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Micromeritics

Micromeritics involve the study of small particles and of the order of a few microns size. This study involves the characterisation of individual particles, particle size distribution and powders. Further, their relevance as pharmaceutical attributes and biological necessities are important to the pharmacist, owing to their use in the manufacture of dosage forms. Particles are characterised by the following properties.

size	shape
volume	surface area
density	porosity
flow	associated properties

Particle size is normally denoted in micrometers (formerly called as microns, μ) μm. One micrometer is equal to 10^{-3} mm (millimeters) or 10^{-6} m. The term 'millimicrometer' is presently called nanometer (nm) and equal to 10^{-9} meters or 10^{-6} millimeter or 10^{-3} μm (micrometer). Knowledge and control of these properties is important in pharmacy.

The **applications** of micromeritics in pharmacy are as follows:

Release and dissolution : Particle size and surface area influence the release of drug from a dosage form that is administered orally, rectally, parenterally and topically. Higher surface area brings about intimate contact of the drug with the dissolution fluids *in vivo* and increases the drug solubility and dissolution. In general, higher the surface area, better the release. Hence faster is the dissolution.

Absorption and drug action : Particle size and surface area influence the drug absorption and subsequently the therapeutic action. Higher the dissolution, faster the absorption. Hence, quicker and greater is the drug action.

Physical stability : Particle size influences the physical stability of suspensions and emulsions. Smaller the size of particles, better the physical stability of the dosage form owing to Brownian movement of the particles in the dispersion.

Dose uniformity : Good flow properties of granules and powders are important in the manufacture of tablets and capsules. The distribution of particles should be uniform in terms of its number and weight. At the same time, the flow of granules should be uniform in order to ensure precise weight of the tablet and drug content.

Comment 6-1. Physical stability of a suspension depends on the surface area of particles. True or false. Justify.

PARTICLES—CHARACTERISTICS

Particle characteristics influence the dissolution rate, absorption rate, content uniformity, taste, texture, colour and stability. Each particle can be characterised and expressed by the following properties.

- size
- shape
- volume
- surface area

Some of these are discussed here.

Particle Size

The shape of particles present in a powder is normally not spherical, but asymmetrical (uneven). Therefore, it is difficult to express the size as a meaningful diameter. However, particle size is expressed as the diameter which is related to an equivalent spherical diameter. Size of the particles may be expressed as follows:

(i) *Surface diameter, d_s* : is the diameter of a sphere having the same surface area as that of the asymmetric particle.

(ii) *Volume diameter, d_v* : is the diameter of a sphere having same volume as that of the asymmetric particle.

(iii) *Projected diameter, d_p* : is the diameter of a sphere having the same area of the asymmetric particle as observed under a microscope.

(iv) *Stokes' diameter,* d_{st} : is the diameter of an equivalent sphere undergoing sedimentation at the same rate as the asymmetric particle.

(v) *Sieve diameter,* d_{sieve} : is the diameter of a sphere that passes through the same sieve aperture as the asymmetric particle.

(vi) *Volume-surface diameter,* d_{vs} : is the diameter of a sphere that has same volume to surface area ratio as the asymmetric particle.

From the above descriptions, it is possible to conclude that same particle possesses different values for the diameter. Appropriate diameter should be selected depending on the intended purpose for which it is being applied in pharmacy. Accordingly, a suitable method of measurement should be selected. In addition to these, there are a number of descriptions for a particle diameter, which are available in books given in bibliography.

Comment 6-2. Particle size is mostly expressed in terms of an equivalent spherical diameter. Why?

Particle Shape

Particle shape is related to geometric shape and surface regularity (rugosity) (Figure 6-1). Particle shape will influence the surface area, flow of particles, packing and compaction properties of the particles. The surface area per unit weight and unit volume are important in the studies of adsorption and dissolution.

