International Journal of Pharmaceutics, 4 (1980) 317–326

POWDER FLOW STUDIES I. POWDER CONSOLIDATION RATIO AND ITS RELATIONSHIP TO CAPSULE-FILLING–WEIGHT VARIATION

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(Received October 29th, 1979)
(Accepted December 11th, 1979)

SUMMARY

The consolidation of loosely packed powders and powder mixtures in cylindrical containers was studied by applying a series of loads to the surface of the powder bed. The results were plotted as the logarithm of the change in volume versus the logarithm of the applied pressure. The slopes of these plots were similar and the intercepts (consolidation ratio) suggested a relationship to powder flow. The effects of the cylinder diameter and initial height of the powder bed on the powder consolidation ratio were investigated to optimize the method. The application of the powder consolidation ratio to powder flow in hoppers was studied by filling capsules of several formulations on an automatic capsule filling machine. The plots of the coefficient of variation of filled weight versus powder consolidation ratio were linear, indicating a direct relationship between the powder consolidation ratio and capsule-filling–weight variation.

INTRODUCTION

The densification of a powder during compaction or compression is usually described as compactibility or compressibility. It was proposed (Schwarzkopf, 1947) that compaction be defined as the minimum pressure needed to produce a given green strength, while compressibility be used to indicate the extent to which the density of a powder is increased by a given pressure. The term compressibility, when used in connection with a powder, was defined (Carr, 1965) to determine a decrease of volume brought about by any means, including vibration or tapping or simply (Neumann, 1967) a change of volume caused by a compressive load acting on the surface.

Using the former concept, the following equation was proposed:

$$\% \text{ Compressibility} = 100\,\frac{\gamma_p - \gamma_a}{\gamma_p} \quad (1)$$

Where γ_p = packed bulk density and γ_a = aerated bulk density.

The results of simple measurements in which the decrease of powder volume was measured as a function of the compressive load were plotted (Neumann, 1967) as graphs of log (Vo – V)/V vs log pressure acting on the powder bed surface. These plots were linear after an initial compression was achieved by a very small force. The following relationship was proposed:

$$\log\left(\frac{Vo - V}{V}\right) = K \log P + C \quad (2)$$

Where Vo = the initial powder volume, V = the powder volume at a given surface pressure, P = the pressure acting on the powder bed surface and K and C are constants.

Comparisons of these results and the results of the reduction in powder bed volume resulting from prolonged tapping without any pressure indicated that the technique of studying powder compression by applying a load on the powder bed surface did not produce as great a reduction in powder bed volume as prolonged tapping without any pressure.

Since Eqn. 2 is not dimensionally homogeneous, P should be replaced by P/P_0, where P_0 equals 1 kg/cm^2 (Eqn. 3)

$$\log\left(\frac{Vo - V}{V}\right) = K \log(P/P_0) + C \quad (3)$$

In the present investigation, the consolidation (preferable terminology than compression) of loosely packed powders and powder mixtures in cylindrical containers was investigated by applying a series of loads on the surface of the powder bed. The intercept (powder consolidation ratio) of the log (Vo – V)/V vs P/P_0 plots was studied in some details to test any relationship to powder flow. For optimizing the method, the effects of the cylinder diameter and initial height of the powder bed on the consolidation ratio were investigated. This ratio was linearly related to the coefficient of variation of capsules filled on an automatic capsule filling machine. The data suggested that the powder consolidation ratio may be a useful tool in predicting flow properties of powders and powder mixtures.

MATERIALS AND METHODS

Materials

The drug, tromethamine salt of ±-2-benzoyl-l-azabicyclo(3,3,0)-octa2,4-diene-6-carboxylic acid, was obtained from the Institute of Organic Chemistry (Syntex Research, Palo Alto, Calif.) with a purity of at least 99%. The excipients used in these studies were spray dried lactose USP (Foremost Co., San Francisco, Calif.), starch USP (Staley Manufacturing Co., Decatur, Ill.) and magnesium stearate USP (Mallinckrodt Chemical Works, St. Louis, Mo).

Powder consolidation ratio determination

Different size cylinders were used in this study. The internal diameter of the cylinders were 2.5 cm, 3.5 cm and 4.5 cm and the heights of the loosely packed powders were 9.5 cm, 18 cm and 27 cm.

