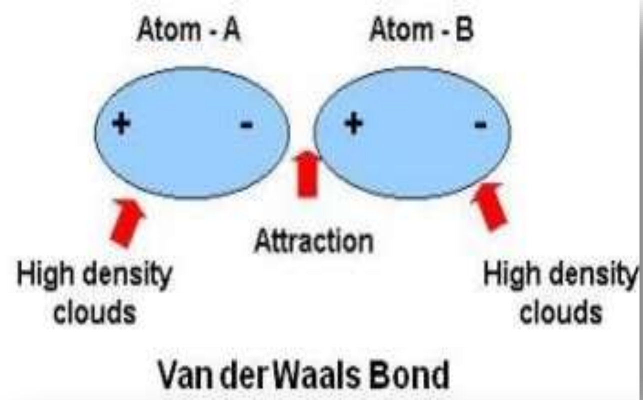
a) Granule is placed between anvils and the force required to break the granule is measured
b) Friability measurement.

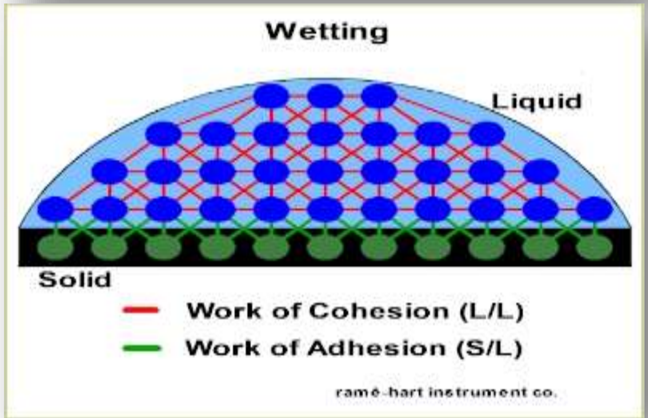
5. Flow properties.

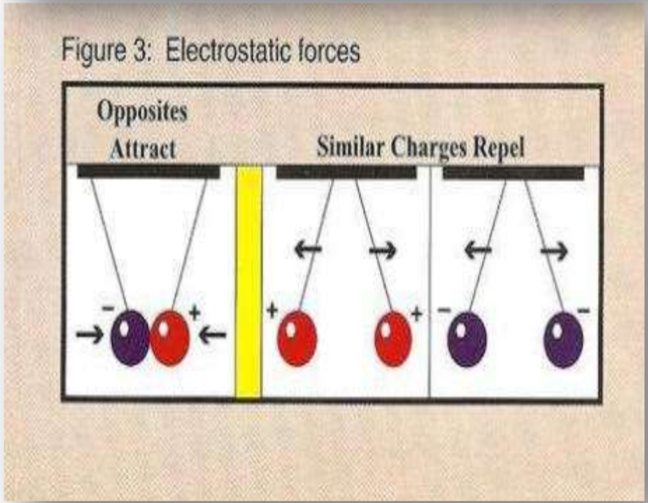
Solid particles attract one another, and forces acting between particles when they are in contact are predominately surface forces.

There are many types of forces that can act between solid particles:

1. Frictional forces
2. Surface tension forces
3. Mechanical forces caused by interlocking of irregular shape
4. Electrostatic forces
5. Cohesive or van der Waals forces.







- **All of these forces can affect:**

1. **Flow properties of a solid.**
2. **Granule properties:**
   a) **Particle size**
   b) **Particle size distribution**
   c) **Particle shape**
   d) **Surface texture or roughness**
   e) **Residual surface energy**
   f) **Surface area.**

Ex: With fine powder (≤ 150μm), the magnitude of the frictional and van der Waals forces usually predominate.

For larger particles (≥ 150μm) such as granules produced by a wet granulation technique, frictional forces normally predominate over van der Waals forces.

