POWDER DOSAGE FORM

(Lect. 5)

Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems, 9th Edition 2011

Chapter 6

Powders and Granules

Powder

- **Most active and inactive pharmaceutical ingredients occur in the solid state as amorphous powders or as crystals of various morphologic structures.**
- **The term "powder" has more than one meaning in pharmacy.**

1. **It may be used to describe the physical form of a material, that is, a dry substance composed of finely divided particles.**
2. **Or, it may be used to describe a type of pharmaceutical preparation, that is, a medicated powder intended for internal (i.e., oral powder) or external (i.e., topical powder) use.**

Powders and granules

- **Powders (as a dosage form) are mixtures of dry, finely divided drugs and/or chemicals that may be intended for internal or external use.**
- **Granules, which are prepared agglomerates of powdered materials, may be used per se for the medicinal value of their content, or they may be used for pharmaceutical purposes, as in making tablets**

The use of powders

a) **Medicated powders for therapeutic effect (limited),**

b) **The use of powdered substances in the preparation of other dosage forms is extensive. For example, powdered drugs may be blended with powdered fillers and other pharmaceutical ingredients to fabricate**

1- solid dosage forms as tablets and capsules;

2- they may be dissolved or suspended in solvents or liquid vehicles to make various liquid dosage forms;

3- or they may be incorporated into semisolid bases in the preparation of medicated ointments and creams.

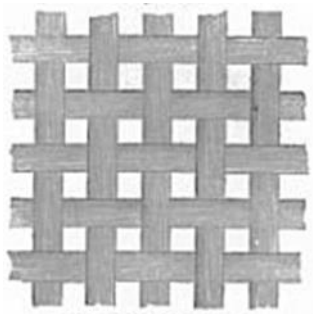
Characterization of powders

- **Before their use in the preparation of pharmaceutical products, solid materials first are characterized to determine their chemical and physical features, including**

1. **morphology,**
2. **purity,**
3. **solubility,**
4. **flowability,**
5. **stability,**
6. **particle size,**
7. **uniformity, and**
8. **compatibility with any other formulation components**

Particle size

- **The adjustment and control of a drug and other materials powder's particle size; enable both the efficient production of a finished dosage form and the optimum therapeutic efficacy.**
- **United States Pharmacopeia (USP) uses these terms: very coarse, coarse, moderately coarse, fine, and very fine, which are related to the proportion of powder that is capable of passing through the openings of standard sieves of varying fineness in a specified period while being shaken, generally in a mechanical sieve shaker**
- **Sieves can be referred to either by their aperture size or by their mesh size (or sieve number).**
- **The mesh size is the number of wires per linear inch**



OPENING OF STANDARD SIEVES

	SIEVE NUMBER	SIEVE OPENING			SIEVE NUMBER	SIEVE OPENING
Very coarse	2.0	9.50 mm			70.0	212.00 µm
Coarse	3.5	5.60 mm			80.0	180.00 µm
coars	4.0	4.75 mm	4-12		100.0	150.00 µm
Fine	8.0	2.36 mm	Granules		120.0	125.00 µm
e	10.0	2.00 mm			200.0	75.00 µm
Moder ately	20.0	850.00 µm	12-20 Tableting		230.0	63.00 µm
	30.0	600.00 µm			270.0	53.00 µm
	40.0	425.00 µm			325.0	45.00 µm
	50.0	300.00 µm			400.0	38.00 µm
	60.0	250.00 µm				

Very fine

Source: USP 31-NF 26.

Terminology of powders

Very coarse (No. 8):	**All particles pass through a No. 8 sieve and not more than 20% pass through a No. 60 sieve.**
Coarse (No. 20):	**All particles pass through a No. 20 sieve and not more than 40% pass through a No. 60 sieve.**
Moderately coarse (No. 40):	**All particles pass through a No. 40 sieve and not more than 40% pass through a No. 80 sieve.**
Fine (No. 60):	**All particles pass through a No. 60 sieve and not more than 40% pass through a No. 100 sieve.**
Very fine (No. 80):	**All particles pass through a No. 80 sieve. There is no limit to greater fineness.**

