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Powder flowability as an indication of capsule filling performance

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Summary

The flowability of size fractions of 5 pharmaceutical excipients has been related to their capsule filling performance. Using angular, packing and shear tests, the samples were ranked in different relative orders of flowability. The powders were filled on an instrumented mG2 capsule filling simulator fitted with a size 1 dosator. Capsule fill weight and weight uniformity were monitored and the coefficient of variation (X_{cv}) of the fill weight of 20 capsules was used as an indicator of capsule filling performance. Flowability was dependent on the particle size, morphology and bulk density of the powder. There was a significant correlation between the values of X_{cv} and the flow parameters of Carr's compressibility, Hausner's ratio, angle of repose, Kawakita's equation constant (a) and Jenike's flow factor. X_{cv} was also related to the coefficient of variation of the powder bed bulk density and the variation in the compression stress. There was, however, no correlation between the values of X_{cv} and the angle of internal flow and the angle of effective friction.

Introduction

For a successful capsule filling operation and the production of capsules with uniform fill weights, it is essential that the powders have optimal flow and packing properties. There is thus a need for test methods which can accurately assess the powders' flowability for use in predicting capsule fill weight variation during filling. Whilst numerous methods such as the angle of repose, flow through orifices, compressibility on tamping, tensile strength and shear parameters have been used to assess the flowability of powders, few attempts have been made to relate these flow parameters to capsule fill weight variation.

To date, some correlations between capsule fill weight variation and parameters such as orifice flow rate (Irwin et al., 1970), angle of repose (Kurihara and Ichikawa, 1978), tensile strength and consolidation ratio (Chowhan and Yang, 1981) have been reported. However, little effort has been made to correlate capsule fill weight variation with parameters such as the Jenike's flow factor, FF (Jenike, 1961, 1964), angle of effective friction, δ (Jenike, 1961, 1964), Carr's compressibility, (Carr, 1965), Hausner's ratio (Hausner, 1967), angle of internal flow, Θ (Varthalis and Pilpel, 1976) and Kawakita's equation constants, a and $1/b$ (Kawakita and Lüdde, 1971).

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A major problem in capsule manufacture is that although doses are specified by weight, the filling system measures by volume. Whilst different types of capsule machines are currently available, the only significant difference amongst them is in the mechanism of dosing the powder into the capsule body (Cole, 1987). Automatic filling machines which employ the dosator nozzle system (e.g., Zanasi and mG2 machines) require the accurate dosing, retention and transfer of a powder plug within a cylindrical nozzle before its ejection into a receiving capsule body.

The present work describes the use of an instrumented mG2 simulator (dosator nozzle system) to study the capsule filling characteristics of sized fractions of Starch 1500, Avicel PH 101, calcium carbonate, maize starch and lactose powders. Capsule filling performance in terms of fill weight and weight uniformity is correlated with the powders' flowability which had been assessed by angular, packing and shear tests.

Materials and Methods

Materials

Microcrystalline cellulose, Avicel PH101 (Honeywill & Stein Ltd., Surrey, U.K.), heavy, precipitated calcium carbonate (BDH, Dorset, U.K.), milled, fine lactose, B170 (Dairy Crest, Surrey, U.K.), maize starch 'Windmill' (Beehive Industries, Amsterdam, The Netherlands) and pregelatinized starch, Starch 1500 (Colorcon Inc., Orpington, U.K.) powders were used for the present study.

Fractionation and characterisation of the powders

A zig-zag classifier (Alpine Multiplex 100 MZR) was used to prepare the different size fractions of the powders. Only particle size ranges of less than 45 μm were selected. For the Starch 1500, Avicel PH101 and calcium carbonate powders, size fractions of: < 11, 11–23 and 23–45 μm were prepared. Due to the narrow size distribution of maize starch, only the < 11 and 11–23 μm size fractions were obtained. Size fractions of < 5, 5–11 and 11–19 μm were prepared for the lactose B170.

