DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 12(11-13), 1947-1966 (1986)

EFFECT OF COMPRESSIBILITY AND POWDER FLOW PROPERTIES ON TABLET WEIGHT VARIATION

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ABSTRACT

A powder flowmeter has been designed to provide both quantitative and qualitative data relating to powder flowability. Three directly compressible powders, Emdex, Emcompress and magnesium oxide as well as a three component powder mixture was assessed for flowability, angle of repose and particle size. Compressibility indices were determined for all the above materials as well as for the fractions of each which consisted of a particle size below 315 µm. Sieve analysis was performed on the above powders in order to establish groups consisting of cohesive, mildly cohesive and non-cohesive fractions and their respective flow-time profiles were subsequently determined. Scanning electron microscopic analysis was performed to obtain information on the particle size, shape and size distribution. The interrelationships between flow rate, angle of repose, compressibility index and

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coefficient of tablet weight variation were established using both a single punch and a high-speed rotary tabletting machine.

A three-dimensional plot was constructed to illustrate the influences of flow rate, angle of repose and compressibility index on the coefficient of tablet weight variation. Whilst it was established that particle size has a significant effect on uniformity of flow, the data also indicated that when the compressibility index exceeded a value of about 20% a significant increase in tablet weight variation resulted irrespective of the powder flow rate.

INTRODUCTION

Particulate systems consist of a complex arrangement of individual components of various chemical composition, size, shape, size distribution, density, texture and hygroscopicity. The total bulk and flow properties of this heterogeneous mixture are generally non-uniform. Solid dosage forms produced with high-speed tablet machines (± 4 000 tablets min^{-1}) are manufactured on a volumetric basis. Hence, powder inhomogeneity can influence powder flow which may then result in tablet weight variation since the die must fill to within a few percent of target weight within a fraction of a second.

A survey of the literature on the flow properties of pharmaceutical powders reveals that although a large amount of work has been done on individual variables,[1-8] comparatively little has been done to clearly define any interrelationships between the key parameters. The flow rates of powders depend on many variables which include the shape and size of the container orifice, the ratio of the orifice diameter (D_o) to that of the containing vessel and the shape, size, density, roughness and moisture content of the particles[6, 9]. It has been well documented that particle size can influence the rate of flow and that flow rate initially increases with an increase in particle size (D_p) up to a maximum of between 100 and 400 μm (depending on the nature of the powder) and then decreases as the ratio of D_p/D_o increases towards a value of 0.2[10, 11]. The relationship between angle of repose, flowability and particle diameter has previously been investigated[12-16]. The rates of flow of powders are given by the following relationship[17], $D_o = A\ (4W/60\pi\rho_p\sqrt{g})^{1/n}$, where W is the flow rate in g min^{-1}, D_o is the orifice diameter in cm, ρ_p is the particle density in g ml^{-1}, g is the gravitational constant, and A and n are numerical terms depending upon material and particle size. Jones,[18] investigated the influence of changes in bulk density with increasing amount of fines and found that an increase in flow rate is not merely due to the filling of the void spaces. The porosity or void space can range from 26% to 48% depending upon the arrangement of the particles in the packing[19]. Carr[20] defined the compressibility index 'c' as: $c = \rho_T - \rho_B/\rho_T$ where ρ_T is the tamped density and ρ_B is the bulk density, good powder flowability being associated with powders having a low compressibility index. Many types of forces can act between solid particles and directly affect the flow properties and the angle of repose[21]. Different methods have been used to measure the angle of repose and powder flow[22-27]. The most comprehensive treatment of the various parameters involved in studies of powder flow, interparticulate forces and relevant mathematical relationships have been critically assessed and described by various authors[17, 28].

The objectives of this investigation were to determine not only the overall characteristics of a powder mass, but also to define the interrelationships between angle of repose, flowability, compressibility and other variables on the coefficient of tablet weight variation thereby providing quantitative information on materials used for solid dosage form manufacture. The importance of uniformity of flow and optimum compressibility index to produce a product of consistent quality has been evaluated.

EXPERIMENTAL

Materials

The directly compressible materials used were: Emcompress[R], Emdex[R], magnesium oxide U.S.P. and mixtures of various fractions of all the three to make a mixed powder (all received from Edward Mendell Co. Inc.). Magnesium stearate B.P. was used as lubricant.

Electron Micrographs

Pictures of powder samples were taken with a Jeol J.S.M. 840 scanning electron microscope. The samples were coated with gold prior to the microscopic examination using ion sputter.

Assessment of Intrinsic Physical Properties of Powders

Moisture Content - The moisture content of each powder was determined after placing samples in a hot air convection type oven for 5 to 10 hours at 60°C and the percent weight loss on drying calculated.

Particle Size Distribution - Particle size distribution was determined by the use of a series of B.S. sieves using a mechanical siever.

Bulk Density and Compressibility - The bulk density of each powder was determined from the weight of a 25 g sample, carefully charged into a 100 ml graduated cylinder. The powder was tamped until a constant volume was obtained. The compressibility index was calculated from the equation: % compressibility = $(\rho_T - \rho_B/\rho_T)100$, where ρ_T = tamped density, ρ_B = bulk density.

