

## A Study on Analysis of Particle Size Distribution

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**Abstract** □ Analysis of particle size distribution of a sample of fine aluminum hydroxide powder was carried out by four different methods, *i. e.*, conductivity, air permeability, gas-adsorption and sedimentation. Each method was reproducible. The results obtained by Coulter counter and sedimentation balance were similar, and the data obtained by Lea and Nurse permeameter and Stroeblein areameter were also similar. But the results differ considerably between the former and the latter. The advantages and disadvantages of each method were discussed briefly and a means of comparing the results with those obtained by surface area measurements was shown.

**Keywords** □ Determination of particle size aluminum hydroxide powder. Four methods of conductivity, air permeability, gas adsorption and sedimentation— comparison of these methods.

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Knowledge and control of the size and size range of particles are of profound importance in pharmacy. One of the most significant occurrences in recent years is the realization that size, and hence surface area, of a particle can be related in a significant way to physical, chemical and pharmacological properties. The field of particle size measurement and analysis are extensive and complex. The measurement of particle size and particle size

distribution may be carried out in a large number of ways.<sup>1~2)</sup>

Different analytical methods measure different particle size parameters or different properties of the particles. It is therefore often said that the analytical method should be chosen to match the end use of the product. The analytical methods differ considerably in range and sensitivity. Proper choice of method may depend merely on the size range of the sample and on the particle size of the distribution for which information is required. As a consequence, results produced by different method often are mutually inconsistent, limited in application and uncertain in interpretation. Often there will be uncertainty as to which particle-size parameter is relevant to a particular application.

In a period when the automation and operating speed of analytical instruments are becoming as important as accuracy, a frequent and careful appraisal of techniques available for fine particle analysis should be made to facilitate meeting the needs of industry rapidly and effectively.

It is the purpose of this paper to compare briefly four different methods of particle size analysis, *i.e.* conductivity, air permeability

gas adsorption and sedimentation method. Aluminum hydroxide fine powder was chosen as a sample.

## MATERIALS AND METHODS

### Equipment

Coulter counter model A (Coulter Electronics Ltd.) Lea and Nurse permeameter (Baird Tatlock Ltd.) Stroehlein Areameter (Stroehlein Co.), Sartorius 4600 sedimentation balance (Sartorius), and Computer CDC cyber 72.

### Material

Apumine A (Aluminum hydroxide) (AFN-OR), Sodium chloride injection 0.9% w/v (BP), Calibration latex (diameter 12.92  $\mu$ ) (Coulter Electronics Ltd.), Nitrogen gas (British Oxygen Co.), Liquid nitrogen Dewar (Union Carbide), Sodium pyrophosphate (BDH Chemicals), and Nonidet p 40 (BDH Chemicals)

### Method of Size Analysis

#### 1) Coulter counter

##### A) Calibration

Two drops of calibration latex (monodisperse polystyrene spheres) were mixed in 100ml of 0.9% w/v sodium chloride injection. The orifice diameter selected was 100  $\mu$ . Background and coincidence corrections were made in the ordinary way.

##### B) Preparation of suspension.

About 20mg of Apumine A were mixed with a drop of Nonidet p 40 and suspended in 1000 ml of 0.9% w/v sodium chloride injection. The solution were placed on a ultrasonic bath for a period of several seconds. The final concentration of Apumine A suspen-

sion was adjusted to count about 20,000 particles when t' is kept 30 and I is set at 10.

##### C) Calculation

Calibration constant was obtained from:

$$K = \frac{dV}{\frac{3}{2} \sqrt{t}}$$

Where K is calibration const., dv is the diameter of the monosized particles, in microns, t is equivalent particle volume (t' x F) and F is expansion factor.

The diameter, dv, of sample was calculated according to the expression.

$$dv = K \cdot \sqrt[3]{t}$$

The cumulative oversize and diameters of particles were calculated by using computer.

#### 2) Lea and Nurse permeameter

A) Calibration Calibration was carried out with air.

##### B) Preparation of sample

Apumine A was weighed to give, when compacted in the powder bed, 1cm deep x 2.54cm diameter. The cell is then tapped four times by allowing it to fall from a height of about 1cm onto the bench.