The powder mixtures contained drug, lactose (in indicated proportions), 10% starch and 0.5% magnesium stearate, and were prepared by mixing the drug and the excipients in geometric dilutions on a piece of glassine paper. The powder mixtures were screened through a no. 20 mesh screen to ensure proper mixing and to avoid powder compaction. Six 50 mg spot samples were withdrawn from each powder mixture, two from top, two from middle and two from bottom. Each sample was analyzed by dissolving in purified water and measuring the ultraviolet absorption at 332 nm (Unicam SP 1800 ultraviolet spectrophotometer, Pye Unicam, Cambridge, England). The results indicated that the coefficient of variation for each formulation was less than 5%.

The powders or the powder mixtures were loosely packed in graduated cylinders and a close-fitting plastic disc was placed on the powder bed. The plastic disc was perforated in the center to avoid air compression (Fig. 1). The initial height of the powder bed in the cylinder was kept close to the chosen height of the cylinder. For the 2.5 cm and 3.5 cm cylinders, the metal weight was loosely screwed to a stainless steel rod and gently loaded over the plastic disc by unscrewing the weight. For the 4.5 cm cylinder, the weight was lowered in a plastic weight holder which was loaded gently over the plastic disc. Thirty seconds were allowed for equilibration after each loading. The reduction in

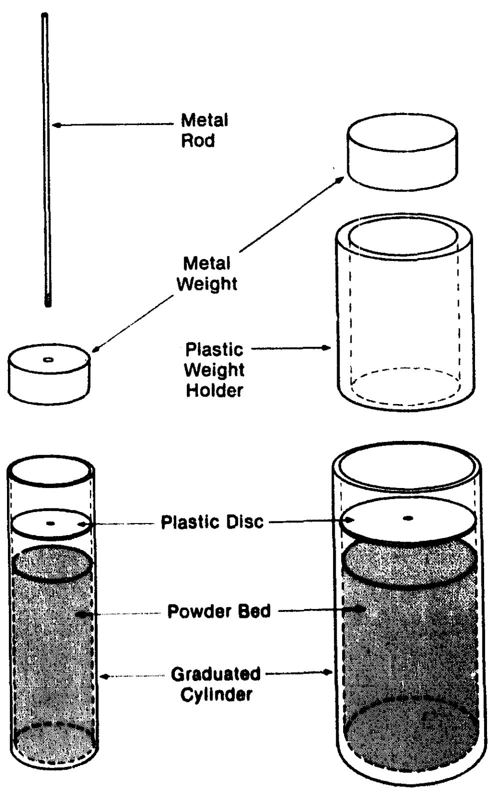


Fig. 1. Apparatus used to study powder consolidation ratio.

the powder bed height was obtained by subtracting the height of the powder bed after compaction from the initial height. For each experiment, 4 determinations were made and the mean results were plotted as log (Vo – V)/V vs log (P/P_0).

Capsule-filling–weight variation study

An automatic capsule filling machine (Zanasi) was used to study the weight variation. The target weight per capsule was 100 mg. The machine was run continuously and 100 capsule samples were taken at equal intervals. The capsules were individually weighed and the coefficient of variation was calculated from the mean and the standard deviation.

RESULTS AND DISCUSSION

The plots of the relative volume change as log (Vo – V)/V of powders and powder mixtures versus applied pressure as log (P/P_0) are given in Figs. 2–6. The effect of the powder bed height on powder consolidation at constant cylinder diameter is shown in Figs. 2–4. The results of the effect of the cylinder diameter at constant powder bed height are given in Figs. 3, 5 and 6.

Table 1 gives the values of the slopes obtained from Figs. 2–6. At constant cylinder

