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Unit: IV

Topic: Methods for determining particle size by different methods

Sieving Method

Particles having size range between 50 and 1500 μm are estimated by sieving method. In this method, the size is expressed as d_{sieve}, which describes the diameter of a sphere that passes through the sieve aperture as the assymmetric particle. This method directly gives weight distribution.

The sieving method finds application in dosage form development of tablets and capsules. Normally 15 per cent of fine powder (passed through mesh 100) should be present in granulated material to get a proper flow of material and achieve good compaction in tabletting. Therefore, percent of coarse or fine powder can be quickly estimated.

Sieves for pharmaceutical testing are constructed from wire cloth with square meshes, woven from wire of brass, bronze, stainless steel or any other suitable material. Sieves should not be coated or plated. There must be no reaction between the material of the sieve and the substance to be sieved. Standard sieves and their dimensions as per IP are given in Table 6-5.

TABLE 6-5

Designations and Dimensions of I.P. Specification Sieves

Sieve number	*Aperture size micrometer*	*Sieve number*	*Aperture size micrometer*
10	1700	44	325
12	1400	60	250
16	1000	85	35
22	710	100	36
25	600	120	34
30	500	150	36
36	425	170	35

Method : Standard sieves of different mesh numbers are available commercially as per the specifications of I.P. and U.S.P. Sieves are

arranged in a nest with the coarsest at the top. A sample (50 g) of the powder is placed on the top sieve. This sieves set is fixed to the mechanical shaker apparatus and shaken for a certain period of time (20 minutes). The powder retained on each sieve is weighed. Frequently, the powder is assigned the mesh number of the screen through which it passes or on which it is retained. It is expressed in terms of arithmetic or geometric mean of the two sieves. For example, a powder passing through a 36 mesh and retained on 44 mesh sieve is assigned an arithmetic mean diameter of (425 + 325)/2 or 375 μm. This is reported as undersize. Data are analyzed for normal, log-normal, cumulative per cent frequency distribution and probability curves (Figures 6-3, 6-4, 6-5 and 6-6). The relevant diameters such as geometric mean weight diameter and standard deviation can be obtained. Data processing for a granular material is shown in Table 6-6.

TABLE 6-6
Weight-size Distribution of a Granular Materials as Measured by the Standard Sieves

Sieve number (passed/ retained)	*Arithmetic mean size of opening μm*	*Weight retained on a sieve g*	*Per cent weight retained (undersize)*	*Cumulative per cent retained*
30/45	470	57.3	13.0	13.0
45/60	300	181.0	41.2	54.2
60/80	213	110.0	25.0	79.2
80/100	163	49.7	11.3	90.5
100/140	127	20.0	4.5	95.0
140/200	90	22.0	5.0	100.0

Practical considerations : Care should be taken in order to get reproducible results. The type of motion influences sieving; vibratory motion is most efficient, followed by side-tap motion, bottom-pat motion, rotary motion with tap and finally rotary motion. The type of motion (intensity) of the shaker is fixed and standardized. Shakers are commercially available.

Other factors are weights of samples and duration of shaking. Sieves produced by photoetching and electroforming techniques are used to get a better estimate of the size distribution analysis with a lower limit of estimation of particle diameter 5 μm.

Advantages : It is inexpensive, simple and rapid with reproducible results.

Disadvantages:

(a) Lower limit of the particle size is 50 μm.

(b) If powder is not dry, apertures become clogged with particles, leading to improper sieving.

(c) During shaking, attrition (particles colliding with each other) occurs causing size reduction of particles. This leads to errors in estimation.

Sedimentation Method

Sedimentation method may be used over a size range of 1 (one) to 200 μm. In this method, size is expressed as Stokes' diameter, d_{st}, which describes the diameter of an equivalent sphere having the same rate of sedimentation as that of the asymmetric particle. Sedimentation of particles may be evaluated by different methods. Some of these are Andreasen pipette method, balance method and hydrometer method. Andreasen pipette method is discussed here.

