DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 6(1), 1-13 (1980)

POWDER FLOW STUDIES II. POWDER COMPACTIBILITY FACTOR AND ITS RELATIONSHIP TO POWDER FLOW

Z.T. Chowhan and Y.P. Chow

ABSTRACT

The powder compactibility factors of a drug, an excipient and several drug-excipients combinations were determined by plotting the logarithm of the change in the powder bed volume contained in cylindrical containers versus logarithm of the applied pressure. The powder compactibility factor increased as the powder bulk density decreased and the plots of these two properties were linear at lower powder bulk densities. The plots of the logarithm of flow rate and the coefficient of variation versus the compactibility factor were also linear indicating the usefulness of this method in predicting flow properties of powders and powder mixtures.

INTRODUCTION

The compactibility of loosely packed powders and powder mixtures in cylindrical containers was investigated recently (1) by applying a series of loads on the surface of the powder bed. For optimizing the method, the effects of the cylinder diameter and the initial height of the powder bed were examined. The intercepts (compactibility factor) of the linear plots of the logarithm of the change in volume versus the logarithm of the applied pressure were linearly related to the coefficient of variation of the capsules filled on an automatic capsule filling machine (Zanasi).

This paper reports the relationship between the powder compactibility factor, powder bulk density and powder flow. The data confirms earlier findings that the powder compactibility factor may be a useful tool in predicting flow properties of powders and powder mixtures.

MATERIALS:

The drug, tromethamine salt of ± 2-benzoyl-1-azabicyclo (3,3,0) octa-2,4-diene-6-carboxylic acid, was obtained from the Institute of Organic Chemistry (Syntex Research, Palo Alto, CA)

with a purity of at least 99%. The excipients used in these studies were spray dried lactose USP, crystalline lactose USP (Foremost Co., San Francisco, CA), starch USP (Staley Manufacturing Co., Decatur, IL) and magnesium stearate USP (Mallinckrodt Chemical Works, St. Louis, MO).

METHODS:

Powder mixing:

The powder mixtures contained drug, lactose (in indicated proportions), 10% starch and 0.5% magnesium stearate. The powders of each formulation were mixed by the geometric dilution method on a piece of glassine paper and the mixture was screened through a #20 mesh screen to ensure proper mixing and to avoid powder compaction. Analyses of the powder mixtures carried out by dissolving in purified water and measuring the absorption at 322 nm (Unicam SP 1800 Ultraviolet Spectrophotometer, Pye Unicam Ltd., Cambridge, England) indicated good homogeneity.

Powder Bulk Density:

The powder or powder mixture was slowly sifted into a 100 ml graduated cylinder by means of a funnel. The powder weight (w) and volume (v) were recorded to calculate the powder bulk

density (P_b = w/v). The reported values are the average of four determinations.

Angle of Repose:

The powder or powder mixture was gently sifted by means of a vibra-flow feeder through a funnel with an opening diameter of 1.5 cm onto a glass plate (10 x 10 cm). The tip of the powder cone was kept at 0.5 cm from the lower end of the funnel by lowering the plate which was resting on a laboratory jack. The radius (r) and height (h) of the cone were recorded and the angle of repose was calculated ($\theta = \tan^{-1} h/r$). The reported values are the average of four determinations.

Compactibility Factor:

The powder or powder mixture was 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. The cylinder height was close to the powder bed height which was kept constant at 27 cm. The inside diameter of the cylinder was 3.5 cm. The metal weight was loosely screwed to a stainless steel rod and gently loaded over the plastic disc by unscrewing the weight. Thirty seconds were allowed for equilibration after each loading. The reduction in the powder bed height was obtained by subtracting the height of

the powder bed after compaction from the initial height. For each experiment, four determinations were made and the mean results were plotted as log (Vo-V)/V versus log P.