##### C) Calculation

The average value of the flowmeter constant was calculated from

$$C = \frac{V}{t} \cdot \frac{P_1 - P_2}{P_1} \cdot \frac{\eta}{h_2 \rho_L}$$

where v is the measured volume of damp air in ml collected in t seconds at atmospheric pressure. P<sub>1</sub>, P<sub>2</sub> is the vapor pressure of water at room temperature,  $\eta$  is the viscosity in cgs units of air at room temperature and  $\rho_L$  the density of the flowmeter fluid in gm.<sup>-3</sup> The specific surface area pergram of material (S<sub>w</sub>) is given by the formula:

$$S_w = K \sqrt{h_1/h_2}$$

$$\text{Where } K = \frac{14}{\rho(1-\varepsilon)} \sqrt{\frac{\varepsilon^3 A}{C \cdot L}}$$

$\varepsilon$  is the porosity, A the area (cm<sup>2</sup>) and L the depth (cm) of the bed,  $\rho$  is the density of the powder, C the flowmeter constant and  $h_1$  and  $h_2$  are the difference in reading in cm of manometer and flowmeter, respectively.

### 3) Stroehlein areameter

#### A) Preparation of sample

Ten grams of Apumine A, accurately weighed, were put into an adsorption vessel. The vessels with samples were placed into the heating block, set at 200°C, and purged, by means of the capillaries with nitrogen for half an hour to remove adsorbed impurities.

#### C) Calculation

The specific surface area of the sample ( $S_w$ ) was evaluated from the equation:

$$S_w = \frac{A \cdot \Delta h}{m} + \frac{B}{d}$$

Where  $\Delta h$  is the pressure difference (mm) indicated on the differential manometer, m is weight (g) of the sample of density d, and A and B are coefficients determined from the pressure difference and atmospheric pressure.

### 4) Sedimentation balance

#### A) Calibration

In about 550ml of distilled water 2.23g of sodium pyrophosphate were dissolved. The calibration was carried out in the ordinary way with this solution.

#### B) Preparation of suspension

After calibration of the instrument with the sedimentation liquid, about 670 mg of Apumine A was then poured into the sedimentation liquid. By continuous stirring (up and down movement) and turning of the

collecting pan the suspension is homogenized. The uniformity of particles is inspected by microscopy.

#### C) Calculation

Filling weight was calculated as follows:

$$\text{Filling weight} = \frac{500 \times \rho_K}{\rho_K - \rho_F}$$

where  $\rho_K$  is specific gravity of sample and  $\rho_F$  is specific gravity of liquid.

According to Stoke's equation the Stoke's diameter ( $d_{st}$ ) of particles was calculated.

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

Where  $\eta_0$  is the viscosity of the medium, h is the distance of fall in time t,  $\rho_s$  is the density of the particles and  $\rho_0$  that of the dispersion medium, g is the acceleration due to gravity. From the tangents at the inner curve the residue was determined.

The residue value was also determined by calculation, which is possible due to the steplike curve.

$$R' = G - \frac{\Delta G}{\Delta t} \times t$$

$$R = R' / E g \times 100 \%$$

Where R is residue value, R' is residue value on the abscissa t is the chosen time on the ordinate, G is the deposited sediment of the time t,  $\Delta G$  is the weight increase per step (0.08cm),  $\Delta t$  is the time in cm, within which the weight increase  $\Delta G$  occurred and E g is the theoretical end weight.

## RESULTS AND DISCUSSION

### Method of Analysis

The four common methods of sizing in the fine particle size range, Coulter counter, Lea