Angle of Repose and Flow Rate - A novel light-emitting flowmeter was used to measure powder flow rate, angle of repose and uniformity of flow. One hundred grams of powder was allowed to flow through the flowmeter orifice and the powder collected in a calibrated receptacle which facilitated the direct measurement of the resulting angle of repose. Flow rates and uniformity of flow were recorded with the aid of a strip-chart recorder. The angle of repose of each powder was confirmed by measuring the height and diameter of the base of the powder cone using a cathetometer.

Preparation of Tablets - Each of the powders were mixed with 0.3% magnesium stearate* for 3 minutes in a tumbler mixer at a rotation speed of 40 r.p.m. Flat and concave tablets of various dimensions were produced using either a single punch (Manesty type F3) (60 tablets min^{-1}) or a rotary (Manesty Unipress Sentinel 3) tabletting machine (3300 tablets min^{-1}).

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* Addition of 0.3% magnesium stearate increased the flow rate by not more than 1.5 g S^{-1} whilst the compressibility index was reduced by not more than 1%.

TABLE 1

Particle Size Distribution: Sieve Analysis

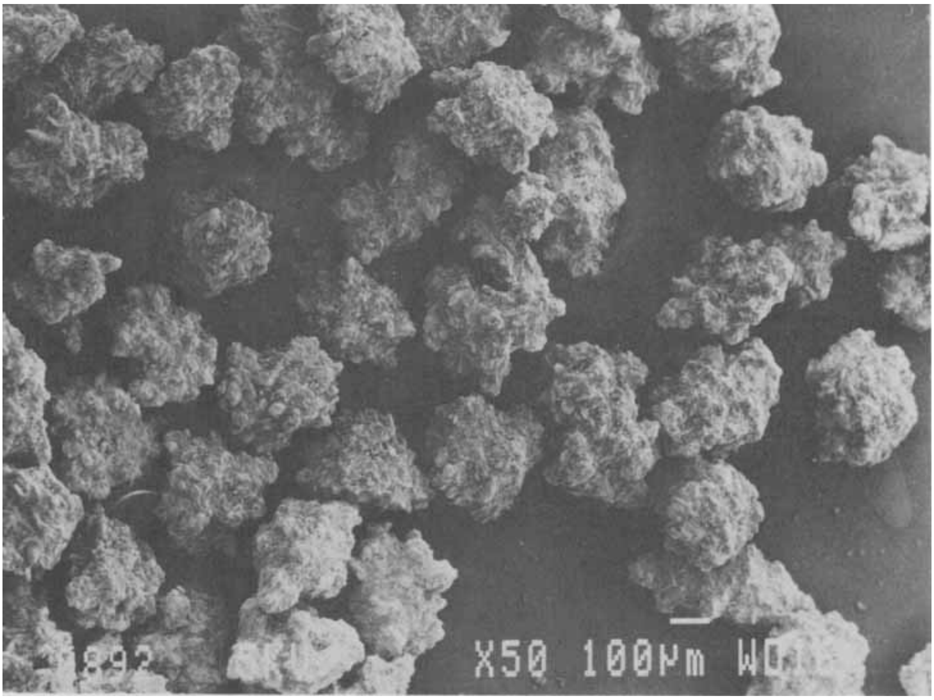
Powder \ Sieve Size (μm)	Weight Percent of Samples Greater than Stated Sieve Opening					
	<100	100	177	250	315	400
Emdex	0.6	7.2	27.4	25.1	39.1	0.3
Emcompress	8.3	46.6	37.4	4.7	2.9	-
Magnesium Oxide	4.0	12.8	25.4	11.9	45.8	-
Mixed Powder (three component powder)	0.9	35.2	28.2	6.3	28.0	1.3

Uniformity of Tablet Weight

The coefficient of tablet weight variation was determined by weighing 50 individual tablets.

RESULTS AND DISCUSSION

The results obtained from sieve analysis and the particle shapes of the powders studied are shown in Table 1 and Figures 1-4. The photomicrographs in Figures 1-4 reveal the particle shapes of different directly compressible materials as well as the percent size distribution by weight. The results indicate that all the powders follow a log-normal distribution pattern. Emcompress particles fall within a much narrower size distribution range and are associated with a relatively uniform particle shape compared to