Particle size analysis of each fractionated powder in terms of its length (dimension A), breadth (dimension B) and elongation ratio (where E/R = length/breadth) was determined using a digital image and analysing technique linked to a microcomputer to process the digitised data. The system consisted of three components: an image projection apparatus (Vickers M75 laboratory microscope); a sonic digitiser unit (Science Accessories Corp.) and a microcomputer (Commodore Pet). For each particle, 2 points corresponding to its length (A) and 2 points corresponding to its breadth (B) were determined. Between 300 and 600 particles of each size fraction were digitised. The A and B dimensions and the elongation ratio A/B were computed from each set of digitised coordinates (Tan, 1987).

Scanning electron photomicrographs (SEMs) were also taken to examine the morphology and size of the different fractionated systems. The particle density and moisture content of each powder were determined with an air comparison pycnometer (Beckman Model 930) and by drying to constant weight in a vacuum oven (Heraeus) at 85 °C, respectively.

Flow characterisation

The value of the angle of repose (α) for each fractionated powder system was determined using a static, fixed-bed cone method as described by Train (1958). Five determinations were made for each size fraction and the mean value of α computed.

The minimum and maximum bulk density and the rate of packing down of each powder system in a 50 cm^3 graduated cylinder were determined using a tapping device similar to that of Neumann (1967) and a procedure recommended by BS 1460 (1967). Each experiment was repeated four times to obtain mean values of loose and tapped bulk density. The data obtained from the tapping experiments were also used to calculate the values of Carr's (1965) compressibility, (C.C), Hausner's (1967) ratio (H.R.), Kawakita's (Kawakita and Lüdde, 1971) equation constants (a, $1/b$) and angle of internal flow Θ (Varthalis and Pilpel, 1976).

The shear and failure properties of each powder system were characterised using an annular shear cell (Technigraphic Bristol Ltd.) similar in design to that of Carr and Walker (1967). From these experiments values of Jenike's flow factor (F.F) and angle of effective friction, δ (Jenike, 1961) for each powder were derived from their yield loci.

Capsule filling studies

The instrumented mG2 capsule filling simulator used for the current work was similar to that of Jolliffe et al. (1982). A notable difference for the present system involves the use of an instrumented size 1 dosator and a digital storage oscilloscope (Gould Model OS 4040) interfaced to a microcomputer (BBC Model B) for data acquisition (Tan, 1987). The procedure for capsule filling was essentially similar to that described by Jolliffe et al. (1982) but the initial piston height was maintained at 15 mm, i.e. with the piston tip just touching the powder surface during dosing when no piston compression was applied. For each experiment, 20 capsules were filled and the piston displacement and the compression and ejection forces for each filling cycle were recorded by the data capture system. Each capsule was then fitted with a cap and numbered and weighted to ± 0.1 mg. This minus the mean weight of the empty shell gave the weight of powder fill. The change in weight of the nozzle was also noted after each filling cycle thus enabling the weight of powder coating to be determined. Capsule filling studies were carried out for all the powders and for each system the procedure was performed over a range of compression settings and their effects on the capsule filling process monitored. Piston compression adjustments were made approximately from the position of the machine scale (Cm) and more precisely using measurements taken from the piston displacement transducer. The compression ratio, Cr (Takagi et al., 1969) was calculated from the depth of the powder bed and the distance travelled by the piston during powder compression, i.e.

$$\mathrm{Cr} = \frac{\text{change in height of the powder bed on compression}}{\text{original height of powder bed}}$$

The effect of filling powder with a coated nozzle in contrast to a clean one was also investigated. This involved the filling of approx. 500 powder