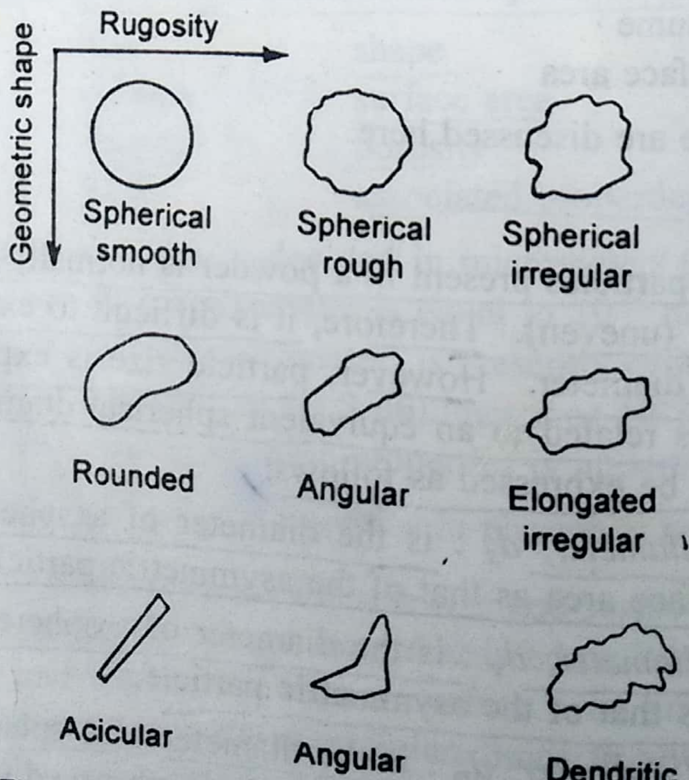

Figure 6-1. Characteristic particle shapes related to geometric shape and surface irregularity.

It is possible to determine whether the shape of a particle is spherical or asymmetric. A sphere has minimum surface area per unit volume. Therefore, these properties can be compared for spheres and asymmetric (consider projected diameter, d_p) particles, in order to decide the shape. The following expression can be obtained.

Property	*Sphere*	*Particle*
Surface area	πd_s^2	$\alpha_s \times d_p^2$
Volume	$(1/6)\pi d_s^3$	$\alpha_v \times d_p^3$

where α_s and α_v are the surface area factor and the volume factor, respectively, for the asymmetric particle. Solving for α_s and α_v by equating the appropriate properties (surface area and volume) provides:

$$\alpha_s = \frac{\pi d_s^2}{d_p^2} \quad \text{and} \quad \alpha_v = \frac{\pi d_s^3}{6 d_p^3}$$

When d_s is made equal to d_p, the relationship may be written as:

$$\alpha_s = \pi = 3.124 \text{ and } \alpha_v = \pi/6 = 0.524$$

The *shape factor* of particle can be expressed as the ratio of surface to volume factors, then

$$\text{Shape factor} = \frac{\alpha_s}{\alpha_v} = \frac{3.124}{0.524} = 6 \qquad (1)$$

The minimum possible value for shape factor is 6, which represents a sphere. If the ratio exceeds this factor 6, the particle is considered as asymmetric.

Comment 6-3. The shape of particles is an important parameter to study the rate of dissolution of drugs. True or false. Explain.

Comment 6-4. Shape factor ratio a_s/a_v is 6 for a spherical particle. For an asymmetric particle, this ratio will be more than 6. True or false. Justify.

POWDERS—CHARACTERISTICS

Powder is considered as a collection of particles. Therefore, the properties (examples are taste, texture, colour etc.), that are ascribed to a particle, can as well be applied to powder. At the same time, particles also collectively contribute certain properties to the powder. Thus, powder is characterised and expressed by the following properties.

- powder size
- surface area
- flow properties
- particle number
- volume
- density

Some of them are described here.

Powder Size

Powder is considered as a collection of particles. If the powder contains particles of one size, the powder is termed monosize or *monodisperse*. Uniform size particles are normally obtained by passing the powder through the sieves of the desired aperture. Mono-size particles are important in pharmacy in the following areas.

(a) Standardisation of instruments, particle size analyser.

(b) Accurate determination of pore size in case of filters.

(c) For effective immunisation, normally, antigens are made to adsorb on uniform sized particles.

(d) For diagnostic purposes.

Most of the pharmaceutical powders are *polydisperse*, i.e., contain particles of different sizes. There is no universal way of defining size of a powder. However, it is necessary to assign powder with a characteristic value. Attempts have been made to describe the powder by arithmetic mean, geometric mean and harmonic mean.

Particle Number

The number of particles present in a dosage form should remain constant in order to maintain dose uniformity. This is important when drug particles are mixed with other ingredients to prepare tablets and capsules. The number of drug particles vis-a-vis number of particles of other ingredients should be maintained constant for a given weight of dosage form. Larger the number of drug particles, smaller is the error. Errors are large, when the number of drug particles are small. Particle number is more important in case of low dose drugs or potent drugs.

The number of particles per unit weight, N, is expressed in terms of volume-number mean diameter, d_{vn}. Assuming that the particles are