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A COMPARATIVE EVALUATION OF AIR-JET SIEVE FOR PARTICLE SIZE ANALYSIS OF PHARMACEUTICAL POWDERS

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ABSTRACT

The performance of the air-jet sieve (AJS) , for the particle size analysis of pharmaceutical powder, was evaluated and compared with the conventional sieve shaker (ESS). Two grades of acetaminophen (APAP) were used as test pharmaceutical powders. The particle size analysis by the AJS was simple, reproducible, efficient and accurate. The problematic powder, possessing excessive electrostatic charges and ranging in mean diameter from 17 nm to 800 nm (beyond the scope of ESS) could be evaluated accurately by AJS. The analysis time required by AJS was relatively less than that

required by ESS. The accuracy of the determination by AJS was not affected by the sample size. Both the speed of rotation (vibrations and/or shaking) and the total time of sifting affected the results of the determination by ESS. The particle size value of APAP-special determined by ESS and AJS were 680.0 $\pm$ 0.14 nm and 40.0 $\pm$ 0.32 respectively, whereas the value assigned by the manufacturer was below 74 nm (-200 mesh). The precision of either method for particle size analysis of powder possessing excessive electrostatic charge was improved by the use of carbon black as an anti-static agent.

INTRODUCTION

The knowledge of particle size and particle size distribution, in dealing with powders, is of considerable importance to pharmacists engaged in the preformulation, formulation development and routine production of pharmaceutical dosage forms. The influence of particle size on the rate of most chemical and physical reactions between solids and liquids, the dissolution and absorption rate of drugs, the drying rate of granules, the rate and degree of mixing of drug-excipient combinations and hence content uniformity in dosage forms, flow properties and compressional characteristics of powder, taste and color and texture of dosage forms, and the stability

of drugs in the dosage form, has been well documented in pharmaceutical and chemical engineering texts. (1-6).

The pharmaceutical powder technologist, for the most part, relies on the conventional sieve shaker, due to its simplicity and low cost, for the control and monitoring of particle size in pharmaceutical powders. However, sieve shakers possess disadvantages in the large sample size requirement, limitation to particle sizes larger than 100 nm, and the blinding of the screen by particles which get lodged in the mesh openings, mechanically or due to electrostatic charges (1,7). The United States Pharmacopeia (7) suggests the use of a device other than a sieve shaker for the quality control of powders with particles below 100 nm mean diameter; however, no specific device is specified.

The air-jet sieve, an instrument operating on the principle of fluidization, has been reported (8) to be a useful tool for the quality control of the fineness of cement powder. Since the nature of pharmaceutical powders is considerably different than that of cement powder, and since no published data pertaining to the application of the air-jet sieve for particle size analysis of pharmaceutical powder could be found in the literature, the objective of the present communication is to report the results of a study on the relative performance of the air-jet sieve and conventional sieve shaker.

EXPERIMENTAL

Acetaminophen (APAP) - special[1.] and APAP granules,[2.] were used as test pharmaceutical powder to evaluate the performance of the air-jet sieve[3.] and sieve shaker.[4.]

Particle Size Determination by Sieve Shaker:

A nest of sieves, comprising 20, 40, 60, 80, 100, 120, 200, 270, and 400 U.S. Standard mesh, in a series of five sieves per nest, was assembled on a sieve shaker. The test drug powder sample weighing 5.0 g, 10.0 g or 25.0 g was placed on the topmost sieve and the percent of powder retained on each sieve, after a shaking period of thirty minutes, was determined. The procedure was repeated with samples of powder which were coated with 0.1% carbon black. The coating of the particles, in the powder, was achieved by gently rolling and tumbling the sample with the carbon black in a screw capped glass bottle. The speed of the drive shaft on which the sieve nest is attached was set at 40 rpm for the main study and at 30 or 20 rpm (ESS-30 or ESS-20) for supplementary studies.