TABLE 1

Particle size, particle density and moisture content of the powders

	Starch 1500			Avicel PH101			Calcium carbonate			Maize starch		Lactose B170		
Code:	S1	S2	S3	A1	A2	A3	C1	C2	C3	M1	M2	L1	L2	L3
Size fraction (μm)	< 11	11–23	23–45	< 11	11–23	23–45	< 11	11–23	23–45	< 11	11–23	< 5	5–11	11–19
Size dimension (μm)														
A	13.7	29.7	66.7	16.7	58.9	88.7	6.8	14.5	25.2	10.2	15.2	6.6	13.2	25.9
($\pm$S.D.)	(4.3)	(9.3)	(15.0)	(9.3)	(25.9)	(34.3)	(1.9)	(3.4)	(5.1)	(3.3)	(4.1)	(2.4)	(6.5)	(10.0)
B	10.2	20.8	48.6	9.6	26.0	38.1	5.6	12.6	31.7	8.7	12.7	4.1	8.6	16.6
($\pm$S.D.)	(3.1)	(6.4)	(11.6)	(4.9)	(8.9)	(14.9)	(1.7)	(3.1)	(4.1)	(2.8)	(3.4)	(1.4)	(3.9)	(5.8)
ER.	1.4	1.5	1.4	1.8	2.3	2.4	1.3	1.2	1.2	1.2	1.2	1.6	1.6	1.6
($\pm$S.D.)	(0.3)	(0.3)	(0.3)	(0.7)	(1.0)	(0.9)	(0.2)	(0.1)	(0.1)	(0.2)	(0.2)	(0.4)	(0.4)	(0.4)
Particle density (g cm^{-3})														
x	1.47			1.60			2.69			1.5		1.55		
($\pm$S.D.)	(1.6×10^{-3})			(4.4×10^{-3})			(6.5×10^{-3})			(3.3×10^{-3})		(3.6×10^{-3})		
Moisture content (%)	8.6	8.6	8.7	4.0	4.3	4.2	0.2	0.2	0.4	9.6	9.7	0.3	0.3	0.3

S.D., standard deviation; ER., elongation ratio; x, mean value.

plugs (to form a constant coating on the nozzle surface) prior to capsule collection.

All flow characterisations and capsule filling studies were performed in an environment of controlled humidity (35 ± 5% R.H.).

Results and Discussion

Powder characterisation

The designation for the different powders (A, C, L, M and S) and their particle size, particle density and moisture content data are listed in Table 1.

Scanning electron photomicrographs illustrate the shape of the particles to differ from being spherical as in maize starch to those of Avicel which were elongated. All other powder particles were angular. Fine size fractions of lactose (L1) and calcium carbonate (C1) also contained a fair amount of fines and appeared agglomerated.

Flow characterisation

Values for the angle of repose and data relating to the packing behaviour during tap consolidation are presented in Tables 2 and 3. It is clear (Table 3) that angle of repose measurements show powders C3 and S3 ($\alpha = 42$ and 43°, respectively) to be relatively 'free flowing', while L1 appears cohesive ($\alpha = 60°$).

Data for the flow parameters (Tables 2 and 3) derived from the packing characteristics of the powders during tap consolidation, (such as C.C., H.R., Θ and 'a') also indicate coarse powders C3 and S3 to have good flowability whilst fine powders L1 and M1 exhibit very poor flow. Other powders show intermediate flowability.

Clearly, for a particular excipient, flowability is dependent on particle size and the above tests may be used as qualitative indices of flow for ranking the different powder systems.

Table 4 shows the values of Jenike's flow function (F.F) and angle of effective friction (δ) derived from shear cell experiments for the different powders. It is evident that powder C3 (with a FF value of 10.8) is free flowing whilst powders S1, A1, C1, M1, M2 and L1 (with FF values < 4) are cohesive. Other powders exhibit intermediate flow

