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FLOW STUDIES ON DIRECTLY COMPRESSIBLE TABLET VEHICLES

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ABSTRACT

A number of methods of estimating 'flowability' of some direct compression vehicles have been evaluated as to their usefulness in predicting weight variation on tabletting. There was little or no inter-relationship between angle of repose, compressibility on tamping and flow rate values. In addition there was no correlation between any of these three values and tablet weight variation. In contrast cohesiveness and the reciprocal of the flow factor as determined from shear cell studies exhibited a fair correlation with weight variation of tablets produced on both a single punch and a rotary machine. It is suggested that the reciprocal of the flow factor is a direct measure of the tendency of the powder to arch or bridge during tabletting.

INTRODUCTION

There is a need in the pharmaceutical industry for simple tests to characterise the flow properties of materials to be used in tabletting or capsule-filling. It has been adequately demonstrated that poor flow can result in dosage forms possessing unacceptably high weight variation (1-4). Such tests could be used to characterise powders routinely before compression or filling to reduce down-time on machinery or in the development laboratory to optimise flow properties of experimental formulations. Methods used to estimate 'flowability' of powders include measurement of flow rates through orifices (1,2,4-6), angle of repose (5-8), per cent compressibility on tamping (9,10), tensile strength (11-13), and even weight variation on tabletting (1-3,5,6) or capsule-filling (4). More recently some authors (14-17) have suggested the use of the shear cell as a means of characterising flow of pharmaceutical powders. However, as yet there have been few attempts to relate the shear parameters obtained to weight variation of tablets or capsules.

The direct compression technique of tablet manufacture is being increasingly used in preference to traditional granulation processes. The advantages are well documented (18) and a large number of commercial direct compression vehicles have appeared. These vehicles must be inherently free flowing without the aid of granulation. This paper describes an attempt to characterise the flowability of a number of commercially available direct compression tablet vehicles. Estimates of flowability as determined by flow rate measurement, angle of repose, compressibility on tamping, tensile testing and shear cell measurements are assessed for their value in predicting tablet weight variation on both a single punch and a high speed rotary tablet machine.

EXPERIMENTAL

Materials

The direct compression vehicles are listed in Table I. Details of manufacturers, particle densities, particle size analysis and moisture content have been reported previously (17).

Methods

Angle of Repose

The drained angle of repose was determined using an apparatus similar to that described by Pilpel (7). The reported value was the mean of ten measurements.

Flow Rates

Volume flow rates were determined from a 100ml. graduated glass cylinder (internal diameter, 2.5cm; length 18.5 cm.) through a 2 cm. circular orifice by timing flow from the 100 ml. to the 50 ml. calibration.

Also the mass flow rate from the hopper of a Manesty SP1 tablet machine was determined. This was converted to a volume flow rate by dividing by the bulk density. In each case the flow rate reported is the mean of ten estimations.

Bulk Density and Compressibility on Tamping

Bulk density was determined from the weight of powder filling a 100 ml. graduated cylinder. The powder was then tamped 60 times per minute until the volume became constant. Compressibility was then determined from the equation.

$$\% \text{ Compressibility} = \frac{\text{Tamped density-bulk density}}{\text{Tamped density}} \times 100 \quad (1)$$

Shear Cell Studies

Values for cohesiveness, C, and the flow factor, FF, were determined under a 50 gcm^{-2} normal consolidating stress using a Jenike shear cell as described previously(17).

Tensile Strength

Estimates of tensile strength were obtained using an Ajax-Warren Spring tensile tester. The values were determined at the same bulk density of the powder as achieved in the shear cell (17).

Tablet Compression

To each vehicle, 1% magnesium stearate was added as a lubricant. Tablets were compressed on both a Manesty SP1 single punch tablet machine producing 3600 tablets/

hour using either 8 mm. or 10 mm. punches and a Manesty Betapress multiple punch machine producing 66,000 tablets/hour. The vehicles were compressed at constant die volume. Compression was allowed to proceed before tablets were collected. Samples of 100 tablets were weighed and the coefficient of variation (CV) of weight estimated.

RESULTS AND DISCUSSION

Mean tablet weights from Table 1 are shown plotted against bulk density in Fig 1. The linearity of the plot for the tablets produced on the multiple punch machine suggests that die filling was truly volumetric. For tablets produced on the single punch machine, the plots are not linear particularly for the heavy tablets. Here incomplete die filling occurs probably explaining why weight variation is greater than for the rotary tablets. It is not possible to use weight variation data from the single punch machine to directly predict weight variation on the multiple punch machine. However, it is interesting to note that the rank order of the vehicles with respect to weight variation is the same on both machines.

Values for angle of repose, flow rates and compressibility on tamping for the eight vehicles are listed in Table 2.