Particle Size Determination by Air-Jet Sieve:

The working principle of the air-jet sieve is illustrated in the diagrammatic sectioned view in Figure 1. The powder to be sieved is placed on the sieve surface (A) and fluidized in the closed chamber (B) by an upward jet of air (C) supplied

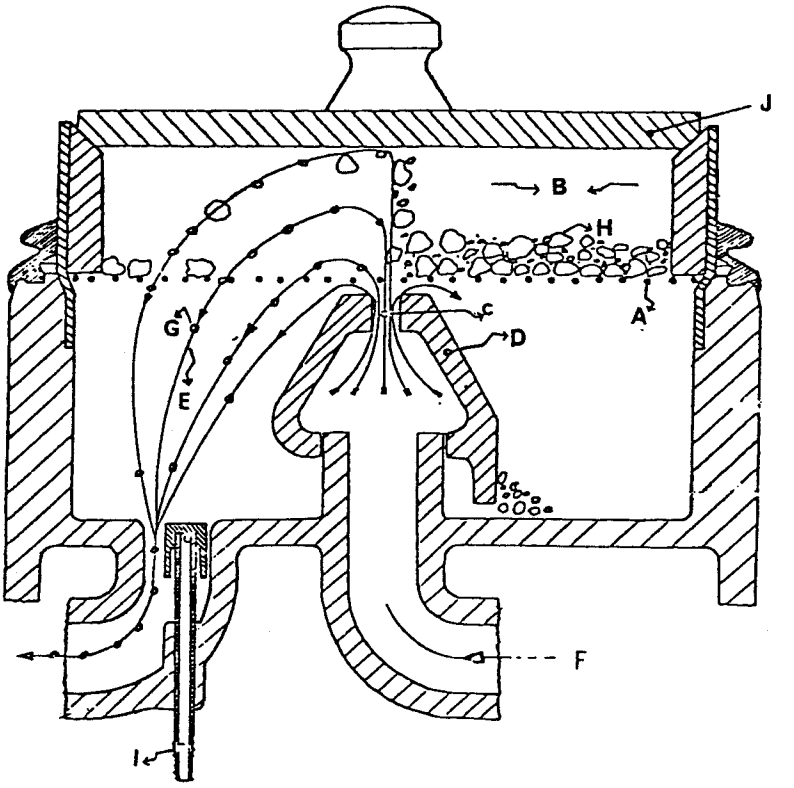

Figure 1 The Diagramatic Sectional View of the Air-Jet Sieve

A) Sieve Surface, B) Sieving Chamber,

C) Upward jet of air, D) Air-Jet Scanner

E) Reversed jet of air, F) Fan blower

G) Undersize particles, H) Oversize particles

I) Manometer

J) Plexiglass Cover

under the screen through a rotating air-jet scanner (D). The fines are separated from the coarse particles in mid-air without any mechanical contact with the sieve. Thus, particle size essentially remains constant and the strain on the sieve mesh is negligible. The upward jet of air keeps the screen from clogging. The reverse jet of air (E) moving at slow velocity flows down the screen carrying with it the undersize particles, (G) leaving the oversize particles (H) on the screen. The air-jet is provided by a suitable fan blower and the pressure in the chamber is controlled by a manometer (I) to give 150-200 mm gauge pressure (just enough to prevent aggregation on the screen). A domestic vacuum cleaner is used for extraction of the reverse air-jet carrying undersize particles.

A weighed quantity of the powdered drug, 1.0 to 25.0 gram, was placed on the sieve, the chamber was closed by the plexiglass cover (J) which was secured in place by suction in the sieving chamber. The machine was run for 3-5 minutes of fluidization and extraction of undersize particles, and the percent of oversize particles retained on the screen was determined. The procedure was repeated with the samples coated with carbon black, as described earlier.

RESULTS AND DISCUSSION

The essentials of the USP procedure (7) for the particle size analysis of pharmaceutical powders is summarized in

Table I. It is evident that the USP procedure, in addition to being time consuming, is unsuitable for assessing the particle sizes of powders, below 100 nm, which are of importance from a biopharmaceutical viewpoint. The sample size required is large and the shaking time required for adequate analysis is thirty minutes or more.

Table II illustrates a typical set of particle size analysis results compiled for computation of arithmetic mean diameter (D_a) of the particles. The average arithmetic diameter (D_a) of a sample of granular APAP was 409.95 nm. Since the

TABLE I

THE USP SPECIFICATIONS FOR PARTICLE SIZE ANALYSIS OF PHARMACEUTICAL POWDERS

1. Instrument recommended - mechanical or vibratory sieve shaker
2. Sample size
   a) 25.00 g - 100 g for coarse powder
   b) 25.00 g - for fine powder
3. Time - 20-30 minutes or until sifting is complete
4. Limitation - not suitable for powders below 100 nm average diameter

   Other device for measurement of particles below 100 nm mean diameter is directed but not specified.

