AL-Mustaqbal university college
Pharmacy department

Physical pharmacy II

lec7

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objective

1-Understand the concept of particle size as it applies to the pharmaceutical sciences.
2- Discuss the common particle sizes of pharmaceutical preparations and their impact on pharmaceutical processing/ preparation.
3- Be familiar with the units for particle size, area, and volume and typical calculations.
4 -Describe how particles can be characterized and why these methods are important.
5 -Discuss the methods for determining particle size.
6- Discuss the role and importance of particle shape and surface area.
7 -Understand the methods for determining particle surface area.
8- State the two fundamental properties for any collection of particles.
9- Describe what a derived property of a powder is and identify the important derived properties.

Micromeritics

Micromeritics

The science and technology of small particles was given the name micromeritics .Colloidal dispersions are characterized by particles that are too small to be seen in the the **ordinary microscope**, whereas the particles of pharmaceutical emulsions and suspensions and the "fines" of powders fall in the range of the **optical microscope**. Particles having the size of coarser powders, tablet granulations, and granular salts fall within the **sieve range**. The approximate size ranges of particles in pharmaceutical dispersions are listed in Table 1. The unit of particle size used most frequently in micromeritics is the micrometer, **µm**, also called the micron, µ, and equal to 10^{-6} m, 10^{-4}cm, and 10^{-3}mm. One must not confuse µm with mµ, the latter being the symbol for a millimicron or 10^{-9} m. The millimicron now is most commonly referred to as the nanometer (nm).

Table 1

PARTICLE DIMENSIONS IN PHARMACEUTICAL DISPERSE SYSTEMS

Particle Size, Diameter: Micrometers (μm)	Particle Size, Diameter: Millimeters	Approximate Sieve Size	Examples
0.5–10	0.0005–0.010	—	Suspensions, fine emulsions
10–50	0.010–0.050	—	Upper limit of subsieve range, coarse emulsion particles; flocculated suspension particles
50–100	0.050–0.100	325–140	Lower limit of sieve range, fine powder range
150–1000	0.150–1.000	100–18	Coarse powder range
1000–3360	1.000–3.360	18–6	Average granule size

Any collection of particles is usually **polydisperse**. It is therefore necessary to know not only the size of a certain particle but also how many particles of the same size exist in the sample. Thus, we need an estimate of the size range present and the number or weight fraction of each particle size. This is the particle-size distribution, and from it we can calculate an average particle size for the sample.

Particle Number

A significant expression in particle technology is the ***number of particles per unit weight***, *N*, which is expressed in terms of d_{vn}. The number of particles per unit weight is obtained as follows. Assume that the particles are spheres, *ρ (Rho)* density,the volume of a single particle is $\pi d^3_{vn}/6$, and the mass (volume × density)is

$$N = \frac{6}{\pi d_{vn}^3 \rho}$$

Example

Number of Particles

The mean volume number diameter of the powder, is 2.41 μm, or 2.41×10^{-4} cm. If the density of the powder is 3.0 g/cm^3, what is the number of particles per gram?

We have

$$N = \frac{6}{\pi d_{vn}^3 \rho}$$

$$N = \frac{6}{3.14 \times (2.41 \times 10^{-4})^3 \times 3.0} = 4.55 \times 10^{10}$$

Methods for determining particle size

Many methods are available for determining particle size.

