Particle Size Studies*

I. The Andreasen-Berg Pipette and the Grain Size Distribution of Barium Sulfate U. S. P.

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INTRODUCTION

The importance of proper grain size for such pharmaceutical chemicals as the basic bismuth salts, barium sulfate, calomel, kaolin and zinc oxide is now well recognized. The Pharmacœpia (1), under Barium Sulfate describes a test for bulkiness of powder. Eder (2) has recently reviewed and discussed the significance of the grain size of particles; evaluated the sedimentation methods and suggested a microscopic method for Barium Sulfate. Mutzenberg (3) has described a centrifuge method. The National Formulary Revision Committee (4) has adapted a sedimentation test for particle size for Magma of Colloidal Kaolin. Danckwortt (5), using the Andreasen-Berg (6) pipette has reported on a number of commercial German barium sulfate preparations. More recently, in this country, Loomis (7) has used this method for the study of a number of ceramic kaolins. The authors have used this method to determine the grain size distribution in two samples of Barium Sulfate, U. S. P. The pharmacopial test for bulkiness (1) does not measure this factor.

EXPERIMENTAL

Apparatus.—The apparatus consists of a glass cylinder about 6 cm. in diameter having a capacity of approximately 550 ml. when filled to the upper mark on the scale. It is provided with a ground glass stopper through which passes the stem of a pipette, which extends 20 cm. beneath the surface of the suspension and about 4 cm. from the bottom, the tip being at the level of the zero mark on the scale while the upper surface of the suspension is at the 20 cm. mark. The pipette has a capacity of 10 ml., and it is provided with a three way stop-cock and spout for drainage.

Method.—A one per cent suspension was used in the determination. This was prepared as follows: 5.5 Gm. of barium sulfate was levigated with 100 ml. of water containing 50 mg. of barium chloride and 50 mg. of acacia, transferred to the cylinder and diluted to the 20 cm. mark with distilled water. With the stopper of the pipette in place, the mixture was shaken, with an end over end motion, for 5 min. The exact time was noted and samples were withdrawn at intervals as follows: 5, 15, 30, 60, 120, 240 and 360 min. The samples were transferred to tared, shallow dishes and evaporated to constant weight at 100° C. The number of mg. of residue gives the percentage of material in the sample.

The grain size of the particles is calculated from Stokes Law as follows:

$$r = \sqrt{\frac{9nh}{2(d_1 - d_2)gt}} \qquad (1)$$

where r is the radius of a spherical particle in cm.
n is the viscosity of the water in poises, 0.00894
d_1 is the density of the barium sulfate, 4.50
d_2 is the density of the water, 0.99707
g is the gravitational constant, 980.267
t is the time in seconds from the start of test
h is the distance (cm.) between liquid surface and pipette when liquid is drawn

Simplified, this becomes:

$$r \text{ equals } 0.003416 \sqrt{\frac{h}{t}} \qquad (2)$$

For the purposes of the test, this was further simplified as follows, where r is in microns and t is in minutes:

$$r \text{ equals } 4.41 \sqrt{\frac{h}{t}} \qquad (3)$$

The results are tabulated in the following tables:

Table I.—Grain Size Distribution of Particles of Barium Sulfate, U. S. P. Manufacturer "A"

Time 10:15	Sample No.	t (Min.)	h (Cm.)	r (Micron)	Dia. ($2r$)	% Finer Than Size
10:20	1	5	20.0	8.82	17.64	89.2
10:30	2	15	19.7	5.38	10.75	87.2
10:45	3	30	19.4	3.54	7.08	85.0
11:15	4	60	19.0	2.46	4.92	83.2
12:15	5	120	18.7	1.71	3.42	68.2
2:15	6	240	18.4	1.19	2.38	20.0
4:15	7	360	18.0	1.05	2.10	2.8

Table II.—Comparison of the Grain Size Distribution of Two Samples of Barium Sulfate, U. S. P.

Diameter	17.64	10.76	7.08	4.92	3.42	2.38	2.10
Grain size (1.612r)	14.21	8.67	5.70	3.96	2.75	1.91	1.41

Table III.—Percentage by Weight Finer Than Size

Mfg. "A"	89.2	87.2	85.0	83.2	68.2	20.0	2.80
Mfg. "B"	87.0	85.4	84.8	78.0	45.2	41	33.4

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SUMMARY

1. A method for the determination of grain size distribution of pharmaceutical chemicals has been described.

2. The grain size distribution in two samples of Barium Sulfate have been determined.

CONCLUSIONS

It would seem that a test of this type, incorporating a limit of the per cent of large particles and a requirement for a definite per cent of small particles would be superior to the present pharmacopial test for bulkiness of powder.

REFERENCES

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Syrup of Cranberry, A New Pharmaceutical Vehicle

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INTRODUCTION

Any attempt to minimize a patient's discomfort and resistance to unpleasant medications is a worthy one. The increase in the number and use of efficient vehicles at the physicians service will eventually neutralize present objections to ill-tasting medicines. The trend to the use of true fruit flavors in pharmaceutical vehicles is a meritorious one. The popularity of Syrup of Cherry, N. F. VI, well illustrates this trend as does the investigation conducted by Mason (1) on grapefruit syrup and Fantus and Dyniewicz (2) on pineapple syrup.

Because of its national distribution, low cost, attractive color and pleasant flavor, the cranberry, *Vaccinium macrocarpum*, in the authors' estimation, warrants attention as the source of a potential pharmaceutical vehicle.

REVIEW OF LITERATURE

Production.—The cranberry is grown principally in Massachusetts, New Jersey, Wisconsin, Oregon and Washington. Its active marketing season extends from September to January, though cranberries are often available during winter months. The annual crop is about 50,000,000 pounds. The retail selling price is variable and depends on the total production, but is usually from $6.00 to $10.00 a barrel of 100 pounds. At retail the cost varies from 7 to 15 cents a pound.

Cranberry Syrup.—A cranberry syrup for beverage purposes was produced commercially in this country in 1895 under the name of "Ruby Phosphate." This was produced at Wareham, Massachusetts, by B. P. Waters and R. C. Randall, local pharmacists, and enjoyed a moderate sale.

Constituents.—The pure cold-pressed juice according to Rice, Fellers and Clague (3) has the following percentage composition: soluble solids 6.7, pectin (alcohol precipitate) 0.13, titrable acidity calculated as citric acid 2.60, ash 0.16 and astringency (tannin) 0.5. The p_H of this juice is 2.4, and the specific gravity is 1.058.

Isham (4) determined the nature of the acids in cranberries. The average amounts of the acids in the Early Black Variety expressed as per cent are: citric 1.1, quinic 1.0, malic 0.26 and benzoic 0.065. Nealy (5) has recently reported the presence of ursolic acid from cranberries. This substance has been used in medicine to a limited extent.

Morse (6) found the percentage composition of the ash to be: potassium oxide 0.068, sodium oxide 0.003, calcium oxide 0.018, magnesium oxide 0.009, phosphorus pentoxide 0.019, sulfur 0.005, chlorine 0.004, iron 0.00022 and manganese 0.00057. Rice, Fellers and Clague (3) found 0.00036 per cent of total iron in Early Black cranberries. The copper content varies widely, but Massachusetts cranberries contain approximately five parts per million. Isham and Fellers

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