Values for angles of repose ranged from 49 - 70^{o} and for compressibility from 8 - 31%. It has been suggested that materials exhibiting angles of repose greater than 45^{o} (19) and compressibility greater than 21% (10) are cohesive and would present problems during tabletting. Avicel, StarX, Cornflour and spray-dried lactose all exhibited values above both limits and the first three vehicles would not flow through a 2 cm orifice or the hopper of the tablet machine. However, they all produced tablets well within

TABLE I

DATA FOR BULK DENSITY, MEAN WEIGHT AND COEFFICIENT OF WEIGHT VARIATION OF TABLETS PRODUCED ON BOTH THE SINGLE PUNCH AND MULTIPLE PUNCH MACHINES AT CONSTANT DIE VOLUME

Vehicle	Bulk Density gml^{-1}	Single Punch				Multiple Punch	
		8mm Punches		10mm Punches		5mm punches	
		Mean Weight mg	CV%	Mean Weight mg	CV%	Mean Weight mg	CV%
Avicel PH 101	0.30	107	3.59	154	5.66	56	1.78
StarX 1500	0.60	233	1.58			94	1.69
Cornflour	0.45			323	2.62		
Lactose (spray-dried)	0.73	302	1.37	537	1.71	132	1.05
Dipac (Batch 1)	0.66					106	0.85
Dipac (Batch 2)	0.64	244	0.82	437	0.87	103	0.81
Celutab	0.67	270	0.71	473	0.70		
Encompress	0.90	333	0.53	592	0.62	144	0.66

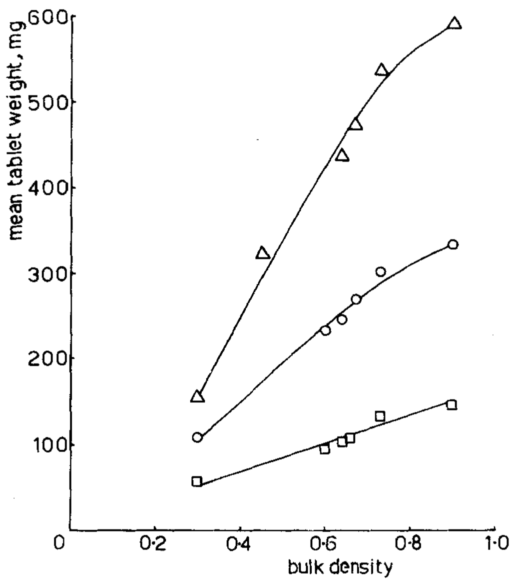

Fig. 1.

Plot of mean tablet weight against bulk density for tablets compressed on the single punch machine using 8mm, O, and 10mm, Δ, punches and on the multiple punch machine using 5mm punches, □.

TABLE 2

FLOW PROPERTIES OF EIGHT DIRECT COMPRESSION VEHICLES

Vehicle	Angle of Repose	Flow rates through 20cm Orifice ml sec^{-1}	Flow rates through Manesty Hopper ml sec^{-1}	Compressibility %	T gcm^{-2}	C gcm^{-2}	FF	1/FF
Avicel	70	No flow	No flow	31	5.58	7.03	3.8	0.263
StarX	70	No flow	No flow	24	2.40	5.17	4.8	0.211
Cornflour	66	No flow	No flow	29	3.38	3.19	6.7	0.148
Lactose(S-D)	65	14.11	No flow	22	1.01	3.19	6.8	0.147
Dipac (Batch 1)	49	77.27	39.55	14	1.22	2.04	12.2	0.082
Dipac (Batch 2)	54	92.03	37.81	16	1.47	2.09	11.7	0.085
Celutab	53	63.73	46.57	8	1.81	2.04	9.7	0.103
Encompress	49	59.56	34.44	19	1.37	1.60	14.8	0.067

official weight variation limits on both the single punch and rotary machines. This suggests that these parameters have little use in predicting flowability during tabletting. There is little correlation between the values themselves. As an example the compressibility of Celutab is half that of Dipac (Batch 2) but the latter has a greater flow rate.

Poor correlation between flow rates and tablet weight variation has been reported previously (5,6). Cole and co-workers (20) observed that there was little relationship between flow rate and variation in flow rate, which is probably the most important factor affecting tablet weight variation. Some flowmeters have been constructed with vibrators attached to facilitate flow of materials which will not flow under gravitational forces alone. These may simulate more closely the hopper of the tablet machine but the amplitude of vibration must be carefully selected. If in addition automatic timing and weighing facilities are incorporated into the flowmeter (20) it will probably be too costly for simple routine use.

Also included in Table 2 are the tensile strength (T), cohesiveness(C), flow factor(FF) and 1/FF values for the eight vehicles. Plots of CV against FF were not linear (Fig 2) but the hyperbolic nature of the plots suggested that there might be a relationship. York (21) has suggested that 1/FF may have more theoretical value because it represents the unconfined yield strength of the powder per unit major consolidating stress. Therefore CV was plotted against 1/FF for both single punch and multiple punch tablets (Fig 3) and reasonable linearity was obtained. Correlation coefficients were greater than 0.92 in all three cases. Plots of CV against C also showed fair linearity with correlation coefficients exceeding 0.94. There was no relationship at all between tensile strength and tablet weight variation. This might be expected as there was shown to be little relationship between T and C or 1/FF in a previous report (17).