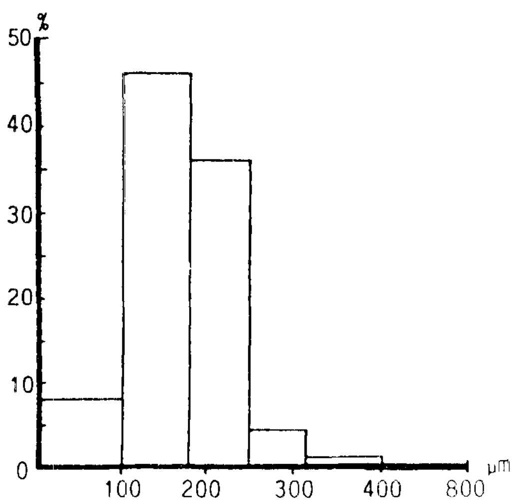
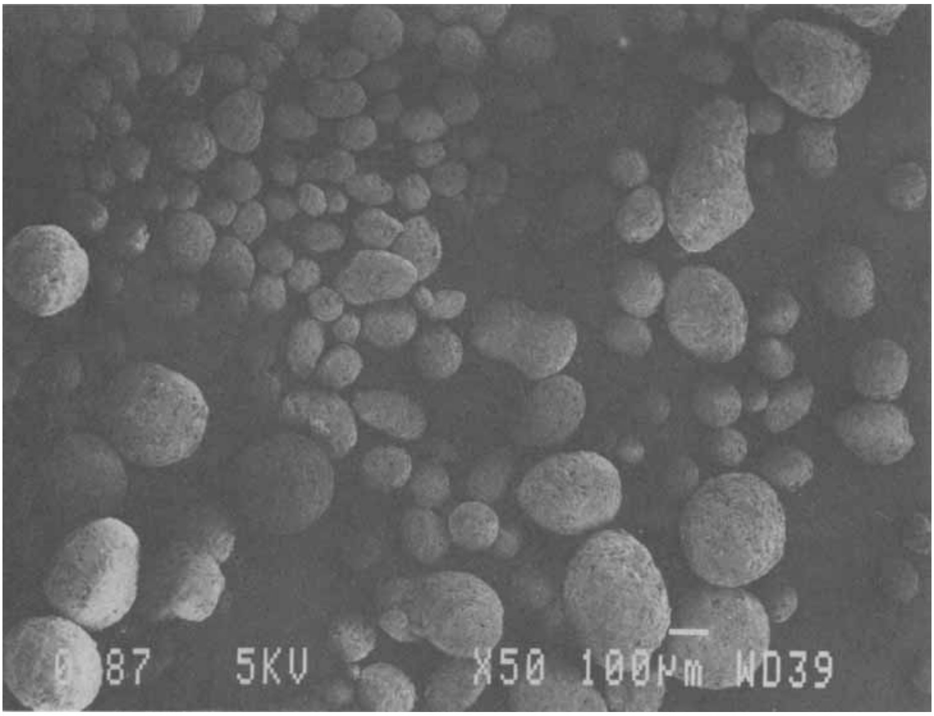


FIGURE 1

Scanning electron micrograph and particle size distribution of Emcompress.



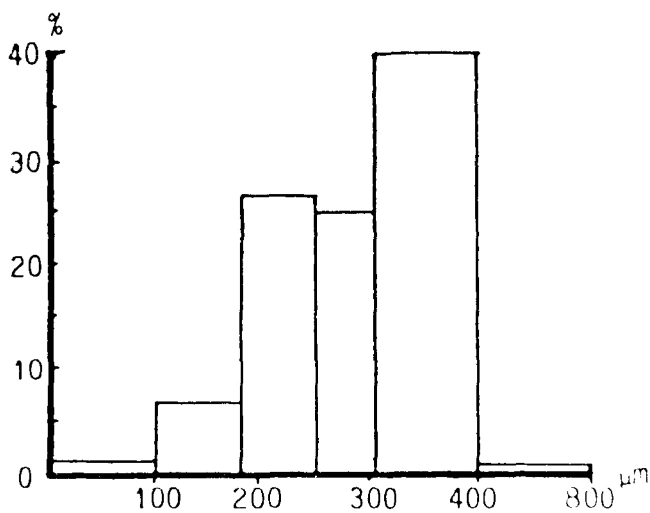


FIGURE 2

Scanning electron micrograph and particle size distribution of Emdex.