TABLE II

DETERMINATION OF ARITHMETIC MEAN PARTICLE SIZE AND PARTICLE SIZE DISTRIBUTION - APPARATUS - SIEVE/SHAKER VIBRATOR

I	II	III	IV	V
Sieve mesh Passed through/ Retained on	Arithmetic mean* opening of sieve nm	% retained	% cum retained	Wt. size (II x III)
Top/20	840	4.579	4.579	3846.36
20/40	630	41.097	45.676	25891.11
40/60	335	22.599	68.275	7570.67
60/80	213.5	5.469	73.744	1167.63
80/100	163	6.08	79.824	991.04
100/120	137	2.388	82.212	327.16
120/200	99.5	6.944	89.156	690.93
200/270	63.5	3.368	92.524	213.87
270/400	45.0	2.373	94.897	106.79
400/base	37.0	5.116	100.013	189.29
				40994.84
Average Diameter=$\frac{\text{Total V}}{100}$		Average Diameter=409.95 (nm)		

*Arithmetic mean screen opening calculated by adding size opening of both screens and dividing by 2.

particle size distribution of APAP was log-normal, it was felt that the computation of geometric mean diameter (D_g) and the geometric standard deviation (σ_g) would be more meaningful then (D_a). The computations of (D_g) and (σ_g) are illustrated in Figure 2. The value of D_g is equal to the 50% value of the distribution and σ_g equal to the ratio of the 84.1% value divided by the 50% value. Stockham and Fochtman (9) have discussed a number of advantages of processing the particle size analysis data by this method, one of the advantages being the ability to ascertain whether two samples of a powder came from the same population or lot. Two samples having identical D_g and σ_g values can be said to have come from the same lot of powder. However, two samples having the same arithmetic mean does not lead to the conclusion that the powder came from the same lot or different lots. Thus, processing problems, such as content disuniformity, flow and compressibility, due to lot to lot variation in particle size distribution of powders, can be minimized through standard quality control methods using D_g and σ_g as criteria for specifying powder characteristics.

Table III summarizes the value of D_a and D_g for the two grades of APAP. The results show that the geometric mean for APAP granular is larger than the arithmetic mean, whereas the D_g for the APAP-special powder is smaller than the D_a. The accuracy of particle size determination of APAP granules by