TABLE 2

Packing properties: minimum and maximum bulk density and compressibility

	Starch 1500			Avicel PH101			Calcium carbonate			Maize starch		Lactose B170		
Code:	S1	S2	S3	A1	A2	A3	C1	C2	C3	M1	M2	L1	L2	L3
Minimum bulk density (g cm^{-3})														
x	0.433	0.551	0.617	0.32	0.29	0.279	0.825	1.161	1.236	0.481	0.479	0.282	0.463	0.654
S.D.	0.015	0.007	0.002	0.005	0.003	0.006	0.007	0.004	0.013	0.019	0.014	0.005	0.007	0.013
Maximum density (g cm^{-3})														
x	0.587	0.695	0.735	0.459	0.385	0.347	1.223	1.394	1.412	0.752	0.703	0.458	0.650	0.802
S.D.	0.006	0.004	0.002	0.004	0.001	0.004	0.002	0.002	0.008	0.011	0.003	0.002	0.006	0.007
Hausner's ratio														
x	1.358	1.261	1.191	1.436	1.327	1.242	1.482	1.2	1.143	1.565	1.468	1.626	1.405	1.227
S.D.	0.046	0.009	0.001	0.032	0.001	0.013	0.011	0.004	0.007	0.076	0.034	0.027	0.016	0.017
Carr's compressibility (%)														
x	26.3	20.7	16.0	30.3	24.7	19.5	32.5	16.7	12.5	36	31.8	38.5	28.8	18.5
S.D.	2.52	0.58	0	1.53	0.58	0.84	0.5	0.289	0.5	3.04	1.61	1.0	0.8	1.1
Carr's flow index														
	poor	fair to passable	good	poor	poor	fair to passable	poor	good to fair	good	very poor	poor	very poor	poor	fair to passable

S.D., standard deviation; x, mean value.

TABLE 3

Angle of internal flow (Θ), angle of repose and Kawakita's equation constants

	Starch 1500			Avicel PH101			Calcium carbonate			Maize starch		Lactose B170		
Code:	S1	S2	S3	A1	A2	A3	C1	C2	C3	M1	M2	L1	L2	L3
Angle of internal flow														
$\text{Tan}^{-1}\Theta$	0.859	0.548	0.474	1.671	2.351	2.753	0.591	0.424	0.409	0.446	0.508	1.59	0.781	0.418
Θ (°)	40.7	28.7	25.4	59.1	67.0	70.0	30.6	23.0	22.3	24	26.9	57.8	38.0	22.7
Kawakita's equation constants														
a	0.392	0.263	0.179	0.369	0.265	0.212	0.372	0.199	0.155	0.379	0.408	0.422	0.408	0.289
$1/b$	67.49	23.47	4.62	42.4	10.8	7.9	28.07	13.89	11.21	16.02	41.27	15.15	77.64	36.45
Angle of repose (α)														
x	56.6	52.7	43.2	58.9	56.3	50.8	57.2	50.0	42.1	57.9	55.5	60.4	55.7	49.4
(±S.D.)	1.4	1.3	1.1	1.8	0.9	1.3	1.6	1.5	0.6	2.3	1.0	4.2	1.7	0.8

S.D., standard deviation; x, mean value.

TABLE 4

Flow function and angle of effective friction

	Starch 1500			Avicel PH101			Calcium carbonate			Maize starch		Lactose B170		
Code:	S1	S2	S3	A1	A2	A3	C1	C2	C3	M1	M2	L1	L2	L3
Tan δ	0.805	0.758	0.674	0.819	0.846	0.808	0.632	0.644	0.608	0.622	0.707	0.823	0.825	0.84
δ (°)	38.8	37.2	34.0	39.3	40.2	38.9	32.3	32.8	31.3	31.9	35.5	39.5	39.5	40.0
F.F.	2.6	3.8	6.5	2.2	4.2	7.0	3.8	7.5	10.8	2.2	3.5	2.4	4.6	7.6
1/FF	0.387	0.26	0.153	0.456	0.24	0.143	0.267	0.134	0.092	0.46	0.289	0.425	0.217	0.132
Jenike's flow classification	Ch	Ch	E.Fl	Ch	Ch to E.Fl	E.Fl	Ch	E.Fl	E.Fl	Ch	Ch	Ch	Ch to E.Fl	E.Fl

F.F. = flow function; Ch, cohesive; E.Fl, free flowing; δ (°), angle of effective friction.