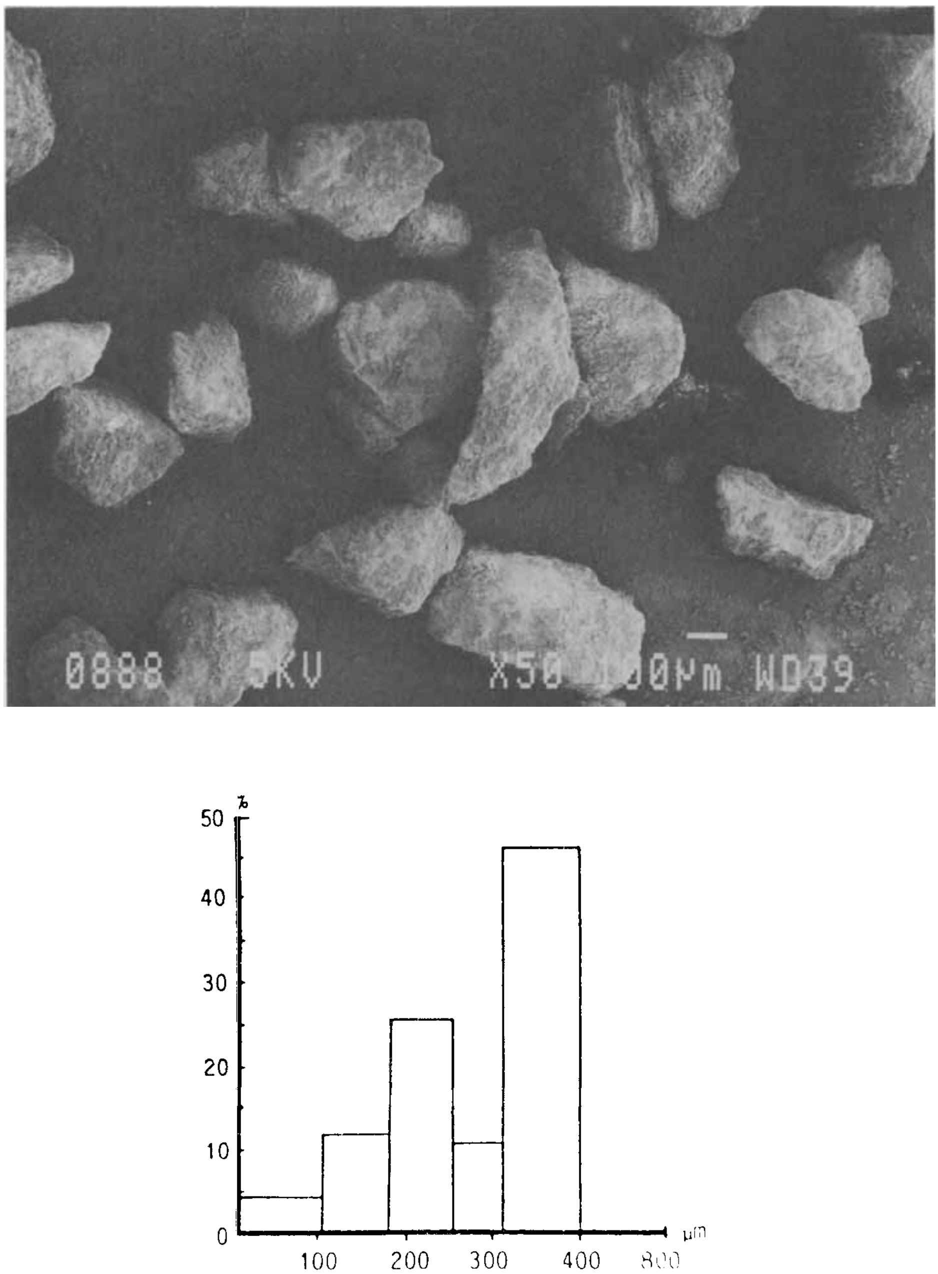
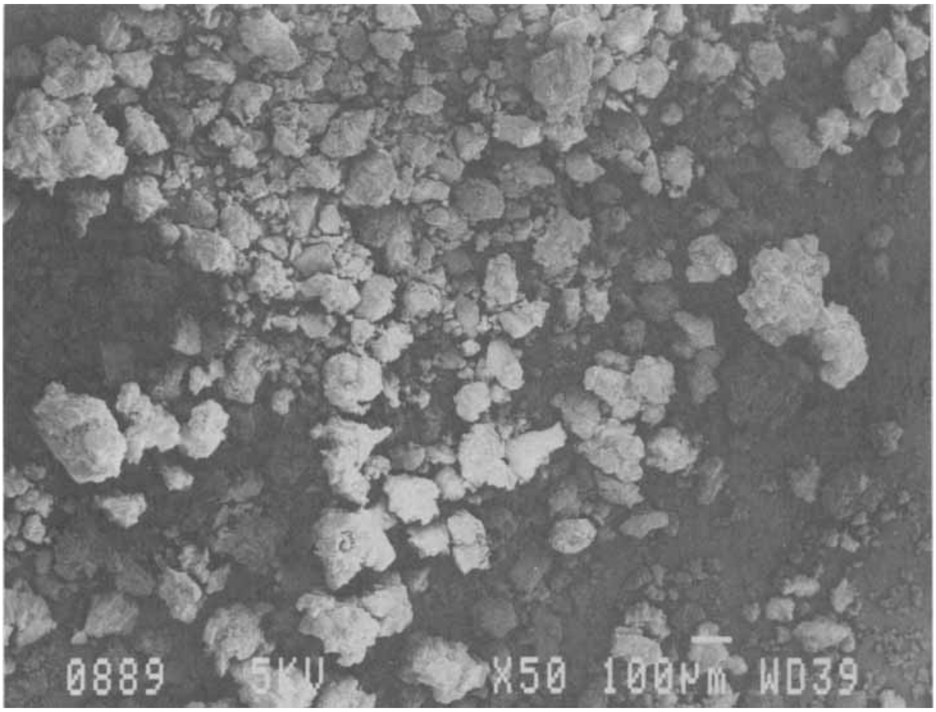


FIGURE 3

Scanning electron micrograph and particle size distribution of magnesium oxide.