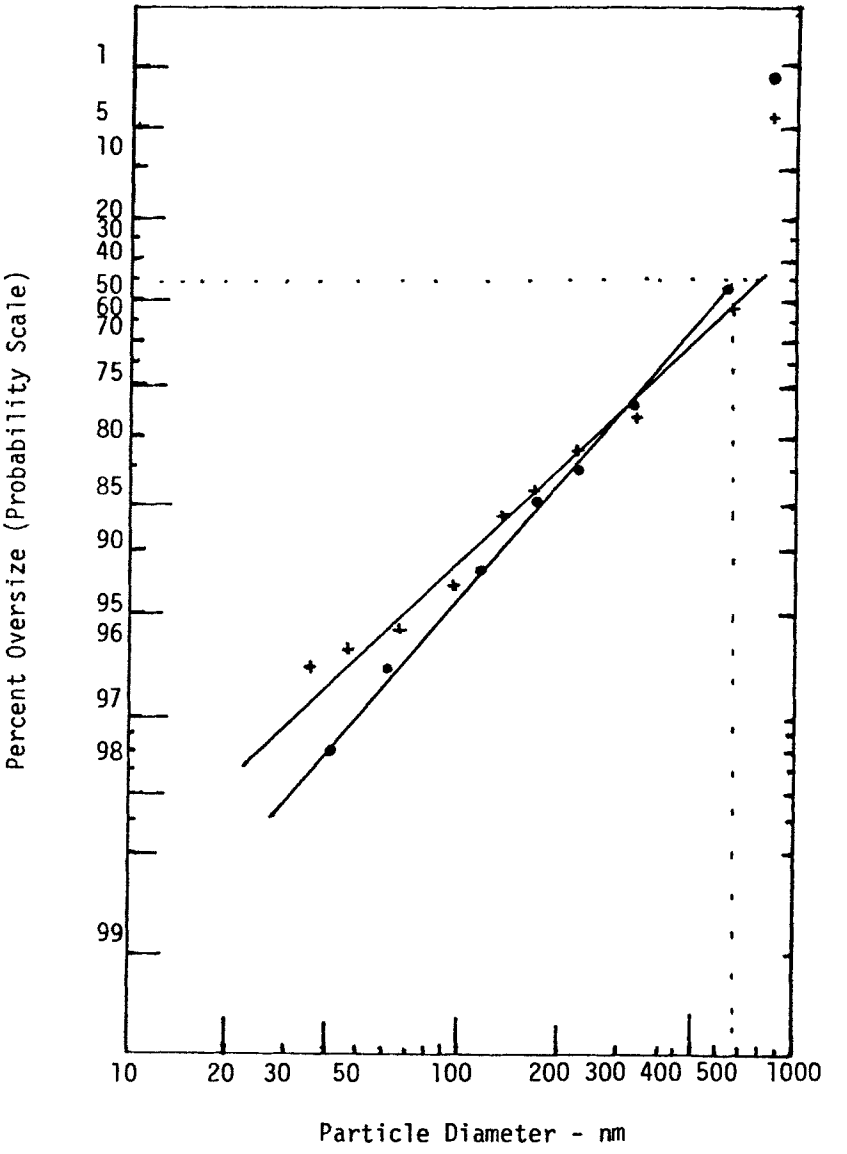

Figure 2 Log-Probability Plot of Granular Acetaminophen

● - % retained on air-jet sieve
+ - % retained on sieve shaker

TABLE III

MEAN PARTICLE SIZE OF ACETAMINOPHEN DETERMINED BY AIR-JET SIEVE AND A SIEVE SHAKER

		Air-Jet Sieve		Sieve Shaker	
		with carbon black as additive	without additive	with carbon black as additive	without additive
Granular Acetaminophen	Arithmetic mean nm	421.47 ± [c]22.98 (5.45) [d]	364.3± 41.11 (11.28)	413.3 ± 21.06 (5.1)	423.73± 6.01 (1.42)
	Geometric mean nm	500± 0.42	450± 0.31	475± 0.25	510± 0.22
Special Acetaminophen	Arithmetic mean nm	103.77± 3.63 (3.5)	106.2± 1.82 (1.71)	104.68± 4.9 (4.7)	568.88± 19.48 (3.42)
	Geometric mean nm	50± 0.24	40±0.32	79±0.32	680±0.14

c- Standard Deviation (N=3)
d- Coefficient of variation

either method is comparable. However, the particle size values obtained for APAP-special powder from the sieve shaker is grossly inaccurate and misleading. The results also indicate that the inherent electrostatic charges on the APAP powder, particularly with APAP-special, make the sieve shaker nearly useless for particle size analysis of problematic pharmaceutical powders.

The use of carbon black as an antistatic agent to coat the powder before particle size analysis was found to increase the precision and accuracy of the determination and permitted easy handling of problematic powder during determination. Figures 3 and 4 illustrate the dramatic influence of carbon black on the estimate of particle size distributions. Figure 3 and Table IV show that almost all of the sample of untreated APAP-special remained on sieve #20 leading to an erroneous D_g value of above 500 nm, whereas the mean particle diameter was in reality below 74 nm. The D_g value for APAP-special untreated, obtained from the air-jet sieve, was within the range claimed (-200 mesh, which is less than 74 nm) by the manufacturer of the powder. Figure 4 further shows that the estimate by two methods on samples coated with carbon black are close to the larger particle size range, but the difference in estimates increases as one moves towards the small particle size range.

