INDUSTRIAL PHARMACY-I

UNIT I-PREFORMULATION

CLASS4

TOPIC: Particle size, shape, flow properties

Fine particle characterization

Particle size of drugs may affect formulation and product efficacy.

Certain physical and chemical properties of drug substances are affected by the particle size distribution including; drug dissolution rate, content uniformity, texture, stability, flow characteristics, and sedimentation rates.

Particle size significantly influences the oral absorption profiles of certain drugs

METHODS TO EVALUATE PARTICLE SIZE AND DISTRIBUTION

1. Sieving or screening
2. Optical microscopy
3. Sedimentation
4. Stream scanning.

Sieving or screening:

Disadvantage: It requires a relatively large samplesize.

Advantage: Simplicity in technique and equipment requirements.

Optical microscopy:

It is the first step in the determination of particle size and shape for new drug substance.

Disadvantage:

Quantitative evaluations need minimum1000 particles (tedious and time consuming).

The slide must be representative of the bulk of the material.

Sedimentation:

It utilize the relationship between rate of fall of particles and their size.

Disadvantage: Proper dispersion, consistent sampling ,temperature control, must be carefully controlled to obtain consistent and reliable results.

Stream scanning:

Technique utilizes a fluid suspension of particles which pass the sensing zone where individual particles are sized, counted & tabulated.

Sensing units are based on ; light scattering transmission, as well as conductance.

The popular unit in the pharmaceutical industry for thispurpose is the Coulter Counter

Advantages:

The unit electronically size, count and tabulate the individual particles that pass through the sensing zone

and data is obtained in a short time with reasonable accuracy.

Thousands of particles can be counted in seconds and used to determine the size distribution curve.

It is a powerful tool and can be used for evaluation ofparameters as crystal growth in suspension formulation.

Sieving	Size range
Optical microscopy	0.5-150mu m
Elecron microscope	0.001-5 mu m
Coulter counter method	1-200 mu m
Laser diffractometer	1-1900 mu m

3. Particle Surface Area

Determination of particle surface area – adsorption method and air – permeability method.

Maximum surface area ensures better solubility

Smaller the drug particle, greater the surface area.

Size and surface area are inversely related to each other.

Determination of particle size – microscopy method and light scattering method

Shape- Particle Shape

Shape also influences rate of dissolution of drugs.

Spherical particles have minimum surface area and better flow properties

has a influence on the surface area, flow properties, packing and compaction of the particles.

Preformulation and flow property

In preformulation stage the drug is available in small quantity so flow property is determined by bulk density and angle of repose.

Importance of flow property in Pharmaceutical Industry

 For easy handling of drug powder in storage

 For easy handling in processing like flow through the hopper of tablet punching machine etc.

 For ensuring good mixing

 For ensuring content uniformity

 For ensuring the particle size uniformity and stability.

 Increase in crystal size or more uniform size leads to smaller angle of repose and smaller Carr's index

Densities of particles should be observed carefully because sometimes particles can be hard and smooth in one case, and rough and spongy in another. Density is defined as weight per unit volume. Four different types of densities are generally observed

- Measure using the gas displacement or liquid displacement method.
- True volume – volume obtained excluding the void volume and intra particle pores
  True density = Powder Weight / True Volume
- Density of the material itself.

Tapped Density

Ratio of the mass of the powders to the volume occupied by powder after it has been tapped for a defined period of time.

Defined as the mass of the powder divided by the bulk volume. ♣

2. Granule Density

Granule density measured using mercury displacement method.
♣Granule density = Granule Weight / Granule Volume
♣for granules that are employed in the manufacture of tablets
3. Bulk Density
Bulk density value indicates the volume of all pores within te powder sample. 4.
Bulk density = Bulk Weight / Bulk Volume

Angle Of Repose:
It is the maximum angle between the surface of a pile of powder and horizontal plane

$$\text{Tan } \theta = h/r$$

The rougher and more irregular the surface of the particles, the higher will be the angle of repose.
Lower values indicates better flow characteristics.
The acceptance criteria for angle of repose are:32

Angle of repose	Type of flow
< 20	Excellent flow
20-30	Good flow
30-34	Passable
>40	Poor flow

. Carr's compressibility index

Carr's index (%) =Tapped density–bulk density x100/Tapped density

By decreasing the bulk and tapped density good flow properties can be obtained.

Carr's index	Type of flow
5-15	Excellent
12-16	Good
18-21	Fair to passable
23-35	Poor
33-38	Very poor
>40	Extremely poor

Hausner `s ratio:

Hausner `s ratio = Tapped density X 100/bulk density

Hausners ratio	Type of flow
< 1.25	Good flow
> 1.5	Poor flow
1.25-1.5	Glidant addition required

Cars index	Hausners ratio	Flow ability
5-15	1.05-1.18	Excellent
12-16	1.14-1.20	Good
18-21	1.22-1.26	Passable
23-35	1.30-1.54	Poor
33-38	1.50-1.61	Very poor
>40	>1.67	vv poor