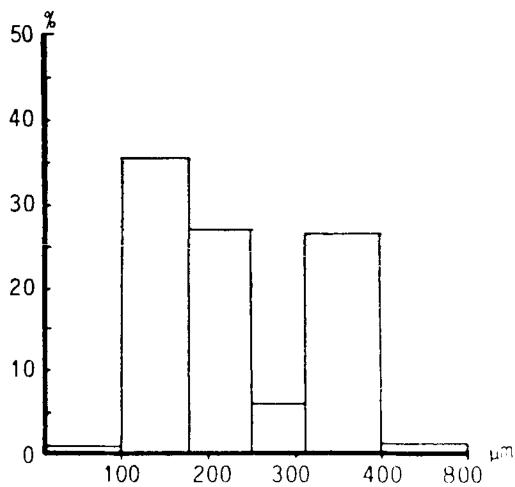


FIGURE 4

Scanning electron micrograph and particle size distribution of mixed powders.

the other powders studied (Figure 1). However, the percentage of particles smaller than 100 μm is significant. The mixed powders, on the other hand consist of non-uniform particles (Figure 4). Table 2 depicts the various powder properties. The moisture content of all the powders was kept to between 0.2 - 0.3%, whilst the tamped density ranged from 0.70 - 1.15 g ml^{-1} and the bulk density from 0.57 - 0.93 g ml^{-1}.

The compressibility index generally increased for powder fractions smaller than 315 μm compared to the unclassified raw material. This trend was more apparent for the mixed powders which have a wider range of particle size distribution. However, particle size did not effect the angle of repose or flow rate of either Emdex or Emcompress. This indicates that for these powders flow rate is independent of particle size under the specific experimental conditions. In contrast, changes in flow rate and angle of repose of both magnesium oxide and the mixed powders were influenced by the particle size of these materials. The latter relationship has previously been established[30-32] and widely accepted in production laboratories. The anomalous behaviour shown by Emdex and Emcompress thus questions the generally accepted concept that a correlation exists between particle size and powder flow rate. Figure 5 depicts the results obtained from the light-emitting flowmeter. These results indicate the considerable potential of the flowmeter in the evaluation of both powder flow rate and uniformity of flow. Steady-state flow is depicted by a linear response at full scale deflection of the initial portion of the flow-time profile. Full blockade is achieved by the

TABLE 2

Properties of Powders

Powder		Particle size µm	Moisture content %	Bulk density g/ml	Tamped density g/ml	Compressibility index %	Angle of repose[+] (α°)	Flow rate g/s
Emdex	a		0.3	0.63	0.72	12.5	51 ± 0.36	9.4
	b	<315	-	0.61	0.70	13.3	47 ± 0.24	9.4
Emcompress	a		0.2	0.83	1.05	20.9	39 ± 0.41	10.6
	b	<315	-	0.80	1.01	21.5	39 ± 0.30	10.6
Magnesium oxide	a		0.2	0.93	1.11	16.3	55 ± 0.50	11.52
	b	<315	-	0.90	1.15	21.3	62 ± 0.44	8.44
Mixed powder (three-component system)	a		0.3	0.81	0.97	16.5	55 ± 0.48	4.33
	b	<315	-	0.57	0.73	22.1	62 ± 0.45	2.77

'a' represents the unclassified powder. 'b' represents the fraction smaller than 315 µm.

[+] (± S.D., n=6).