**Table I: Coulter counter size analysis of Apumine A.**

Gain	Threshold	Current	Scale expansion factor		Counts	Mean	Background	
3.0	300.0	1.0	1.0000000	1.0	1.0	1.0	1.0	
3.0	150.0	1.0	1.0000000	2.0	2.0	2.0	1.0	
3.0	150.0	1.0	1.0000000	6.0	2.0	2.0	1.0	
3.0	90.0	1.0	1.0000000	6.0	2.0	4.0	1.0	
3.0	60.0	1.0	1.0000000	18.0	12.0	15.0	1.0	
3.0	60.0	2.0	.5007400	150.0	166.0	160.5	1.0	
3.0	60.0	3.0	.2513200	2068.0	2351.0	2209.5	1.0	
3.0	60.0	4.0	.1265400	10482.0	10087.0	10284.5	1.0	
3.0	60.0	5.0	.0641420	10742.0	16555.0	13648.5	1.0	
3.0	60.0	6.0	.0329560	18070.0	17664.0	17867.0	1.0	
3.0	60.0	7.0	.0173863	17794.0	17983.0	18349.0	2.0	
3.0	60.0	8.0	.0096300	19193.0	19766.0	20918.0	19959.0	3.0
3.0	60.0	9.0	.0058127	19689.0	20229.0	21159.0	20359.0	4.0
3.0	60.0	10.0	.0040264	20867.0	21128.0	21357.0	21117.3	5.0
3.0	30.0	10.0	.0040264	22074.0	23648.0	23263.0	22995.0	7.0
Aperture diameter	100.00 microns			Manometer volume		50 mls.		
Calibration factor	4.699			Aperture resistance		15000.0 ohms.		
Coincidence	2.50							

and Nurse, Stroehlein areameter and sedimentation balance, were used in this experiment.

Although simple in principle and reliable in operation, the Coulter counter is a highly sophisticated apparatus. The proper methods for using it and in interpreting its results are still being developed.

A second method that of surface area measurement, which may be translated into mean particle size if desired, gives no information on the distribution of particle sizes in the sample.

Two well-known methods of measuring surface area of solids are available: One the permeability of a compressed plug of powder to a fluid, usually air, under ordinary atmospheric conditions, and the other involves

measuring the volume of gas, usually nitrogen adsorbed by a given weight of sample at liquid air temperatures.

In sedimentation methods the property measured is the free falling speed, and the particle size is defined as the diameter of a hypothetical sphere whose falling speed is the same as that of the particle under identical conditions.

Coulter counter:

The upper particle volume diameter, which may be measured with any orifice, is limited to about 40% of the orifice diameter, since frequent blocking of the orifice occurs if larger particles are present in the suspension. Successive counts at different threshold levels gives the data for determining the cumulative frequency oversize curve.

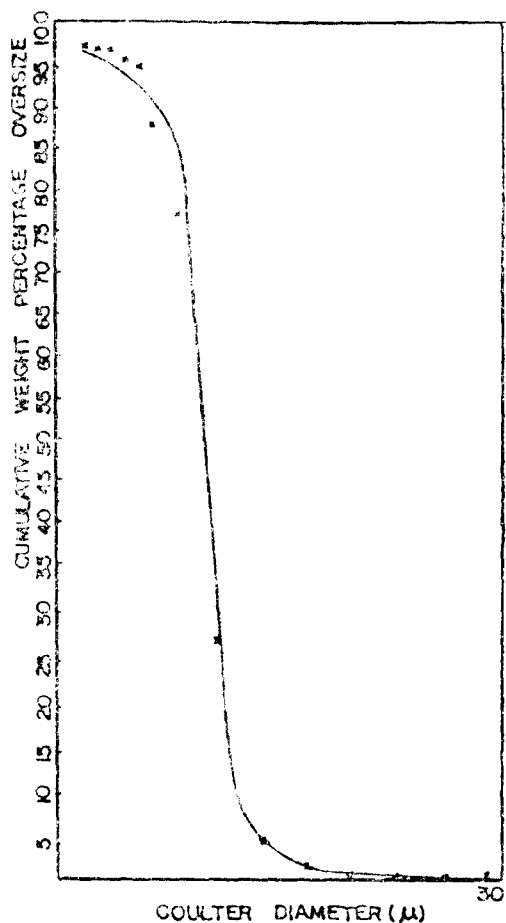


Fig. 1: Cumulative plot of the particle size distribution of Apumine A.

Such changes might occur in a period of 30 minutes. The diameter of the particle is expressed as the cubic root of the particle volume.