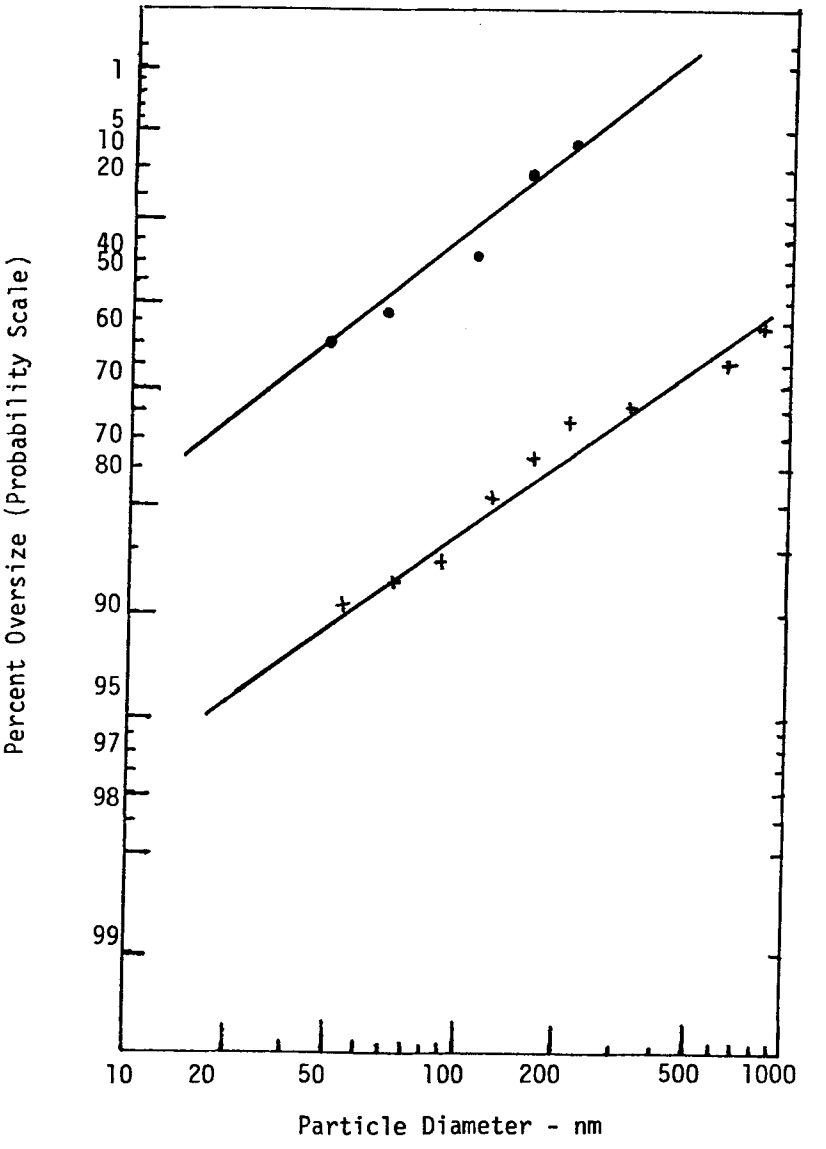

Figure 3 Log-Probability Plot of Acetaminophen Special Powder (Untreated)