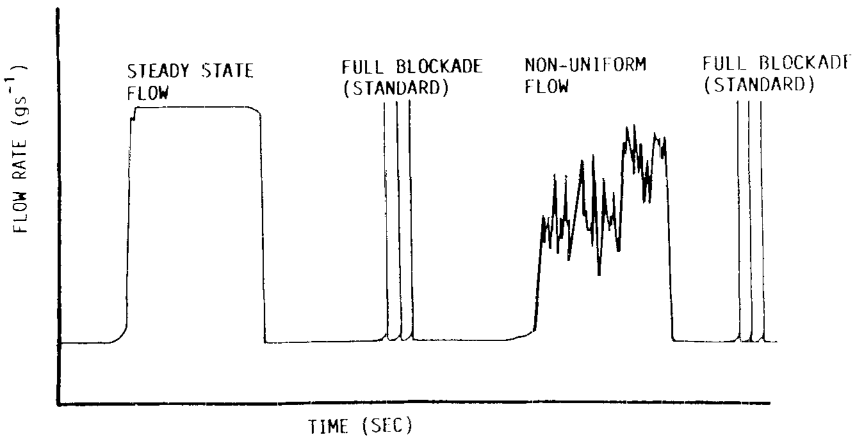
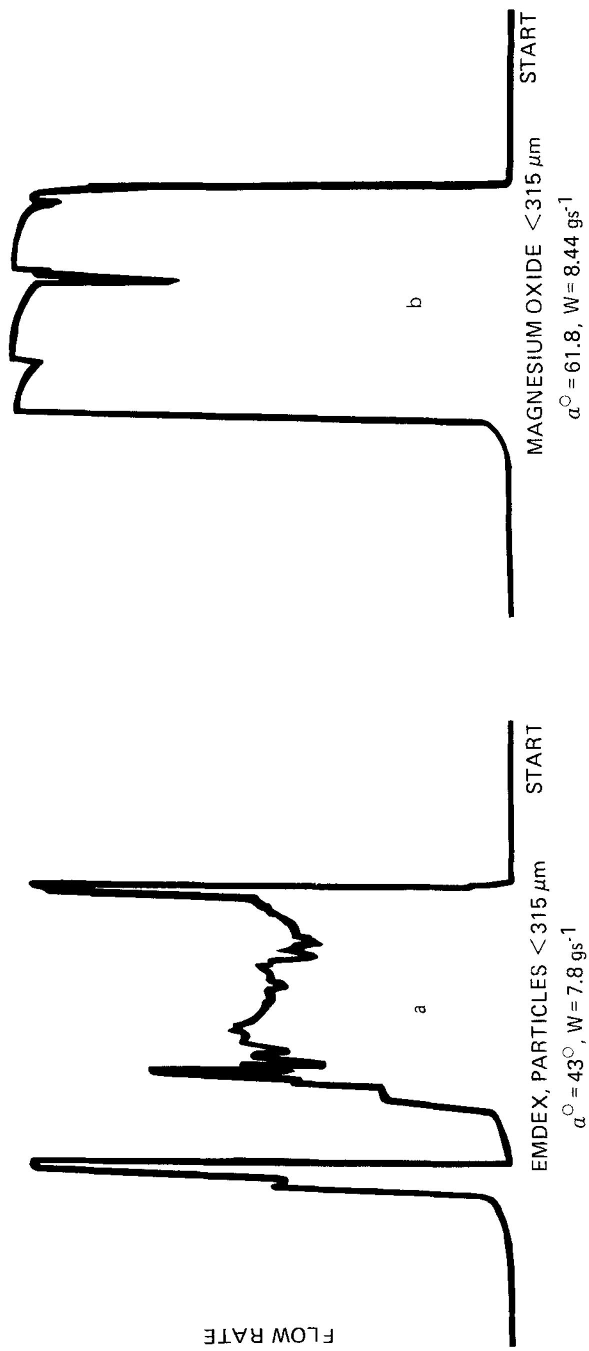


FIGURE 5

A typical flow-time profile showing various flow patterns.

intermittent insertion of an opaque object in the flowmeter orifice. The maximum height of the ordinate inflections correspond to uniform powder flow (or full blockade) whilst any non-uniform flow is easily seen from the irregular responses at lower ordinate values.

The flow-time profiles of non-cohesive powders for these directly compressible materials is given in Figure 6 clearly showing uniform and non-uniform flow behaviour. Emcompress exhibited a uniform flow which is associated with a low angle of repose, good flow rate, narrow size distribution and low compressibility index. The non-uniform flow behaviour of the other powders is obviously due to the wider size distribution and irregular particle shape which contributes to a significant degree of interlocking. It is well documented that flow rate is


START
MAGNESIUM OXIDE <315 μm
a° = 61.8, W = 8.44 gs⁻¹
b
START
EMDEX, PARTICLES <315 μm
a° = 43°, W = 7.8 gs⁻¹
a
FLOW RATE