- Optical Microscopy
- Sieving
- Sedimentation

Optical Microscopy

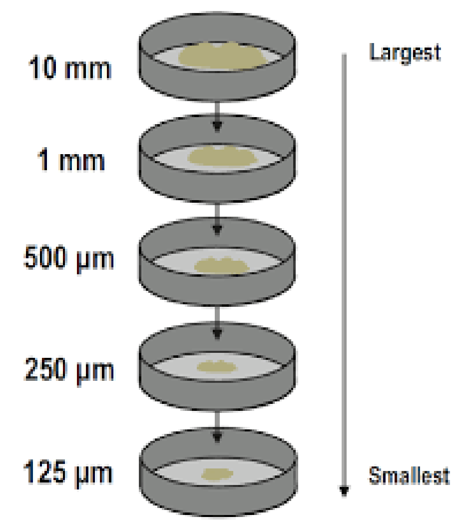
It should be possible to use the ordinary microscope for particle-size measurement in the range of 0.2 to about 100 μm. According to the microscopic method, an emulsion or suspension, diluted or undiluted is mounted on a slide or ruled cell and placed on a mechanical stage. The microscope eyepiece is fitted with a micrometer by which the size of the particles can be estimated.

Disadvantage of microscopic method 1. The diameter is obtained from only two dimensions of the particle. 2. The number of particles that must be counted (300-500) to obtain a good estimation of the distribution makes the method somewhat slow and tedious

Sieving

The sieves can be arranged in a nest of about five with the coarsest at the top .A carefully weighed sample of the powder is placed on the top sieve, and after the sieves are shaken for a predetermined period of time, the powder retained on each sieve is weighed. Sieves produced by photoetching and electroforming techniques are available with apertures from 90 μm to as low as 5 μm

sieving errors can arise from a number of variables including sieve loading and duration and intensity of agitation, the sieving can cause attrition of granular pharmaceutical materials



Sedimentation

The application of ultracentrifugation to the determination of the molecular weight of high polymers. The particle size in the subsieve range can be obtained by gravity sedimentation as expressed in Stokes's law

$$v = \frac{h}{t} = \frac{d_{st}^2(\rho_s - \rho_0)g}{18\eta_0}$$

or

$$d_{st} = \sqrt{\frac{18\eta_0 h}{(\rho_s - \rho_0)gt}}$$

where v is the rate of settling, h is the distance of fall in time t, dst is the mean diameter of the particles based on the velocity of sedimentation, ρs is the density of the particles and ρ0 that of the dispersion medium, g is the acceleration due to gravity, and η0 is the viscosity of the medium

ultracentrifugation

Example

Stokes Diameter

A sample of powdered zinc oxide, density 5.60 g/cm^3, is allowed to settle under the acceleration of gravity, 981 cm/sec^2, at 25 ∘C. The rate of settling, *v*, is 7.30 $\times 10^{-3}$ cm/sec; the density of the medium is 1.01 g/cm^3, and its viscosity is 1 centipoise = 0.01 poise or 0.01 g/cm sec. Calculate the Stokes diameter of the zinc oxide powder.

We have

$$d_{st} = \sqrt{\frac{18\eta_0 h}{(\rho_s - \rho_0)gt}}$$

$$d_{st} = \sqrt{\frac{(18 \times 0.01 \text{ g/cm sec}) \times (7.30 \times 10^{-3} \text{ cm/sec})}{(5.60 - 1.01 \text{ g/cm}^3) \times (981 \text{ cm/sec}^2)}}$$

$$= 5.40 \times 10^{-4} \text{ cm or } 5.40\ \mu\text{m}$$

Particle shape and surface area

The surface area of a powder sample can be computed from knowledge of the particle-size distribution. Two methods are commonly available that permit direct calculation of surface area. **In the first**, the amount of a gas or liquid solute that is ***adsorbed*** on to the sample of powder to form a monolayer is a direct function of the surface area of the sample .