Powder Flow:

The flow of powders and powder mixtures was determined by means of a conical stainless steel hopper, measuring 11 cm (top diameter) by 13 cm (length) and 2 cm (orifice diameter). A shaft with mild vibration (Vibromixer, Chemapec Inc., Hoboken, NJ) was used to facilitate flow. The samples were collected during a period of 5 seconds and weighed. 20 samples were collected for each formulation and the mean, the standard deviation, coefficient of variation and flow rate were calculated.

RESULTS AND DISCUSSION

Some derived properties of the powders and powder mixtures used in this study are summarized in Table I. The bulk density of the drug was very low and the bulk density of the drug-excipients mixtures increased as the lactose percentage was increased. The angle of repose for spray dried lactose was fair and for the crystalline lactose was borderline for flowability (2). For all drug-excipients mixtures, the angle of repose indicated poor flowability.

TABLE I

SOME DERIVED PROPERTIES OF POWDERS AND POWDER MIXTURES

Derived Property	Formulations*								
	100% Drug	40% Drug 49.5% Crystal-line Lactose	40% Drug 49.5% Spray Dried Lactose	20% Drug 69.5% Crystal-line Lactose	20% Drug 69.5% Spray Dried Lactose	10% Drug 79.5% Crystal-line Lactose	10% Drug 79.5% Spray Dried Lactose	89.5% Crystal-line Lactose	89.5% Spray Dried Lactose
Powder Bulk Density (gm/cm^3)	0.182	0.308	0.331	0.451	0.447	0.533	0.564	0.687	0.699
Angle of Repose (^{o})	46.4	49.7	48.6	51.45	46.5	51.27	44.51	44.6	38.4
Powder Flow Rate (cm^3/sec)	1.22	0.91	1.68	1.36	2.48	1.55	5.23	4.81	11.72
Compact-ibility Factor	-3.09	-3.27	-3.45	-3.45	-3.77	-3.78	-4.09	-4.08	-4.78

*All formulations except 100% drug contained 10% starch and 0.5% magnesium stearate.

The plots of the log (Vo-V)/V versus log P are shown in Fig. 1. In these studies crystalline lactose was used. As reported earlier (1), the slopes of these plots were similar and the intercept (powder compactibility factor) may be related to powder flow. The powder compactibility factor obtained from these plots are summarized in Table I. The values of the powder compactibility factors of powder mixtures containing spray dried lactose were taken from a previous report (1) and are summarized in Table I.

Fig. 2 gives the plots of the powder compactibility factor and powder bulk density as a function of the percentage drug in the formulation. The powder compactibility factor increased as the percent drug in the formulation increased and the powder bulk density decreased.

The plots of the powder compactibility factor versus powder bulk density for the drug and the drug-excipient combinations are given in Fig. 3. At lower powder bulk densities straight line relationships were obtained for crystalline and spray dried lactose formulations. At higher bulk densities small increases in powder bulk density caused a large reduction in the powder compactibility factor.