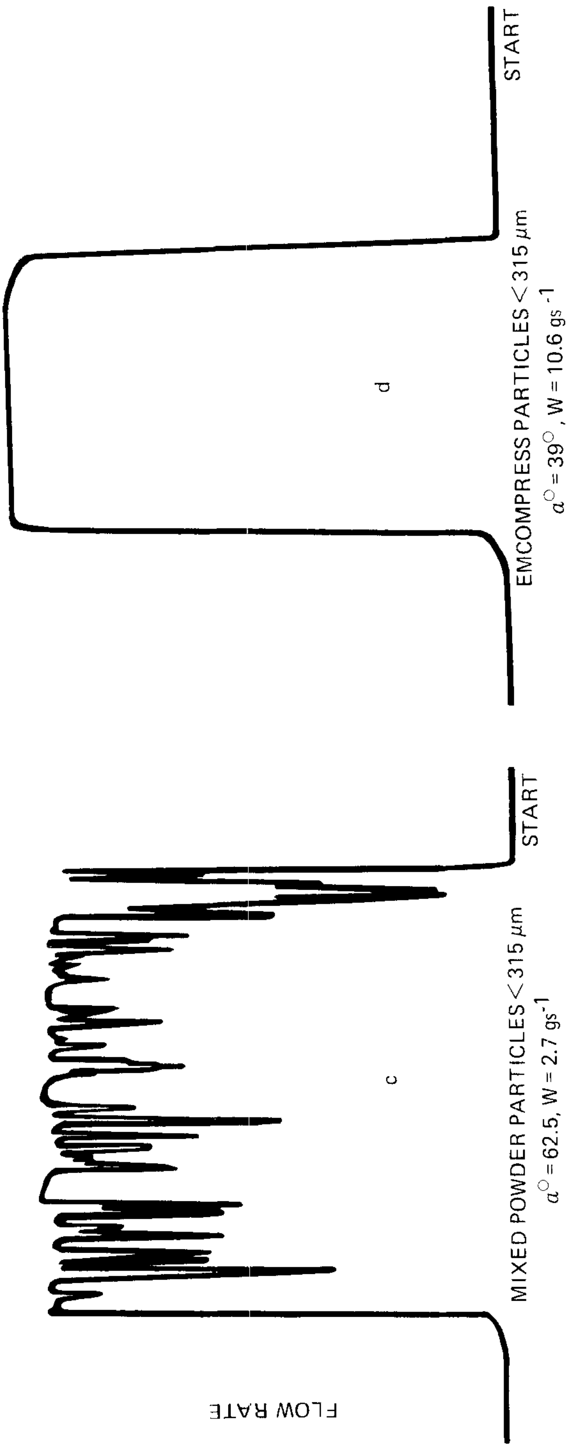


FIGURE 6

Flow-time profiles of non-cohesive powders for directly compressible excipients with various angles of repose ($\alpha°$) and flow rates (W).

influenced by the internal angle of friction associated with the shape of the particles and this will provide some information about their likely behaviour in pipes, chutes, hoppers, tablet and capsule filling machines[33] and therefore such flow-time profiles (Figure 6) will facilitate qualitative assessments of the effects produced by particle shape, size, total bulk and density of powders. The coefficient of tablet weight variation, C.V., can be used as a measure of the flowability. Comparing the C.V. values with the compressibility index, higher weight variation is obtained with increasing compressibility index as shown in Figure 7. A similar relationship has been reported for weight variation versus angle of repose[34] whilst no single relationship has been found to exist between the angle of repose, tamped density, bulk density or compressibility[35].

It is thus important to investigate interrelationships between key parameters such as angle of repose, flow rate, compressibility index and C.V. This will enable useful predictions to be made regarding uniformity of weight. Figure 8 indicates the interrelationships between angle of repose, flow rate, compressibility index and C.V. It is clearly evident that tablets produced from powders having a compressibility index greater than about 20% result in higher C.V. values when compared to tablets produced from powders having a compressibility index below the 20% value. The boundaries of the hatched area were chosen on the basis that powders having an angle of repose greater than about 60° are usually highly cohesive with very poor flow rates whilst powders

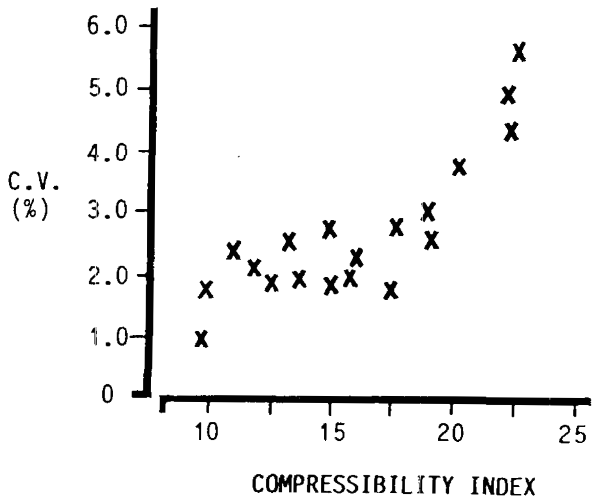


FIGURE 7
Coefficient of tablet weight variation versus compressibility index.

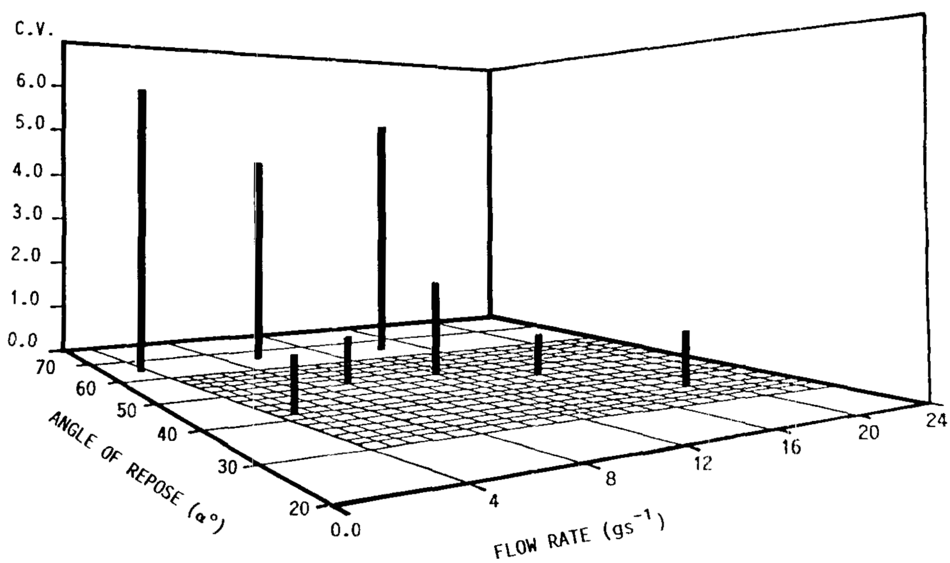


FIGURE 8
Three-dimensional display indicating the interrelationships between flow rate, angle of repose and coefficient of tablet weight variation. The vertical bars beyond the hatched area represent those tablets which were produced from powders having a compressibility index greater than about 20%. The vertical bars within the hatched area represent tablets produced from powders having a compressibility index lower than about 20%.

producing an angle of repose below 30° are generally not readily available for solid dosage form production.