Two of the most common methods are:

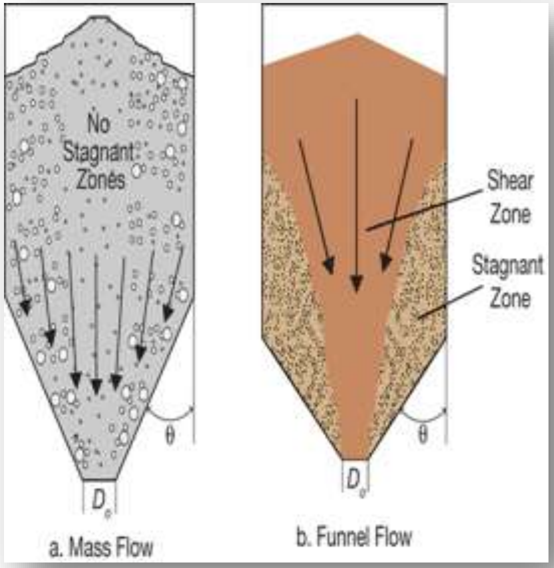
A. Repose angle

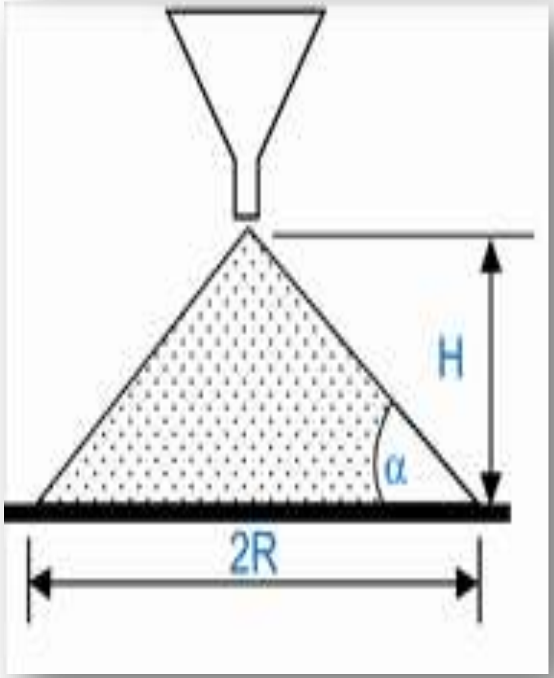
B. Hopper flow rate measurements.

A. Repose Angle.

i. **The fixed funnel and free-standing cone methods**

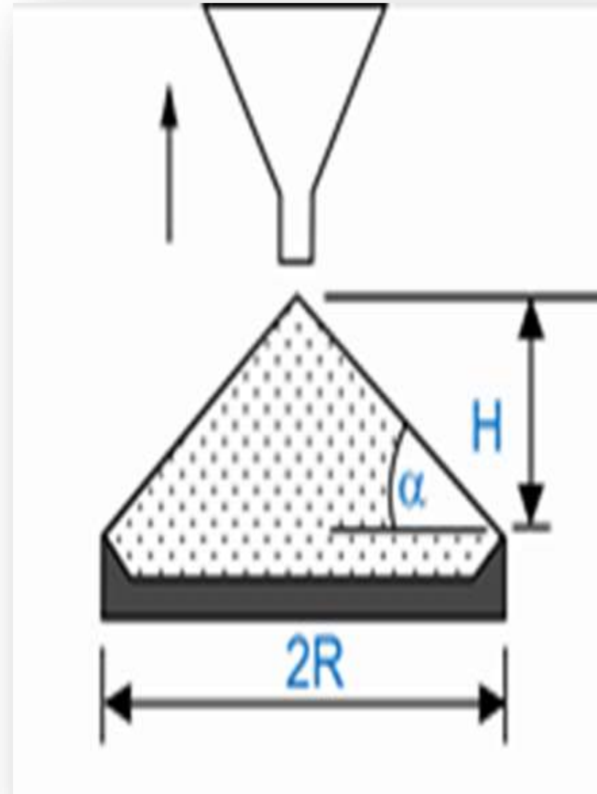
- Employ a funnel that is secured with its tip at a given height, above graph paper that is placed on a flat horizontal surface.
- Powder or granulation is carefully poured through the funnel until the apex of the conical pile just touches the tip of the funnel.





ii. The fixed cone method:

- Establishes diameter of the cone base by using a circular dish with sharp edges.
- Powder is poured onto the center of the dish from a funnel that can be raised vertically until a maximum cone height, H, is obtained. The repose angle is calculated.



$$\tan \alpha = H / R$$

Or

$$\alpha = \arctan H/R$$

The angle determined by these two methods is often referred to as the static angle of repose.

Values for angles of repose ≤ 30° usually indicate a free-flowing material

angles ≥40° suggest a poorly flowing material.