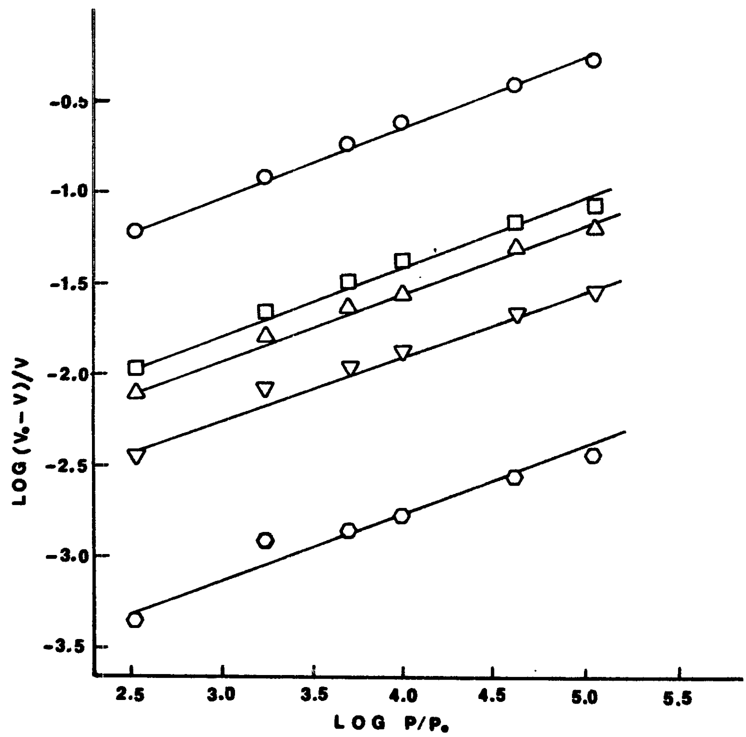


Fig. 2. Relative volume change as log (Vo – V)/V of powders and powder mixtures as a function of the applied pressure as log P/P_0. The inside diameter of the cylinders and initial height of the powder bed were 3.5 cm and 9.5 cm respectively. Key: ○, 89.5% spray dried lactose; ▽, 10% drug, 79.5% lactose; △, 20% drug, 69.5% lactose; □, 40% drug, 49.5% lactose; ○, drug alone. All formulations except drug alone contained 10% starch and 0.5% magnesium stearate.

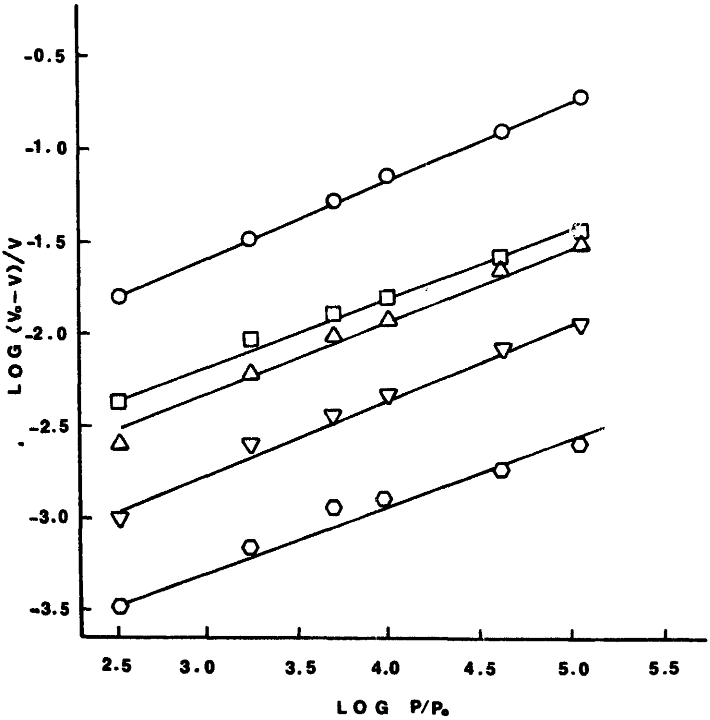


Fig. 3. Relative volume change as log (Vo – V)/V of powders and powder mixtures as a function of the applied pressure as log P/P_0. The inside diameter of the cylinder and initial height of the powder bed were 3.5 cm and 18 cm respectively. Key: o, 89.5% spray dried lactose; ▽, 10% drug, 79.5% lactose; △, 20% drug, 69.5% lactose; □, 40% drug, 49.5% lactose; ○, drug alone. All formulations except drug alone contained 10% starch and 0.5% magnesium stearate.

diameter and at different powder bed heights the slopes of the linear lines were similar. The slopes of the straight lines were higher when the cylinder diameter was 2.5 cm compared to the 3.5 cm and 4.5 cm diameter at constant powder bed height. Only small changes in the slopes of the drug, excipient and their various combinations were observed under similar experimental conditions.

The small changes in the slope of different powders and powder mixtures is due to the fact that the vertical load acting on the powder bed surface is not readily transmitted to deeper layers. It is in fact transmitted in a zig-zag fashion between the particles and is dissipated whenever it reaches the confining wall. Thus the effect of the load on the slope diminishes as the distance from the point of application increases. It should be therefore obvious that the slopes of these plots have no value in studying powder consolidation as related to powder flow.