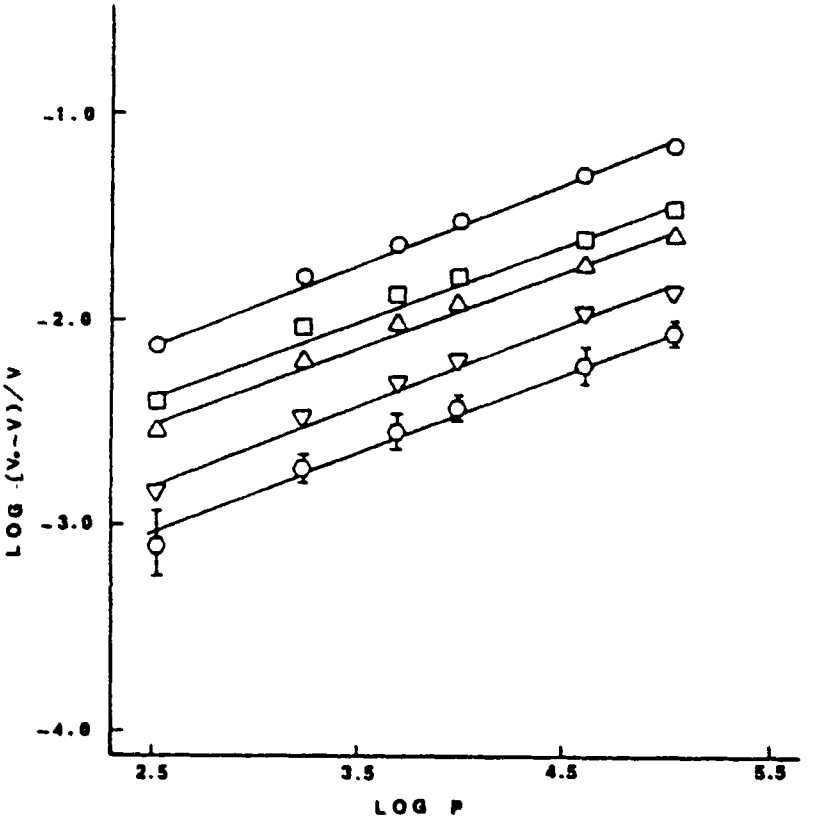

FIG 1:

Relative volume change as log (Vo-V)/V of powders and powder mixtures as a function of the applied pressure as log P. The inside diameter of the cylinder and initial height of the powder bed were 3.5 cm and 27 cm respectively. KEY: ○, 89.5% crystalline 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.

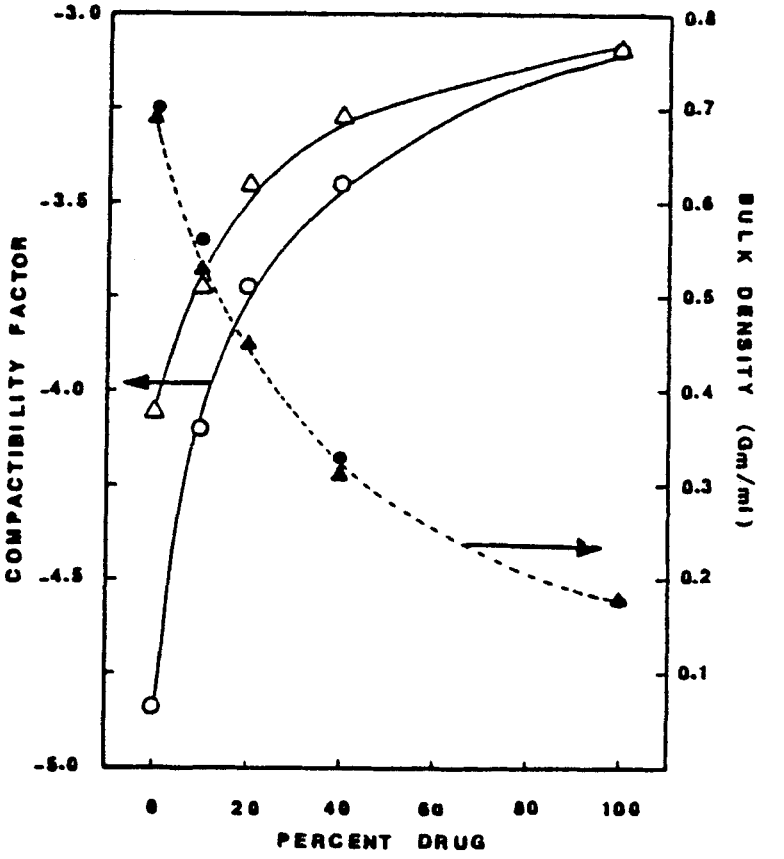

FIG 2:

Powder compactibility factor and powder bulk density of crystalline and spray dried lactose, drug alone and drug-lactose mixtures. KEY: O, spray dried lactose; Δ, crystalline lactose. Open symbols give the powder compactibility factor and closed symbols give the powder bulk density.