● - Percent retained on air-jet sieve
+ - Percent retained on sieve shaker

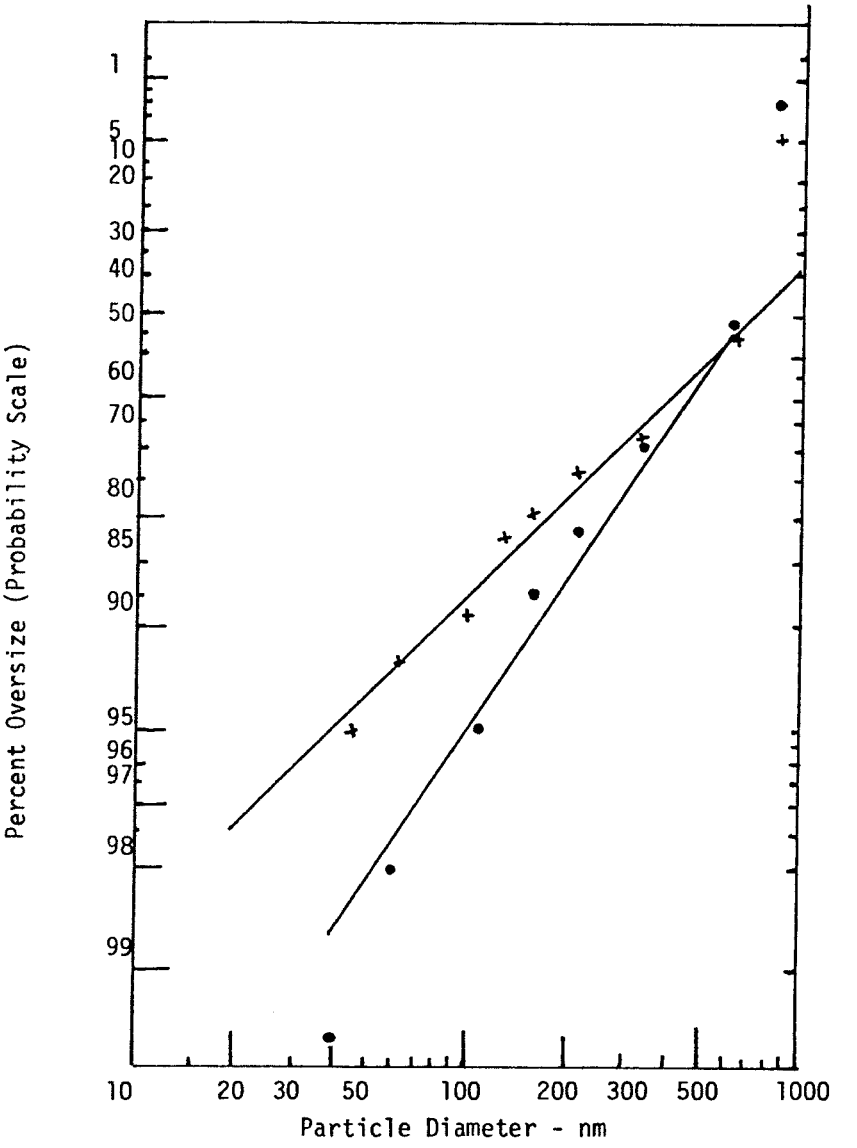

Figure 4 Log-Probability Plot of Granular Acetaminophen USP treated with carbon black

• - percent retained on air-jet sieve
+ - percent retained on sieve shaker

Tables IV and V show the effect of sample size and sieving time on the efficiency of two methods. The sieving efficiency of AJS was relatively independent of the sample size and the optimum sieving efficiency reached within three minutes, confirmed the claims of the manufacturer. Both the sample size and the sieving time influenced the results obtained by ESS. The sieving efficiency of ESS was poorest for APAP-special (Table V). Neither the USP nor the manufacturer of the sieve shaker specify the rpm setting of the drive shaft on which the sieve shaker assembly is fastened. Thus, the reported value of D_a or D_g , determined by different laboratory and different technicians using the sieve shaker,could be considerably different and irreproducible. The results in Tables IV and V indicate that drive shaft rotation speed set below 30 rpm would lead to inaccurate estimates of particle size. Optimum setting of 40 rpm should be used for the universal acceptance of D_a or D_g values computed using ESS.

CONCLUSIONS

1. Estimates of particle size and particle size distribution, by conventional sieve shaker, may be inaccurate and misleading for certain powders possessing electrostatic charge.

TABLE IV

SIEVING EFFICIENCY OF AIR-JET SIEVE AND SIEVE SHAKER AS A FUNCTION OF TIME AND SAMPLE SIZE (APAP - GRANULES)

Sample size (g)		% Remaining on 200 Mesh Sieve Sieve Time (min) 1	2	3	5	10	25
25.0	ESS	-	95.76	-	95.52	95.36	85.44
	AJS	87.56	87.12	86.76	86.24		
10.0	ESS	-	95.0	-	94.7	94.6	81.3
	AJS	87.2	86.5	86.1	85.6		
	ESS 30	-	95.03	-	94.6	94.6	81.2
	ESS 20	-	99.72	-	99.6	99.5	97.5
5.0	ESS	-	93.6	-	93.4	93.2	84.98
	AJS	87.8	87.2	86.6	86.0		

ESS - sieve shaker AJS - air-jet sieve (ESS-30 or ESS-20 indicate sieve shaker set at 30 or 20 rpm)

TABLE V

SIEVING EFFICIENCY OF AIR-JET SIEVE

AND SIEVE SHAKER AS A FUNCTION OF TIME AND SAMPLE SIZE

(APAP SP.)

% remaining on 200 mesh screen

Sample size (g)		sieve time (min) 1	2	3	5	10	25
25.0	ESS		98.22		98.15	98.1	92.06
	AJS	33.95	32.52	31.0	29.68		
10.0	ESS		99.34		99.0	98.8	90.4
	AJS	31.7	30.5	29.5	29.2		
5.0	ESS		99.66		99.4	99.2	93.62
	AJS	33.6	33.0	31.8	31.0		

2. The air-jet sieve is an efficient and dependable instrument for obtaining reproducible and quick estimates of particle size and particle size distribution in the range of 17 nm to 800 nm. (Beyond the limit of a conventional sieve shaker)
3. Problematic powders can be analyzed easily.
4. The total time required for analysis using the air-jet sieve is less than that required by a sieve shaker.
5. Carbon Black can be effectively used to overcome electrostatic charge impeding with the particle size analysis.
6. The sample size required for particle size analysis using AJS could be between 1.0 - 5.0 grams, whereas a minimum 25.0 gram sample is necessary for particle size analysis using ESS.

ACKNOWLEDGEMENT

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FOOTNOTES

1. Acetaminophen, USP, Special Powder, S.B. Penick and Co., New York
2. Acetaminophen, USP, Granular Type I, S.B. Penick and Co., New York.
3. Alpine American Corporation, 3 Michigan Dr., Natick, Mass. 01760
4. Erweka, U.G., G.M.B.H. motor type KOI, Heusentamn, Germany

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