In summary, several key powder parameters have been evaluated and the interrelationships between flow rate, angle of repose, compressibility index and coefficient of tablet weight variation has been established. Uniformity of powder flow was monitored with the aid of a novel powder flowmeter which provided both qualitative and quantitative data. Although particle size was shown to have a significant effect on uniformity of powder flow, the data obtained during this study also indicated that when the compressibility index exceeded a value of about 20% a significant increase in tablet weight variation resulted irrespective of the powder flow rate. Further systematic studies are underway in order to establish the utility of such data and the application thereof in the formulation and production of solid dosage forms.

ACKNOWLEDGEMENTS

The authors thank Ms X K Wakashe for typing this manuscript and Mr E Smith for the photographs.

REFERENCES

1. E.J. Crosby, J.Am. Perfum., 75, 43 (1960).
2. H.G. Kristensen, Dan. Tiddskr. Farm., 43, 205 (1969).
3. R. Ho, D.F. Bagster and M.J. Crooks, Drug Dev. and Ind. Pharm., 3, 475 (1977).
4. J. Carstensen, "Solid Pharmaceutics: Mechanical Properties and Rate Phenomena," Academic Press, 1980, p.86.

5. W.C. Gunsel and L. Lachman, J. Pharm. Sci., 52, 178 (1963).

6. T.M. Jones and N. Pilpel, J. Pham. Pharmacol., 18, 81 (1966).

7. N. Pilpel, in "Advances in Pharmaceutical Sciences," Vol. 3; Bean, Beckett and Carless, eds., Academic Press, New York, 1971, p.173.

8. P.J. Woodhead, J.G. Hardy and J.M. Newton, J. Pharm. Pharmacol., 34, 352 (1982).

9. M. Ahmad and N. Pilpel, Rheol. Acta, 8(4), 448 (1969).

10. A.O. Onyekweli and N. Pilpel, J. Pharm. Pharmacol., 32, 120 (1980).

11. F.Q. Danish and E.L. Parrott, J. Pharm. Sci., 60, 550 (1971).

12. N. Pilpel, Adv. Pharm. Sci., 3, 174 (1971).

13. B. Newman, Adv. Pharm. Sci., 2, 181 (1967).

14. J. T. Carstensen and P. L. Chan, J. Pharm. Sci., 65, 1235 (1976 a).

15. J.T. Carstensen and P.L. Chan, Powder Technol., 15, 129 (1976 b).

16. A.R. Fassihi, M. Falamarzian and M.S. Parker, Drug Dev. and Ind. Pharm. 6(5), 441 (1980).

17. T.M. Jones and N. Pilpel, J. Pharm. Pharmacol., 18, 429 (1966).

18. T.M. Jones, Mfg Chem., 39(3), 38 (1968).

19. L.C. Graton and H.J. Fraser, J. Geol., 43, 785 (1935).

20. R.L. Carr, Chem, Eng. London, 72(2), 163 (1965).

21. J.N. Staniforth, J. Pharm. Pharmacol., 33, 113P (1981).

22. N. Pilpel, J. Pharm. Pharmacol., 16, 705 (1964).

23. G. Gold, R.N. Duvall, B.T. Palermo and J.G. Slater, J. Pharm. Sci., 57, 1291 (1966).

24. G. Gold, R.N. Duvall, B.T. Palermo and J.G. Slater, J. Pharm. Sci., 57, 2153 (1968).

25. G. Gold, R.N. Duvall and B.T. Palermo, J. Pharm. Sci., 57, 1133 (1968).

26. G. Gold, R.N. Duvall and B.T. Palermo, J. Pharm. Sci., 57, 667 (1968).

27. R.P. Jordan and C.T. Rhodes, Drug Dev. and Ind. Pharm., 5, 151 (1979).

28. J.T. Carstensen and S.M. Laughlin, Powder Technol., 23, 79 (1979).

29. E. Nelson, J.Am. Pharm. Assoc., Sci. Ed., 44, 435 (1955).

30. N. Kaneniwa, A. Ikekawa and H. Aoki, Chem. Pharm. Bull., 15, 1441 (1967).

31. C.F. Harwood and N. Pilpel, J. Pharm. Sci., 57, 478 (1968).

32. T.M. Jones and N. Pilpel, J. Pharm. Pharmacol., 18, 182S (1966).

33. N. Pilpel, Mfg. Chem., 41(4), 19 (1970).

34. M. Nicklasson and H. Nyqwist, Int. J. Pharm. Tech. and Prod. Mfr., 3(4), 115 (1982).

35. R.P. Hedge, J.L. Rheingold, S. Welch and C.T. Rhodes, J. Pharm. Sci., 74(1), 11 (1985).