To simplify the work data reduction, which often involves the preparation of a log-probability plot, a programme was developed where by the volume percentages and diameters can be calculated on a computer. Table I shows data illustrative of a change

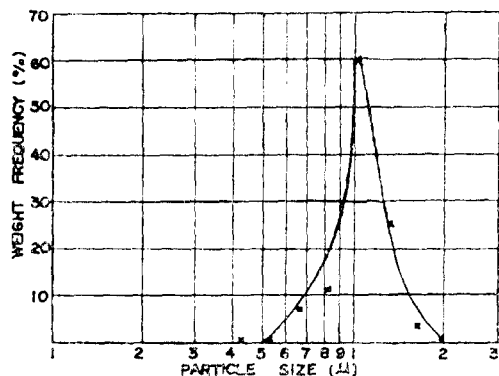


Fig. 2: Frequency distribution plot of log-normal relation of Apumine A.

in the size distribution of a sample during the measuring period and Fig. 1 is the cumulative weight frequency plot of data in Table I.

Fig. 2 is the graph plotted as weight frequency versus the logarithm of the particle diameter. From this it can be seen that 90 percent of the particles are in the range of 7–15 $\mu$ , so it indicates the narrow distribution of the particles.

Lea and Nurse permeameter:

Powder finess can be estimated by measuring the air permeability of a compacted powder bed under the influence of a pressure drop across the bed. Since the principal resistance to air flow through the bed is at the particle surfaces, the permeability is a function of the volume-surface mean diameter ( $d_{vs}$ ) of the particles, or an inverse function of the specific surface. The apparent specific surface varies with porosity<sup>4)</sup> and the experiment should be repeated with beds of various porosities. For any given material a region can be found where the specific surface varies only slightly with porosity; a value of the specific surface determined at a porosity in this region is gene-

rally reported.

A fresh sample should be used for each determination where only a limited amount of material is available, it is permissible to perform the series of tests at decreasing porosities using only small increments of sample as required until a satisfactory porosity is determined.

The useful range of porosity lies between 0.4 and  $0.6\mu$ . The average porosity of Apumine A is  $0.551\mu$  and the specific surface area determined is  $3300 \text{ cm}^2\text{g}^{-1}$ .

Stroehlein areameter:

Gas adsorption as a method of determining the surface areas of finely divided porous or nonporous solid materials is not new.

The Stroehlein areameter employs a single-point BET technique coupled with differential pressure measurement to determine the surface area of powders.

The apparatus enables surface area measurements to be made using low temperature nitrogen adsorption as in the Brunaver, Emmett and Teller (B. E. T.) method<sup>5)</sup>.

Although the full adsorption isotherm can be obtained, normally only a single point is determined for surface area measurements. The surface areas of a wide range of materials can be measured with the apparatus, limitations arise due to the total area of sample that the apparatus is capable of measuring, 7-50  $\text{m}^2$ .

Swintosky *et al.*<sup>6-8)</sup> determined the specific surface area of pharmaceutical powders by the method of nitrogen adsorption method. The specific surface area of Apumine A determined with Stroehlein areameter is 3470

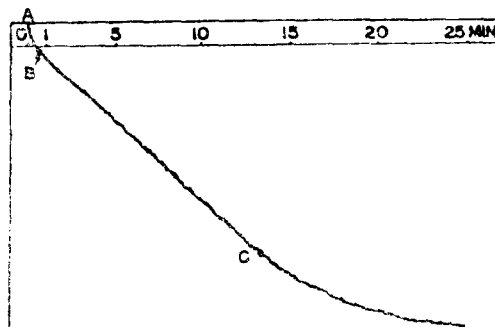


Fig. 3: Sedimentation curve of Apumine A.

$\text{cm}^2\text{g}^{-1}$ .

Sedimentation Balance:

It is necessary to know the final weight to be expected after complete sedimentation since it is rarely possible to prolong a run until all the suspension has settled out. The filling and end weight is calculated as follows: The recording width is 20cm. Each step equals 0.08cm and therefore 250 steps of 2mg(=500 mg) can take place.

In order not to exceed the end weight of 500mg the filling weight of the sample must be calculated as described previously.

The end weight after the complete sedimentation can never reach the 500mg limit. This is due to the diameter of the collecting pan being 1.2mm smaller than the inside diameter of the jar and therefore approximate 3 percent of the sample bypass the pan. Another part of the sample remains right from the start underneath the pan, which is suspended 5mm above the bottom of the jar.