Note: A. **Flow of coarse particles depend on:**

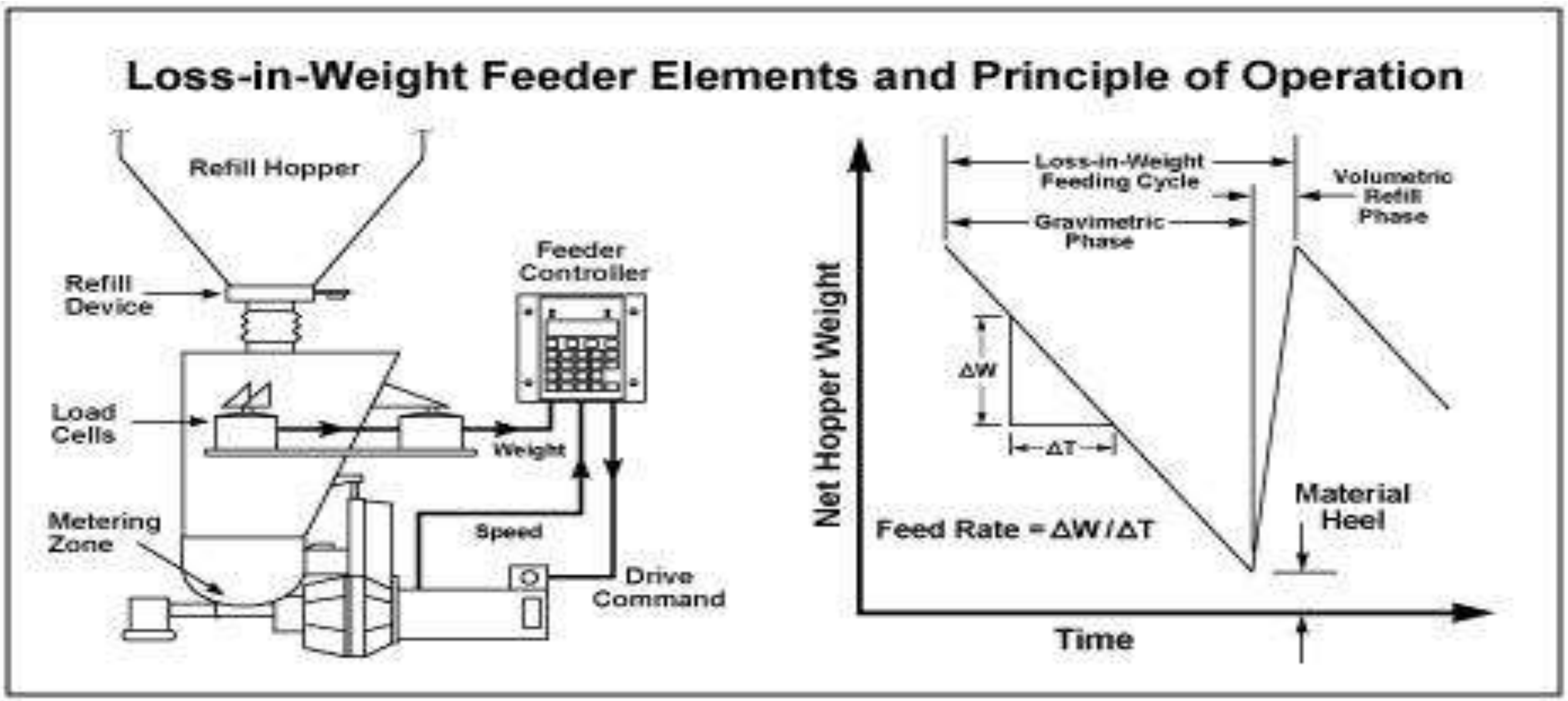
1. Packing densities
2. Mechanical arrangements of particles.

B. **Flow properties affect** angle of repose and compressibility.

B. Hopper flow rates.

Used as a method of assessing flowability.

- Instrumentation to obtain hopper flow rates continually monitors the flow of material out of conical hoppers onto a recording balance device.



6. **Compaction.**

The basic tool for studying the compression process (compacting powder or granule materials) is the instrumented tablet press.

- Tablet presses are instrumented by **affixing transducers** (to measure the forces applied during the compression process).

The signals produced by the transducer system are monitored by computer.


Thank You