Particle size can influence a variety of important factors

1. **Dissolution rate of particles intended to dissolve; drug micronization can increase the rate of drug dissolution and its bioavailability**
2. **Suspendability of particles intended to remain un-dissolved but uniformly dispersed in a liquid vehicle (e.g., fine dispersions have particles approximately 0.5 to 10 μm)**
3. **Uniform distribution of a drug substance in a powder mixture or solid dosage form to ensure dose-to-dose content uniformity**
4. **Penetrability of particles intended to be inhaled for deposition deep in the respiratory tract (e.g., 1 to 5 μm)**
5. **Lack of grittiness of solid particles in dermal ointments, creams, and ophthalmic preparations (e.g., fine powders may be 50 to 100 μm in size**

Micromeritics

- **Micromeritics is the science of small particles; a particle is any unit of matter having defined physical dimensions**
- **Micromeritics is the study of a number of characteristics, including:**
- **particle size and**
- **size distribution,**
- **shape,**
- **angle of repose,**
- **porosity,**
- **true volume,**
- **bulk volume,**
- **apparent density, and**
- **bulkiness**

Methods exist for the determination of particle size

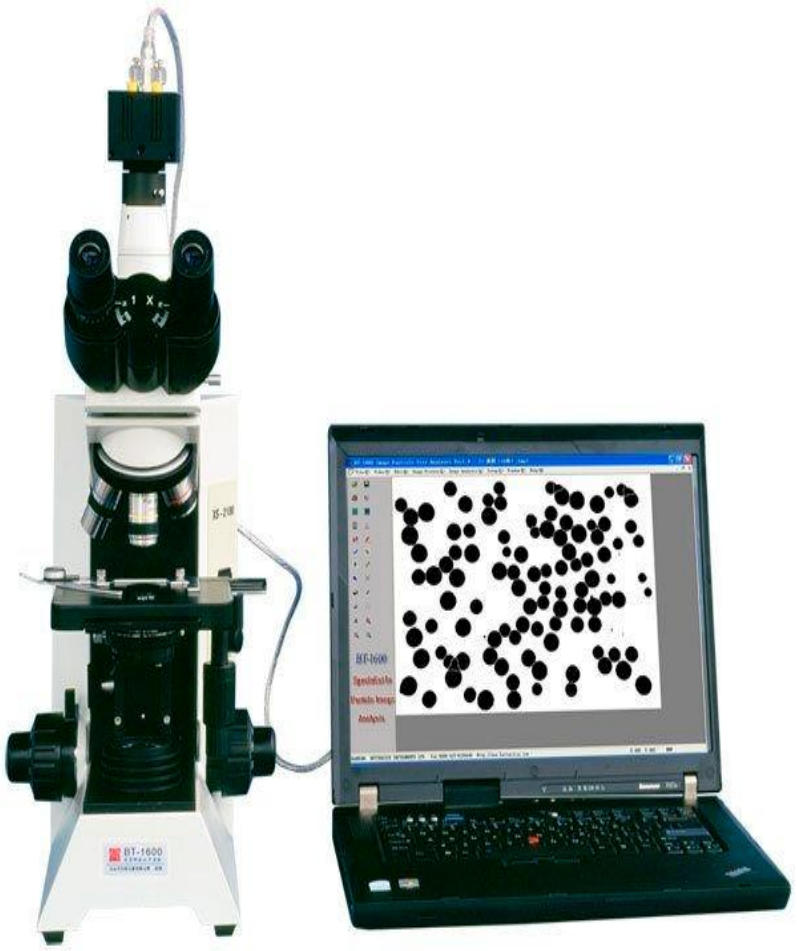
1. **Sieving, in which particles are passed by mechanical shaking through a series of sieves of known and successively smaller size and the proportion of powder passing through or being withheld on each sieve is determined (range about 40 to 9,500 µm, depending upon sieve sizes)**

Sieving

- **The sieving method entails using a set of U.S. standard sieves in the desired size range. A stack of sieves is arranged in order, the powder placed in the top sieve, the stack shaken, the quantity of the powder resting on each sieve weighed**