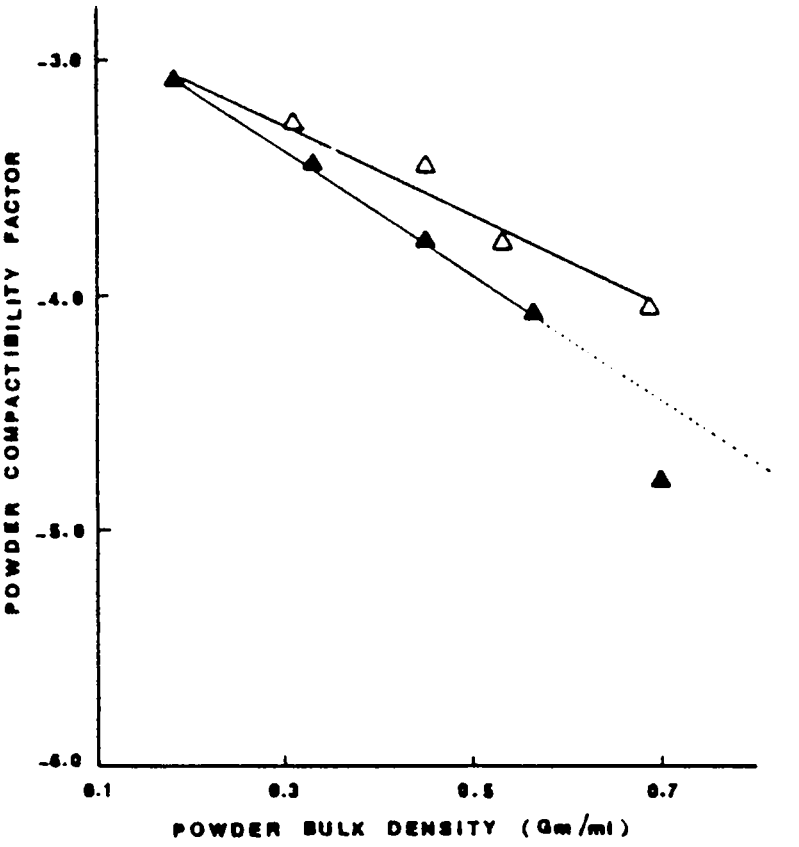

FIG 3:

Relationship between powder, the compactibility factor and the powder bulk density. Δ, crystalline lactose and drug-crystalline lactose mixtures; ▲, spray dried lactose and drug-spray dried lactose mixtures; ▲, drug alone.