This furthermore reduces the end weight so that the total loss amounts to approximate 6 percent.

In order to determine the residue tangents

**Table II: Sedimentation balance size analysis of Apumine A.**

Time (min)	Particle size ( $\mu$ )	Weight oversize in grade (%)	Cumulative weight oversize (%)
0.5	65.30	0.79	0.79
1	46.18	0.53	3.72
10	14.60	0.53	4.25
15	11.92	25.01	29.26
20	10.33	31.38	60.64
25	9.24	17.55	78.19
30	8.43	9.58	87.77
40	7.30	5.85	93.62
50	6.53	2.08	95.70

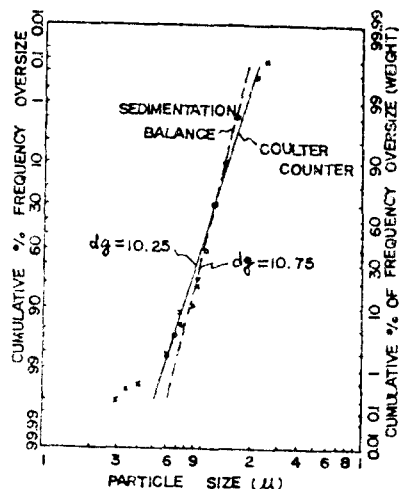
at the inner curve at those points determined by the time intervals are drawn. The extensions of those tangents will cut the abscissa.

The sedimentation curve is running through the zero point of the abscissa and the distance between the zero point and the cutting point equals the residue value in percent provided the distance between the abscissa and the actually obtained end weight is assumed to be 100.

The intersection of the tangents cannot be determined accurately in the flat section of the curve. These residue values must therefore be determined by calculation, which is possible due to the step like curve.

Table II gives the size analysis of the Apumine A sample obtained with the Sartorius 4,600 sedimentation balance. From this it can be seen that almost all of the particles precipitate in an hour.

Fig. 3 is the sedimentation curve. The sedimentation curve from A to B and from B to C is nearly straight line. This indicates that the particle size of this sample is screened one and the parts of the samples precipitate in the region of A-B before recording in the



**Fig. 4:** Logarithmic probability graph of the particle size distributions of Apumine A by two different methods.

recording paper.

The methods described are all generally in use for the size analysis of particles.

Each of these methods gives reproducible results but it is practically impossible to determine which, if any, of them is correct.

Fig. 4 is the logarithmic probability graph of the particle size distribution of Apumine A sample by Coulter counter and sedimentation balance. A linear relationship is obtained when the logarithm of the particle size is plotted against the cumulative percent frequency on a probability scale.

This method of graphical representation of a size distribution as a straight line exaggerates departure from linearity at the "tails" of a size distribution but the effect is nevertheless real and will be more marked when the particles are smaller so that a greater portion is beyond the limit of resolution of the instru-

ment.

The results obtained by Coulter counter method and sedimentation balance method are similar.

From this graph the geometric mean diameter ( $d'g$ ) on a weight basis can be calculated directly. The geometric weight mean diameter is the diameter corresponding to the 50 percent figure.

The geometric standard deviation ( $\sigma_g$ ) which is the quotient of the ratio 50 percent size over 84 percent oversize is the slope of this graph on the probability coordinate.

In sedimentation balance, the calculation is based upon the Stoke's law, which however, refers only to spherical particles. The diameter is then exactly defined if the particles of the sample, however, are not spherical, which will be the case in most tests, only relative values are then obtained.

A cube, which comes geometrically near a sphere, has already three diameters (edge, side diagonal and geometric diagonal) and the diameter term is therefore only a mean value. The further the geometric size of the particles deviates from the sphere (plate, needles), the more relative becomes the result of the so-called diameter and the particle size distribution.

The actual particles are more probably represented by a spectrum sizes, the range varying for different materials and conditioned somewhat by the method of manufacture.

If it is assumed that the particles are spheres then the relationship between the volume surface mean diameter ( $d_{vs}$ ), in microns and the specific surface area, Sw, in  $\text{cm}^2\text{g}^{-1}$  is

Table III: Particle size diameter, standard deviations and surface area values for Apumine A.