2. Microscopy

- In which sample particles are sized through the use of a calibrated grid background or other measuring device (range 0.2 to 100 μm) .
- The microscopic method can include not fewer than 200 particles in a single plane using a calibrated ocular on a microscope



3. Sedimentation rate method

In which particle size is determined by measuring the terminal settling velocity of particles through a liquid medium in a gravitational or centrifugal environment (range 0.8 to 300 μm). Sedimentation rate may be calculated from Stokes' law.

$$dx/dt = d^2(\rho_i - \rho_e)g/\ 18\eta$$

- **dx/dt is the rate of settling,**
- **d is the diameter of the particles,**
- **ρ_i is the density of the particle (ρ = Rho),**
- **ρ_e is the density of the medium,**
- **g is the gravitational constant, and**
- **η is the viscosity of the medium (η = Eta)**

Sedimentation

- **Another method of particle size determination entails sedimentation using the Andreasen pipet, a special cylindrical container from which a sample can be removed from the lower portion at selected intervals. The powder is dispersed in a non-solvent in the pipette and agitated, and 20-mL samples are removed over time. Each 20-mL sample is dried and weighed.**

- **The particle diameters can be calculated from this equation:**

$$V = \frac{h}{t} = \frac{d^2(\rho_i - \rho_e)g}{18\eta}$$

Where

- **d is the diameter of the particles,**
- **h is the height of the liquid above the sampling tube orifice,**
- **η is the viscosity of the suspending liquid,**
- **ρ_i - ρ_e is the density difference between the suspending liquid and the particles,**
- **g is the gravitational constant, and**
- **t is the time in seconds.**

Methods exist for the determination of particle size

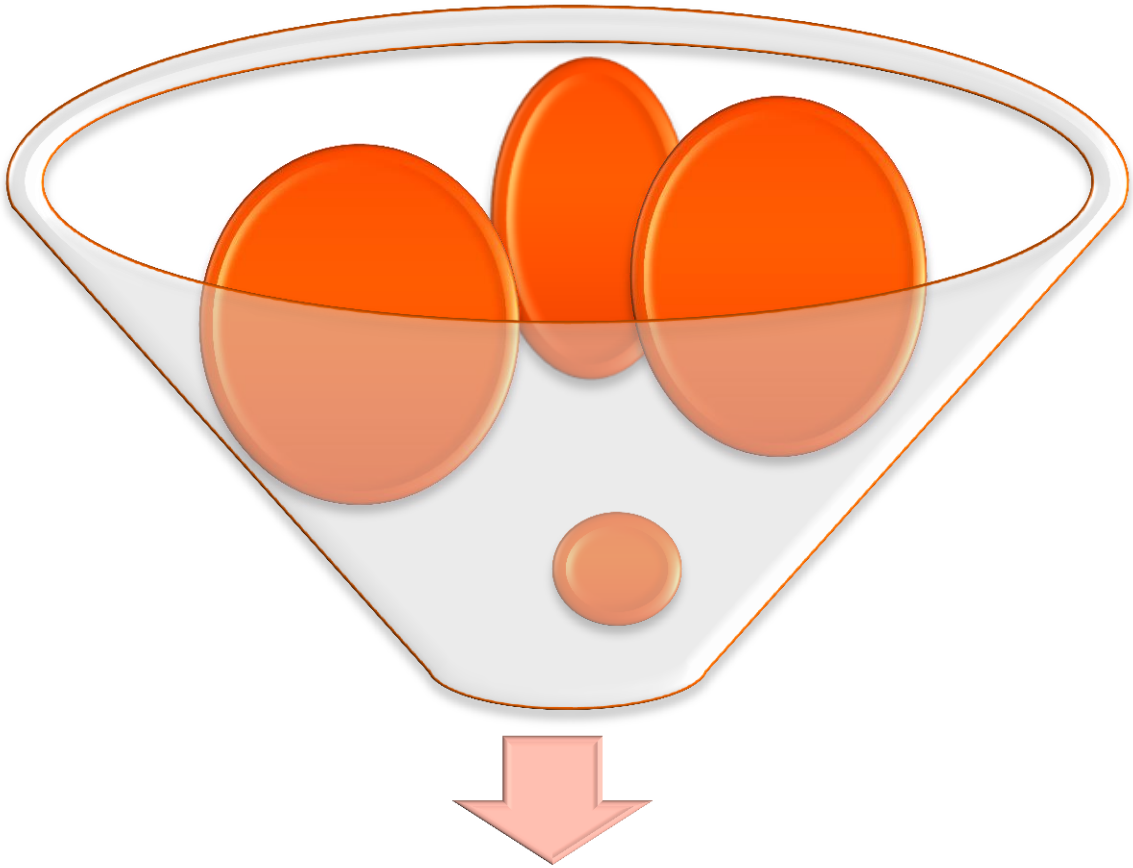
4. **Light energy diffraction or light scattering, in which particle size is determined by the reduction in light reaching the sensor as the particle, dispersed in a liquid or gas, passes through the sensing zone (range 0.2 to 500 µm).**
5. **Laser holography, in which a pulsed laser is fired through an aerosolized particle spray and is photographed in three dimensions with a holographic camera, allowing the particles to be individually imaged and sized (range 1.4 to 100 µm) .**
6. **Cascade impaction.**