Sedimentation method finds applications in:

(a) formulation and evaluation of suspensions

(b) formulation and evaluation of emulsions

(c) determination of molecular weight of polymers

Physical stability of a suspension depends on the rate of settling of particles in the dosage forms. Similar arguments have been proposed for the evaluation of physical stability of emulsions.

Principle : The rate of settling of particles in a suspension or emulsion may be obtained by Stokes' law. The equation is rearranged to get the Stokes' diameter, d_{st}, of particles.

$$d_{st} = \sqrt{\frac{18\eta_0 h}{(\rho_s - \rho_0)gt}} \qquad (11)$$

where h = distance of fall in time, t

η_o = viscosity of the medium

ρ_s = density of the particles

ρ_o = density of the dispersion medium

g = acceleration due to gravity

Equation (11) holds good for spheres falling freely at a constant rate without hindrance. However, equation (11) can be extended to irregu-

larly shaped particles of various sizes. Here it is assumed that the rate of settling of the particle is same as the sphere and therefore, size is expressed as the size of an equivalent sphere.

When the powder is suspended in a vehicle, initially the particles of large diameter settle due to heavy weight. After some time, particles of intermediate diameter will settle. Finally, the particles of smaller size settle. Hence, the study involves the sampling during sedimentation at different time intervals.

Practical considerations : The following points are considered to obtain the size analysis accurately.

1. *The suspension should be dilute* (about 1 to 2 per cent). For the estimation, powder is dispersed in a medium to get a suspension. Some times, particles form aggregates or get clumped together and fall faster due to its weight. This leads to errors. A proper deflocculating agent has to be added to keep particles free and separated, so that each particle sediments individually. Therefore, a dilute suspension is preferred.

2. *Flow should be laminar*, i.e., rate of sedimentation of particles must not be too rapid to create turbulence. Any turbulent flow will affect the sedimentation of other particles thereby causing error in the estimation. The type of flow, (whether turbulent or laminar), is indicated by the dimensionless *Reynolds number*, R_e, which is defined as:

$$R_e = \frac{v d \rho_o}{\eta_o} \tag{12}$$

If Reynolds number is greater than 0.2, the flow is turbulent. Sedimentation method predicts the exact particle size, if the Reynolds number does not exceed 0.2. Thus, the validity of the data can be verified. Combining equations (11) and (12) gives:

$$v = \frac{R_e \eta_o}{d_{st} \rho_o} = \frac{d_{st}^2 (\rho_s - \rho_o) g}{18 \eta_o} \tag{13}$$

or

$$d_{st}^3 = \frac{18 R_e \eta_o^2}{(\rho_s - \rho_o) \rho_o g} \tag{14}$$

Equation (14) allows the calculation of maximum particle diameter, whose sedimentation will be governed by Stokes' law, when R_e does not exceed 0.2. Large, dense particles settle quite fast. In such cases, it may be necessary to increase either the density or the viscosity of the suspending fluid in order to maintain streamline flow.

Method : The Andreasen apparatus is shown in Figure 6-8. It usually consists of a 550 ml cylindrical vessel containing a 10 ml pipette sealed to a ground glass stopper. When the pipette is placed in the cylinder, its lower tip is 20 cm below the surface of the suspension.

The procedure is as follows:

Prepare 1 or 2% suspension of the powder in a suitable medium. A deflocculating agent will help in uniform dispersion of the suspension. Transfer the suspension into the Andreasen vessel. Place the stopper and shake the vessel to distribute the suspension uniformly. Remove the stopper and place the two-way pipette and securely suspend the vessel in a constant temperature water bath.

At different time intervals, 10 ml samples are withdrawn using two-way stopcock and collected in a watch-glass. Samples are evaporated and weighed. The weight or the amount of particles obtained in each time interval is referred to as weight undersize. The weights are converted into cumulative weight undersize.