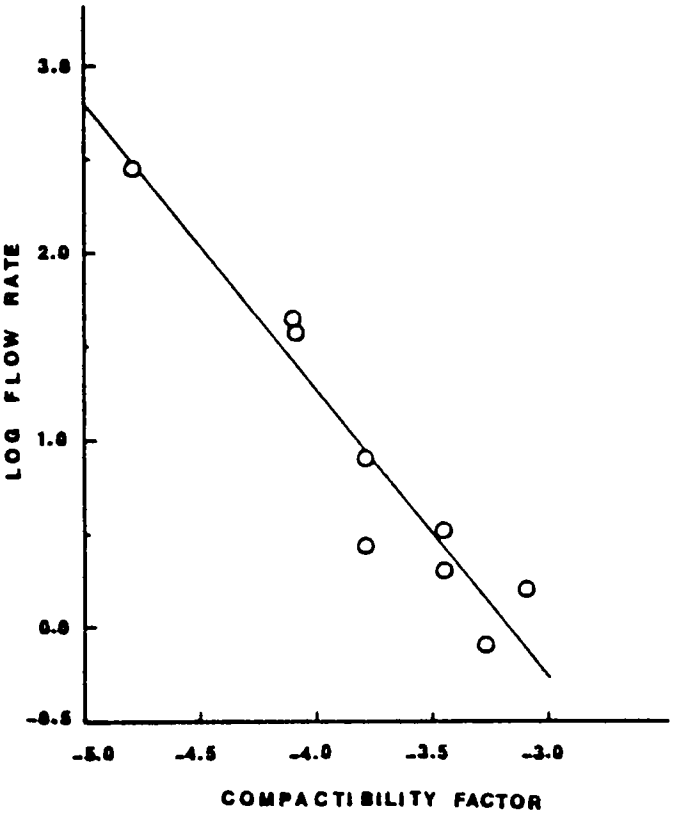

FIG 4:

Relationship between the compactibility factor and the log of the flow rate of crystalline and spray dried lactose, drug alone and their mixtures. The equation of the linear regression line is: $Y = -1.5417X - 4.9015$. correlation coefficient = 0.953.

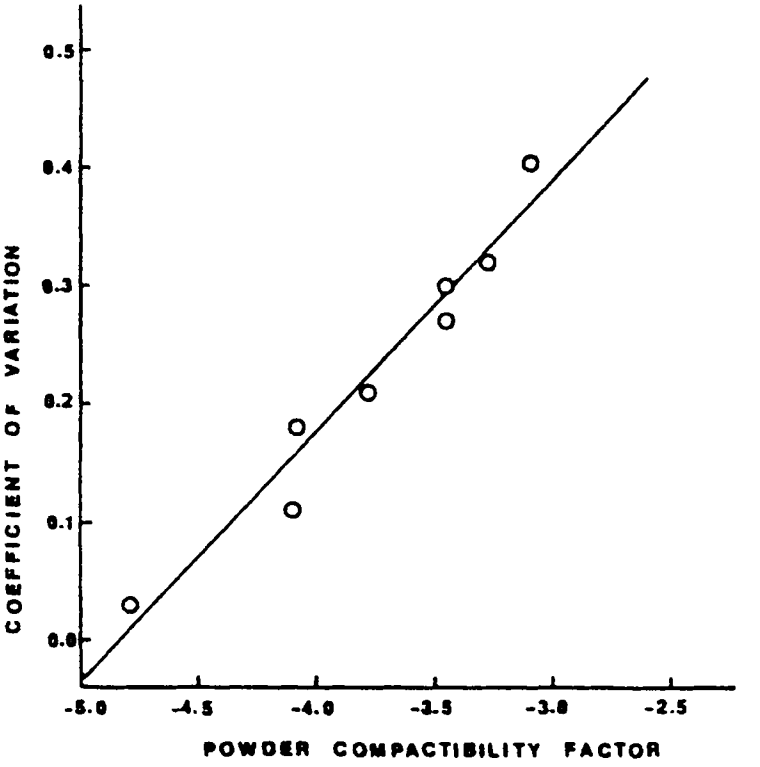

FIG 5:

Relationship between the powder compactibility factor and the coefficient of variation of the flow rate. The equation of the linear regression line is: $Y = 0.2173X + 1.0434$, correlation coefficient = 0.970.

The plots of the logarithm of flow rate versus the powder compactibility factor for formulations used in this study are given in Fig. 4. A linear relationship among these properties

indicated the usefulness of this factor in predicting powder flow.

Fig. 5 gives the plots of the coefficient of variation versus the powder compactibility factor. These results also suggested that the powder compactibility factor may be a useful tool in studying powder flow.

The results of this study in combination with the previous results (1) indicating a linear relationship between the powder compactibility factor and the coefficient of variation of the capsules filled on an automatic capsule filling machine suggest the usefulness of this method in studying flow properties of powders and powder mixtures.

REFERENCES

1. Z.T. Chowhan and Y.P. Chow, International Journal of Pharmaceutics, Submitted for Publication.

2. R.L. Carr, Chemical Engineering, 72, 163 (1965).