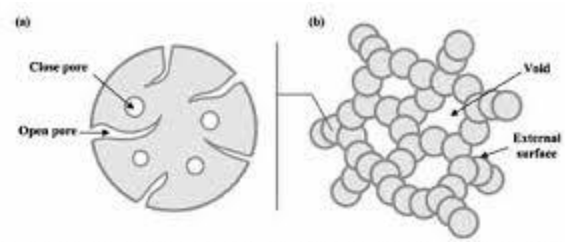
The second method depends on the fact that the rate at which a gas or liquid ***permeates*** a bed of powder is related, among other factors, to the surface area exposed to the permeant.

permeates

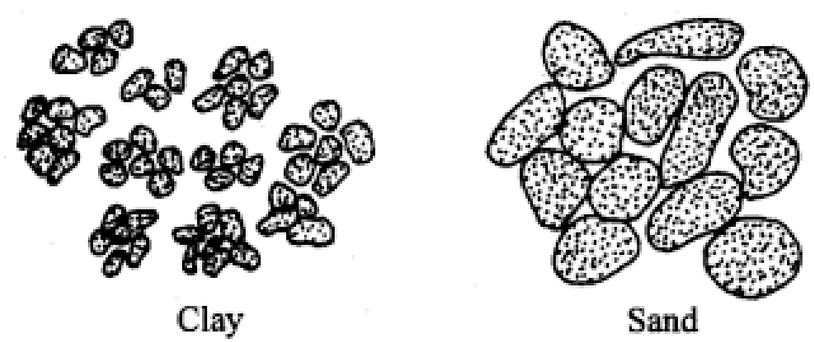
means to "pass through." It's often used to describe smells or liquids that not only pass through, but also spread to fill an entire area

Pore size

Materials of high specific area may have cracks and pores that adsorb gases and vapors, such as water, into their interstices. Relatively insoluble powdered drugs may dissolve more or less rapidly in aqueous medium depending on their adsorption of moisture or air. Other properties of pharmaceutical importance, such as the dissolution rate of drug from tablets, may also depend on the adsorption characteristics of drug powders.



Structure of porous materials: a) a single particle, b) accumulated particles.



Porosity

Suppose a powder, such as zinc oxide, is placed in a graduated cylinder and the total volume is noted. The volume occupied is known as the bulk volume, Vb. If the powder is nonporous, that is, has no internal pores or capillary spaces, the bulk volume of the powder consists of the true volume of the solid particles plus the volume of the spaces between the particles. The volume of the spaces, known as the void volume, v, is given by the equation

$$v = V_b - V_p$$

where V_p is the *true volume* of the particles. The method for determining the volume of the particles will be given later . The ***porosity*** **or** ***voids ε*** of the powder is defined as the ratio of the void volume to the bulk volume of the packing:

$$\varepsilon = \frac{V_b - V_p}{V_b} = 1 - \frac{V_p}{V_b}$$

Porosity is frequently expressed in percent, ε × 100

Example

Calculate Porosity

A sample of calcium oxide powder with a true density of 3.203 and weighing 131.3 g was found to have a bulk volume of 82.0 cm^3 when placed in a 100 mL graduated cylinder. Calculate the porosity.

The volume of the particles is

$$131.3 \text{ g}/(3.203 \text{ g}/cm^3) = 41.0\ cm^3$$

$$v = Vb - Vp$$

$$v = 82.0\ cm^3 - 41.0\ cm^3 = 41.0\ cm^3$$

$$\varepsilon = \frac{V_b - V_p}{V_b} = 1 - \frac{V_p}{V_b}$$

$$\varepsilon = \frac{82 - 41}{82} = 0.5 \text{ or } 50\%$$

Densities of Particles

Because particles may be hard and smooth in one case and rough and spongy in another, one must express densities with great care. **Density** is universally defined as weight per unit volume; the difficulty arises when one attempts to determine the volume of particles containing microscopic cracks, internal pores, and capillary spaces .

For convenience, three types of densities can be defined:

(a) the true density of the material itself, exclusive of the voids and intraparticle pores larger than molecular or atomic dimensions in the crystal lattices,

(*b*) the *granule density* as determined by the displacement of mercury, which does not penetrate at ordinary pressures into pores smaller than about 10 μm, and

(*c*) the *bulk density* as determined from the bulk volume and the weight of a dry powder in a graduated cylinder.


Thank
you