Straight lines were obtained for most log (Vo – V)/V versus log (P/P_0) plots even at very low pressure. At a large cylinder diameter (4.5 cm) initial curvatures were observed for all powder mixtures and lactose. The 100% drug powder gave a straight line when tested with a 4.5 cm diameter cylinder. These results suggest that the plots of log (Vo – V)/V would result in straight lines with proper cylinder diameter selection. The experimental variability increased when the cylinder diameter was 2.5 cm (Fig. 5) and at 3.5 cm

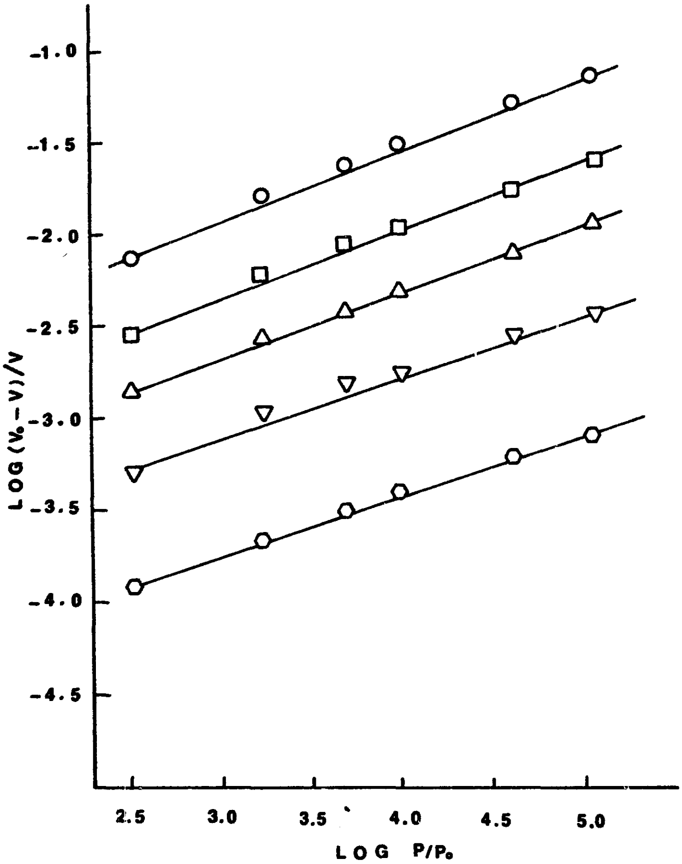


Fig. 4. Relative volume change as log (Vo – V)/V of powders and powder mixtures as a function of the applied pressure as log P/P_0. The inside diameter of the cylinder and initial height of the powder bed were 3.5 cm and 27 cm respectively. Key: ○ 89.5% spray dried lactose; ▽, 10% drug, 79.5% lactose; △, 20% drug, 69.5% lactose; □, 40% drug, 49.5% lactose; ○, drug alone. All formulations except drug alone contained 10% starch and 0,5% magnesium stearate.

TABLE 1

SLOPES OF PLOTS IN FIGS. 2–6

Cylinder diameter	Powder bed height (cm)	Formulation				
		0% Drug	10% Drug	20% Drug	40% Drug	100% Drug
2.5 cm	18.0	0.51	0.53	0.58	0.49	0.50
3.5 cm	9.5	0.34	0.34	0.36	0.36	0.37
	18.0	0.34	0.42	0.43	0.36	0.44
	27.0	0.32	0.33	0.36	0.26	0.39
4.5 cm	18.0	0.39	0.34	0.40	0.39	0.45