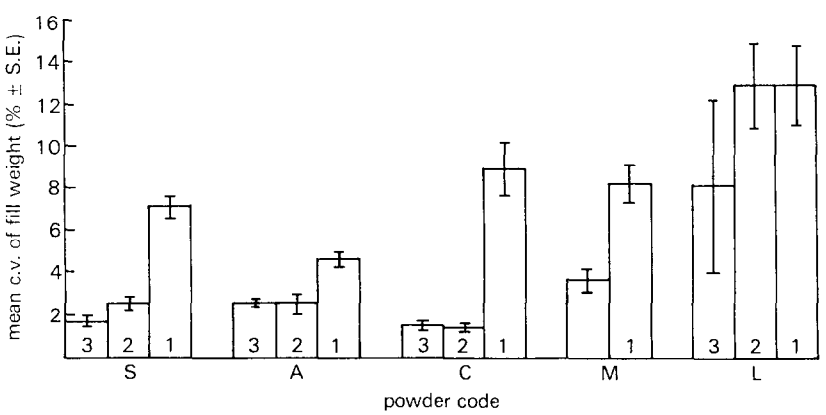

Fig. 1. Histogram of the mean c.v. of fill weight for the different powder systems. Mean = data points from all compression settings. S.E. = standard error of the mean.

properties. For each excipient, the value of FF increases (i.e. better flowability) with increasing particle size. The values of F.F. obtained (Table 4) compared well with those reported by other workers (York, 1975a,b; Marshall and Sixsmith, 1976; Crooks et al., 1977; Ho et al., 1977).

Results obtained for the values of δ are less predictable than that for FF. Large values of δ (39–40°) are observed for powders L1, L2, L3, A1, A2, A3 and S1 while smaller values (31–33°) are exhibited by C1, C2, C3 and M1. For most powders, δ is generally independent of particle size.

As in the case for angular and packing tests, it is clear that values of F.F and δ derived from shear tests may be used as indices of flow and allow powders to be ranked according to their flowability.

Capsule filling studies

The assessment of capsule filling performance will be the coefficient of variation of the fill weight (X_{cv}), the values of which are presented in Fig. 1. Clearly, the highest values of X_{cv} are shown by lactose powders whilst very low values are observed for powders such as C3, C2, S3, S2, A3 and A2. For a particular excipient, the fine size fractions show a much higher value of X_{cv} than the corresponding coarser size fractions. High weight variations observed for lactose powders may be associated with powder binding and piston jamming during capsule filling (Tan, 1987).

Correlation between powder flowability and capsule fill weight uniformity

The methods of Spearman (1904) and correlation coefficient are used to evaluate the relationship between these parameters.

Spearman's rank correlation coefficient (r_s)

Spearman's equation for calculating the rank correlation coefficient, r_s, between any two ranks is given by:

$$r_s = 1 - \frac{6\sum d^2}{n(n^2-1)} \quad (1)$$

where r_s is the rank correlation coefficient, n the number of items in rank and d the difference between each rank.

The rank orders of the various flow parameters and parameters associated with X_{cv} for the different powders (tabulated in Table 5) were derived and the value of Spearman's correlation and coefficient calculated.

From Table 5 it is evident that when parameters commonly used to assess powder flowability, such as Carr's compressibility (C.C), Hausner's ratio (H.R.), angle of repose (α), Kawakita's equation constant (a) and Jenike's flow factor (FF) are compared, all show r_s values which are highly

TABLE 5

Values of Spearman's rank correlation coefficient for the various rank orders

Rank comparison	Spearman's rank correlation coefficient r_s	Significance
C.C. : α	0.903	[b]
C.C. : Θ	0.380	n.s
C.C. : a	0.879	[b]
C.C. : $1/b$	0.490	[a]
C.C. : δ	0.097	n.s
C.C. : F.F	0.859	[b]
C.C. : H.R.	0.996	[b]
Θ : $1/b$	0.051	n.s
Θ : δ	0.585	[a]
Θ : F.F	0.459	[a]
δ : F.F	0.114	n.s
C.C. : X_{cv}	0.780	[b]
H.R. : X_{cv}	0.776	[b]
α : X_{cv}	0.710	[b]
F.F. : X_{cv}	0.596	[a]
X_{cv} : a	0.897	[b]
X_{cv} : $1/b$	0.662	[b]
X_{cv} : Θ	0.275	n.s
X_{cv} : δ	0.363	n.s
X_{cv} : $\gamma_{b.cv}$	0.789	[b]
a : $1/b$	0.686	[b]
X_{cv} : C.S.$_{cv}$	0.692	[b]

[a] Significant at 5% level; [b] significant at 1% and 5% levels; n.s., non-significant.