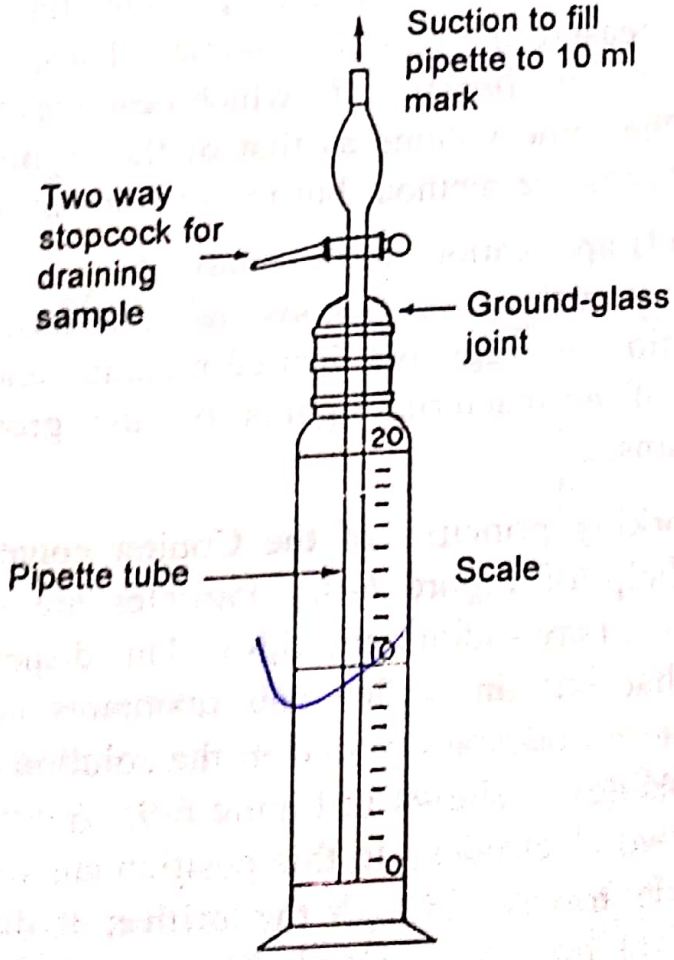

Figure 6-8. Andreasen apparatus for determining particle size by gravity sedimentation method.

Particle diameter is calculated from Stokes' law, with 'h' in equation (11) being the height of the liquid above the lower end of the pipette at

Conductivity Method

Particle size ranging from 0.5 to 500 μm is measured by conductivity method. This method gives number distribution. In fact, particle volume is measured and converted into particle diameter. Coulter counter is used to measure the particle volume. Thus, in this method, size is expressed as *volume diameter*, d_v, which describes the diameter of the sphere having the same volume as that of the asymmetric particle. This is a quick and accurate method, but the instrument is expensive.

This method finds applications in the study of—

(a) particle growth in suspensions and solutions,
(b) dissolution of drugs in a desired medium, and
(c) effect of antibacterial agents on the growth of micro-organisms.

Principle : Working principle of the Coulter counter may be explained with the help of Figure 6-9. Particles are suspended in a conducting electrolyte (say sodium chloride). This dispersion is filled in the sample cell, that has an orifice and maintains contact with the external medium. Electrodes are placed in the solution (inside the cell) and suspension (outside) as shown in Figure 6-9. A constant voltage is applied across the two electrodes. In this position current passes. When a suspended particle travels through the orifice, it displaces its own volume of electrolyte into the beaker. The net result is a change in electrical resistance. This change in electric resistance is termed as voltage pulse, which is related to the particle volume. This voltage pulse is amplified and fed to a pulse height analyzer. This analyzer is previously calibrated in terms of particle size for different threshold settings.