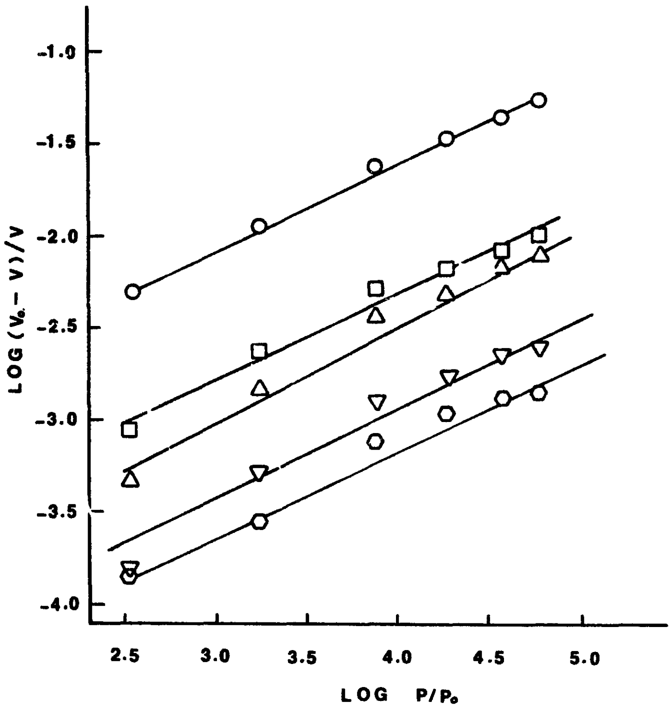


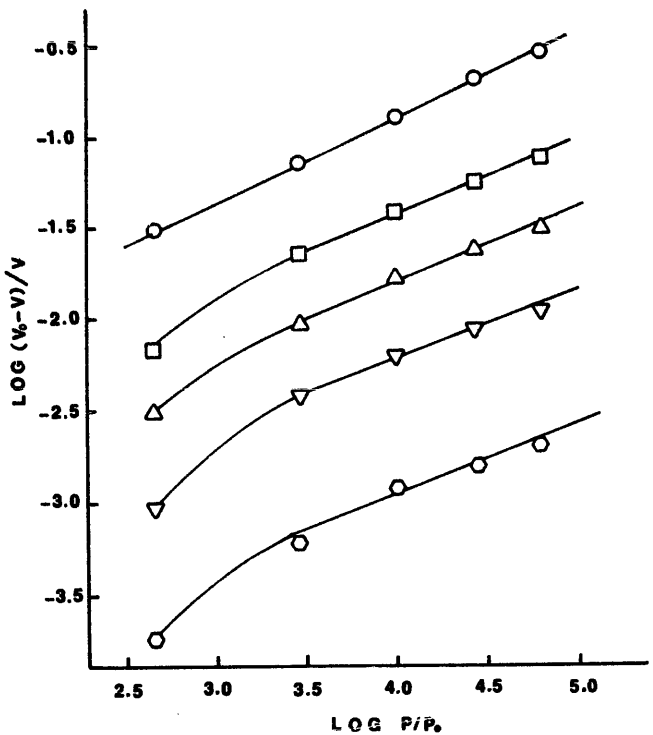
Fig. 5. Relative volume change as log (Vo – V)/V of powders and powder mixtures as a function of the applied pressure as log P/P_0. The inside diameter of the cylinder and initial height of the powder bed were 2.5 cm and 18 cm respectively. Key: o, 89.5% spray dried lactose; v, 10% drug, 79.5% lactose; △, 20% drug, 69.5% lactose; □, 40% drug, 49.5% lactose; o, drug alone. All formulations except drug alone contained 10% starch and 0.5% magnesium stearate.

cylinder diameter when the powder bed height was 9.5 cm and 18 cm. For a given formulation the consolidation ratio varies with the powder bed height and with the diameter of the cylinder because of the lack of deeper transmission of load in the powder bed. Therefore it is important to standardize the powder bed height and cylinder

TABLE 2

INTERCEPTS OF PLOTS IN FIGS. 2–6

Cylinder diameter	Powder bed height (cm)	Formulation				
		0% Drug	10% Drug	20% Drug	40% Drug	100% Drug
2.5 cm	18.0	–5.22	–5.08	–4.74	–4.26	–3.59
3.5 cm	9.5	–4.16	–3.27	–2.99	–2.83	–2.14
	18.0	–4.32	–4.05	–3.66	–3.27	–2.92
	27.0	–4.78	–4.09	–3.77	–3.45	–3.09
4.5 cm	18.0	–4.55	–3.61	–3.40	–3.01	–2.71