Method	$d'g(u)$	g	$dvs(u)$	Sw( $\text{cm}^2\text{g}^{-1}$ )
Coulter counter	10.25	1.28	9.88	1570
Lea and Nurse			4.71	3290
Stroehlein areameter			4.47	3470
Sedimentation balance	10.75	1.24	10.5	1480

given by

$$S_w = 6 \times 10^4 / \rho \cdot d_{vs}$$

Where  $\rho$  is the density.

To use surface area measurements a volume surface diameter must be defined. This can be done by means of the Hatch-Choate<sup>(9)</sup> equations,

$$\log d_{vs} = \log d'_{f-1} - 1.151 \log^2 \sigma_g$$

The derived values for the geometric weight mean diameter, the standard deviation, the volume surface diameter and the specific surface area of the four size distributions are given in Table III.

The Coulter counter operates at a very low concentration, sample is kept in suspension by stirring during analysis, but sometimes a precipitation is occurred in spite of constant stirring and presence of dispersant.

One of the most valuable features of the electrical sensing zone instrument is the wealth of the information it can supply regarding a sample: (1) dispersal or agglomeration tendencies of the sample causing changes of distribution with time; (2) high inherent and realized resolution in size distribution; (3) identification of the presence and often the numbers, of particles in the sample both above and below the actual counting range; and (4) a sufficient number of counts and volume of data to give high statistical significance to the



results, but still in a form convenient to procedure, process, and analysis.

Though the particle diameters determined by the gas adsorption and air permeability method lose some of their significance because of the nonuniformity in size of the powder particles, the specific surface area is a real definite value. The gas adsorption method would be inaccurate for particle-diameter information if the particles were porous or in the form of rods or plated.

A surface area measurement can relate to any number of distributions and therefore such a measurement cannot be used, to define a distribution completely.

Moreover it can be applied only to dry powders.

The only worthwhile application of surface area measurement is, therefore, as a routine check of the grinding efficiency of a mill, for which purpose they are ideally suited.

Because of the simple instrumentation and the speed with which determinations can be made, permeability methods are widely used pharmaceutically for specific surface determinations especially when the aim is to control batch-to-batch variations when using this technique for more fundamental studies, it would seem product to calibrate the instrument.

Bephenium hydroxynaphthoate, official in the British Pharmaceutical Codex 1973, is standardized by means of an air permeability method of Lea and Nurse<sup>10</sup>.

Bryant *et al.*<sup>11</sup> compared the results obtained from whittings with Lea and Nurse air permeability method and Stroehlein area-

meter. The data of the air permeability method are one third of that of the gas adsorption, which suggests that the whiting particles have re-entrant surfaces with an internal area of the same order as the external surface area.

The specific surface area obtained with the gas adsorption and the air permeability method in this experiment are similar, but the results differ considerably from those of Coulter counter and sedimentation balance.

The most important practical requirement of any method is that it be suitable for the particular nature of the sample. Because most measurement methods are sensitive to shape, density, porosity, or other characteristics of the particle, not including diameter itself, size determinations will have different degrees of accuracy depending on the extent to which these factors enter.

For such reasons, agreement of results between various techniques may be good for certain samples but poor for others.

Lack of agreement is much more common, values of particles diameter found by different measurement techniques differing sometimes by various factor.

If two samples differ from each other only at the coarse end of the distribution gravimetric sedimentation analysis and the Coulter counter are more capable of detecting the difference than microscopy. Conversely differences at the fine end of the distribution have more effect on the specific surface and are more readily detected by air permeability methods.

Also limiting the usefulness of some particle size measuring techniques are variations

caused by operational procedures. Still another limitation is the difficulty of specifying or even knowing, either the accuracy or the precision of results.

### CONCLUSION

Four different analytical methods of particle size *i.e.* conductivity, air permeability, gas-adsorption and sedimentation were compared one another

Results of particle size distribution of fine Aluminum hydroxide powder by Coulter counter and sedimentation balance showed similar tendency.

However, the data obtained by Lea and Nurse permeameter and Stroehlein areameter were quite different from those above data.

It may be due to the difference of methods in principle.

The choice of particle size analysis method is very important and the characteristics of each apparatus should be considered.

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