Thus the shear cell appears to be a most useful technique in providing parameters such as C or 1/FF which can be used directly to predict tablet weight variation. The advantage over other methods of assessing flowability is that the shear cell measures fundamental parameters which are more directly relevant. For example 1/FF is a direct measure of the tendency of the powder to arch or bridge causing variation in flow rate and tablet weight. The other methods evaluated are less fundamental and measure derived properties of the powder. These properties will also depend on

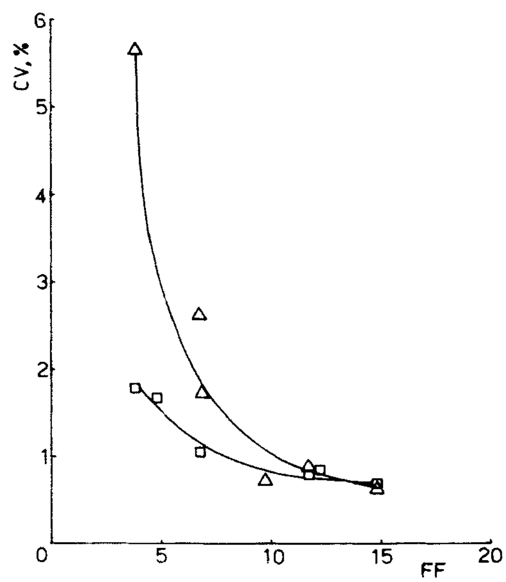

Fig.2

Plot of coefficient of variation of tablet weight versus flow factor. Single punch tablets, △; multiple punch tablets, □.

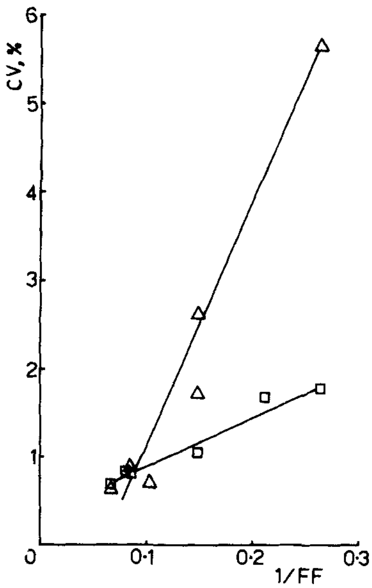

Fig.3.

Plot of coefficient of variation of tablet weight versus reciprocal of flow factor. Single punch tablets, △; multiple punch tablets, □.

experimental factors such as method of pouring or drainage in angle of repose measurement or orifice size and degree of vibration in flow rate determination. In shear cell studies the only factor which must be selected is the normal consolidating stress. This can cause significant differences in FF values for 'complex' powders (17) and should be selected from a knowledge of the stresses applied to a particular powder in a particular hopper. However, even if all the powders are consolidated with the same normal stress, as long as it is fairly representative the FF values obtained will still be more useful than other estimates of flowability.

REFERENCES

1. Gold, G., Duvall, R.M., Palermo, B.T. and Slater, J.G., J. Pharm. Sci., 55, 1133, (1966).

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

3. Augsburger, L.L. and Shangraw, R.F. J. Pharm. Sci., 55, 418 (1966).

4. Irving, G.M., Dodson, G.J. and Ravin, L.J., J. Pharm. Sci., 59, 547 (1970).

5. Kristensen, H.G. Dansk. Tidsskr, Farm., 43, 213, (1969).

6. Kristensen, H.G. and Jensen, V.G., Dansk. Tidsskr Farm. 43, 205 (1969).

7. Pilpel, N., Chem. Process. Engng., 46, 167, (1965).

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

9. Bavitz, J.F. and Schwartz, J.B., Drug and Cosm. Ind., 114, No. 4, 44 (1974).

10. Carr, R. L. Chem. Engng., 72, 163 (1965).

11. Pilpel, N. in "Advances in Pharmaceutical Sciences", 3, Bean, H.S., Beckett, A.H. and Carless, J.E. (Eds) Academic Press, London and New York. (1971) Pp 173-219.

12. Stainforth, P.T. and Berry, R.E.R., Powder Tech., 8, 243 (1973).

13. Kocova, S. and Pilpel, N., J. Pharm. Pharmac., 26, 11P (1974).

14. Pilpel, N., Endeavour, XXVIII, No. 104, 73 (1969).

15. Pilpel, N. and Walton, C.A., J. Pharm. Pharmac., 26, 1P, (1974).

16. Marshall, K. and Sixsmith, D., J. Pharm. Pharmac., 28, 770 (1976).

17. Crooks, M.J., Ho, R. and Bagster, D.F., Drug Dev. Ind. Pharm., Submitted for publication. (1977).

18. Khan, K.A. and Rhodes, C.T., Canad. J. Pharm. Sci., 8, 1 (1973).

19. Neumann, B.S. in "Advances in Pharmaceutical Sciences", 2, Bean, H.S., Beckett, A.H. and Carless, J.E. (Eds) Academic Press, London and New York. (1967). Pp. 181-221.

20. Cole, E.T., Elworthy, P.H. and Sucker, H. J. Pharm. Pharmac., 26, 57P (1974).

21. York. P. Powder Tech., 11, 197 (1975).