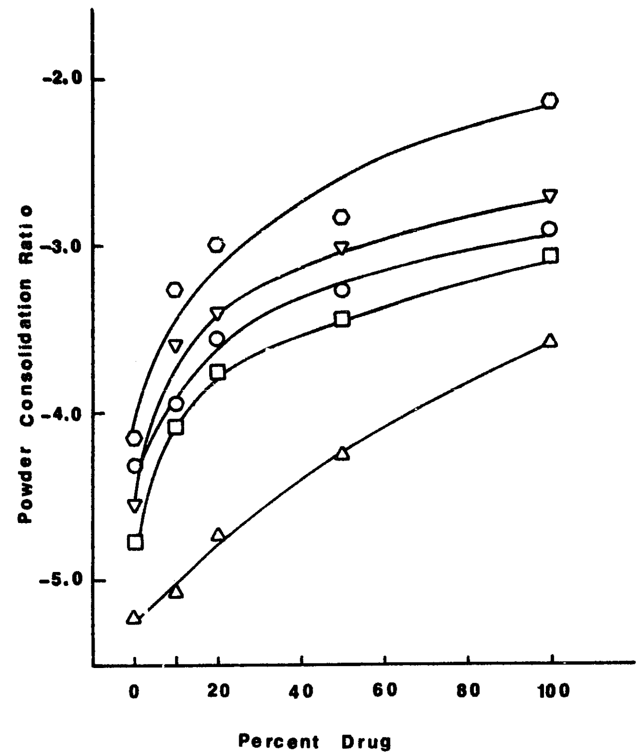


Fig. 6. Relative volume change as log(Vo – V)/V of powders and powder mixtures as a function of the applied pressure as log P/Po. The inside diameter of the cylinder and initial height of the powder bed were 4.5 cm and 18 cm respectively. Key: o, 89.5% spray dried lactose; ▽, 10% drug, 79.5% lactose; △, 20% drug, 69.5% lactose; □, 40% drug, 49.5% lactose; ○, drug alone. All formulations except drug alone contained 10% starch and 0.5% magnesium stearate.

Fig. 7. Powder consolidation ratio vs percent drug plots. Key: the inside diameter of the cylinder and the initial height of the powder bed respectively were: o, 3.5 cm and 9.5 cm; ○, 3.5 cm and 18 cm; □, 3.5 cm and 27cm; △, 2.5 cm and 18 cm; ▽, 4.5 cm and 18 cm.

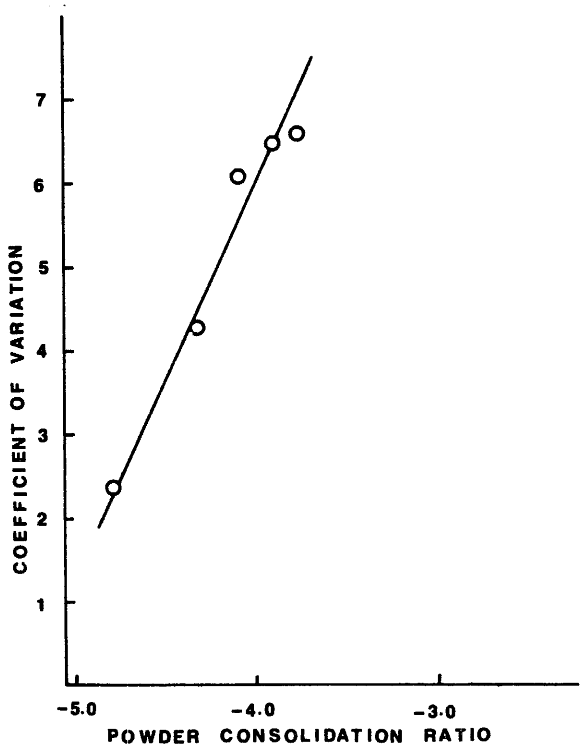


Fig. 8. Relationship between the powder consolidation ratio and the coefficient of variation of capsule weight filled on an automatic machine. The equation of the regression line is: Y = 4.437 X +23.676 correlation coefficient Y = 0.977

diameter. These data suggested that 3.5 cm cylinder diameter and 27 cm powder bed height gave the best results.

Table 2 gives the intercept values (consolidation ratio) obtained from Figs. 2–6. These results indicated that the consolidation ratio increased as the percent drug in the powder increased. These data are plotted as a function of the percent drug for different experimental conditions in Fig. 7. It appears from these results that the cylinder diameter of 3.5 cm in combination with the 18 cm and 27 cm powder bed height and the cylinder diameter of 2.5 cm in combination with the 18 cm powder bed height may be suitable for determining the consolidation ratio. However, in view of the overall results, it was decided to use the 3.5 cm diameter cylinders and 27 cm powder bed height for future evaluations.

Fig. 8 gives the plots of the consolidation ratio vs coefficient of variation of capsules filled on an automatic machine. Because of the poor flow properties of the drug, it was not possible to fill capsules containing more than 20% drug. The consolidation ratio for 5% and 15% drug formulations were obtained from Fig. 7. The results in Fig. 8 indicate a direct relationship between the powder consolidation ratio and coefficient of variation of capsules suggesting that this method should be further investigated to show its usefulness and limitations in predicting flow behavior of powders and powder mixtures.

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