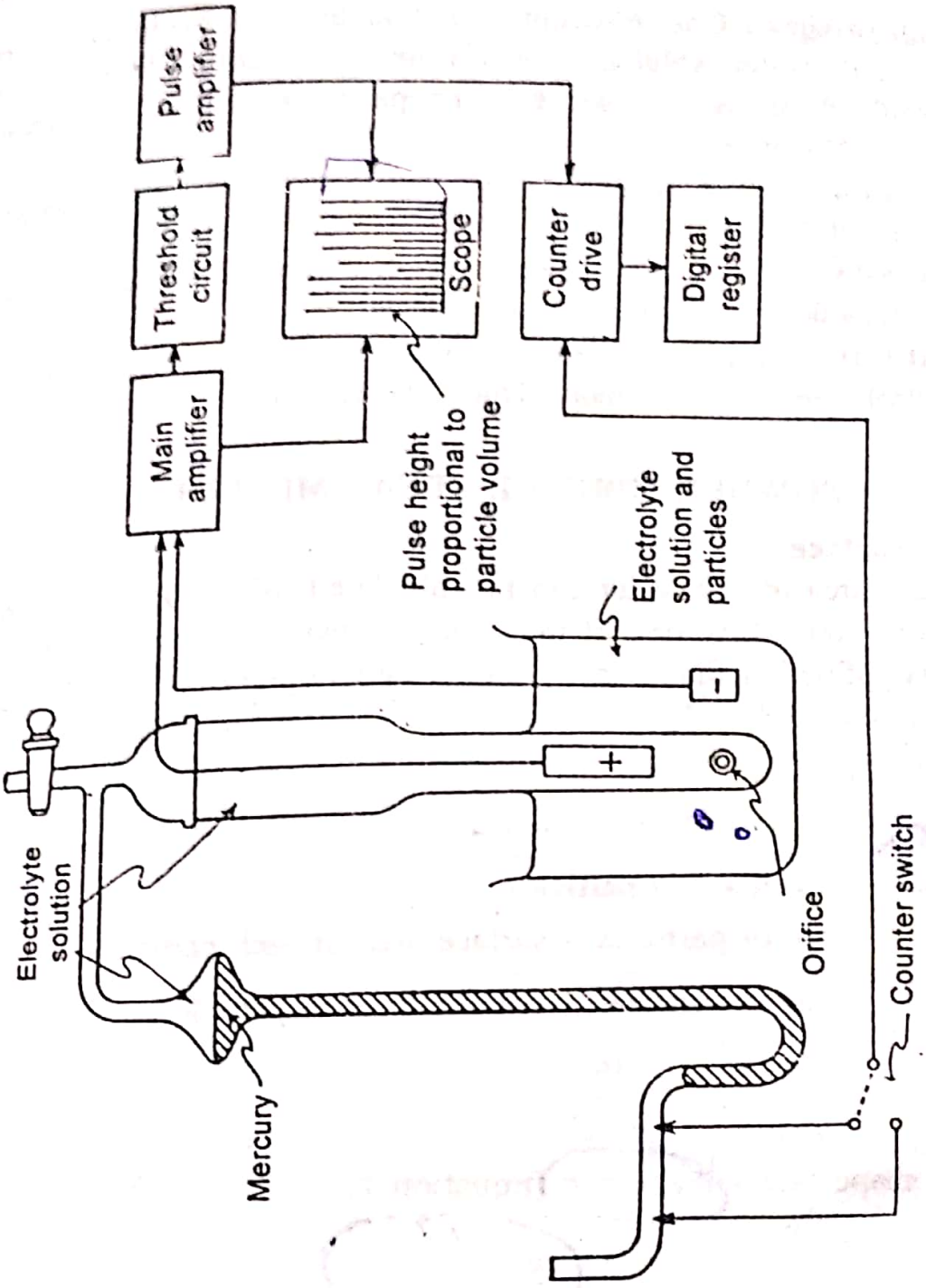

Figure 6-9. Schematic diagram of Coulter counter used to determine particle volume.

For a given threshold value, the pulses are electronically counted. By changing the threshold settings gradually, number of particles of each size range is obtained. Thus the particle size distribution can be obtained.

Conductivity method is also known as *stream scanning*, i.e., a fluid suspension of particles passes through a sensing zone, in which individual particles are electronically sized, counted and tabulated.

Advantages : Using Coulter counter apparatus, approximately 4000 particles per second can be counted. Therefore size distribution analysis can be completed in a relatively short period of time. It gives reasonably accurate results.

Disadvantages : Coulter-counter method may be unsuitable for polar- and highly water- soluble materials due to solvation. In such cases, if a nonsolvent is used to suspend the particles, it may not produce adequate conductance.