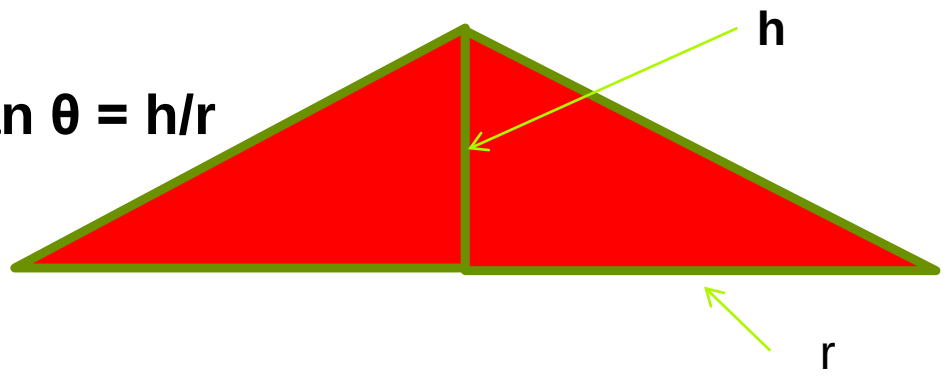
These methods may be used for the analysis of particle size and shape. For some materials, a single method may be sufficient; however, a combination of methods is frequently preferred to provide greater certainty of size and shape parameters.

Most commercial particle size analyzers are automated and linked with computers for data processing, distribution analysis, and printout.

Flowability: Angle of repose

- **The angle of repose is a relatively simple technique for estimating the flow properties of a powder. It can easily be determined by allowing a powder to flow through a funnel and fall freely onto a surface. The height and diameter of the resulting cone are measured and the angle of repose is calculated from this equation:**
- $$\tan \theta = h/r$$
- **where**
- **h is the height of the powder cone and**
- **r is the radius of the powder cone.**




tan θ = h/r
h
r

Example

- A powder was poured through the funnel and formed a cone 3.3 cm high and 9 cm in diameter. What is the angle of repose?
- $\tan \theta = h/r = 3.3/4.5 = 0.73$
- arc tan 0.73 = 36.25°
- Angle of repose as an indicator of powder flow properties

Angle of repose as an indication of powder flow properties	
Angle of repose (degrees)	Types of flow
< 20	Excellent
20 – 30	Good
30 – 34	passable
> 40	Very poor

Flowability

- Powders with a low angle of repose flow freely, and powders with a high angle of repose flow poorly
- A number of factors determine the flow properties of powders, including:
- Shape : Spherical particles flow better than needles.
- Size : Very fine particles do not flow as freely as large particles.
- In general, particles in the size range of 250 to 2,000μm flow freely if the shape is amenable.
- Particles in the size range of 75 to 250 μm may flow freely or cause problems, depending on shape and other factors.
- With most particles smaller than 100 μm, flow is a problem.

THANK YOU