C.C, Carr's compressibility; α, angle of repose; Θ, angle of internal flow; a and $1/b$, Kawakita's equation constants; δ, angle of effective friction; FF, Jenike's flow factor; H.R., Hausner's ratio; X_{cv}, coefficient of variation of mean fill weight; $\gamma_{b.cv}$, coefficient of variation of initial powder bed bulk; C.S.$_{cv}$, coefficient of variation of compression stress.

significant (i.e. at both 1 and 5% levels). This suggests that any of these methods may be used for evaluating powder flowability to yield comparable trends in the results. In contrast, parameters such as angle of internal flow (Θ) and angle of effective friction (δ) show non-significant correlation with the above indices (i.e. C.C, H.R, α, FF), although there is some correlation (at the 5% level) between Θ and δ. Thus, if values of Θ and δ are used to assess powder flowability, very different results would be obtained.

Comparing the rank orders of these flow parameters with that obtained for capsule fill weight uniformity shows that good rank correlations exist between the coefficient of variation of fill weight (X_{cv}) and flow parameters such as C.C, H.R, α and $1/b$. Whilst there is also a significant correlation between X_{cv} of fill weight and FF (at the 5% level), the former appears unrelated to Θ and δ.

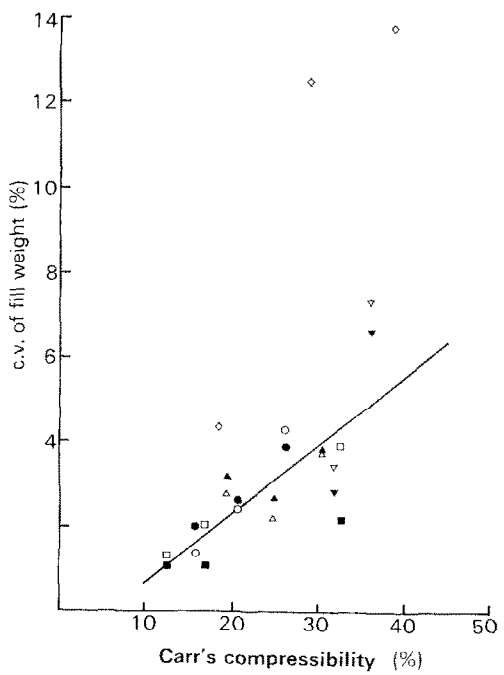

Fig. 2. Coefficient of variation (c.v.) of fill weight as a function of Carr's compressibility ('clean' and 'coated' nozzle). Key to symbols:

Powder code	Nozzle	
	'clean'	'coated'
S	○	●
A	△	▲
C	□	■
M	▽	▼
L	◇	–

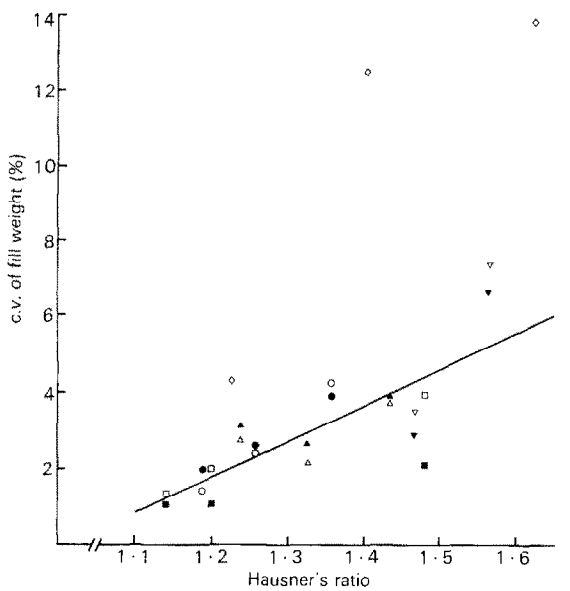

Fig. 3. C.V. of fill weight as a function of Hausner's ratio ('clean' and 'coated' nozzle). Symbols as per Fig. 2.

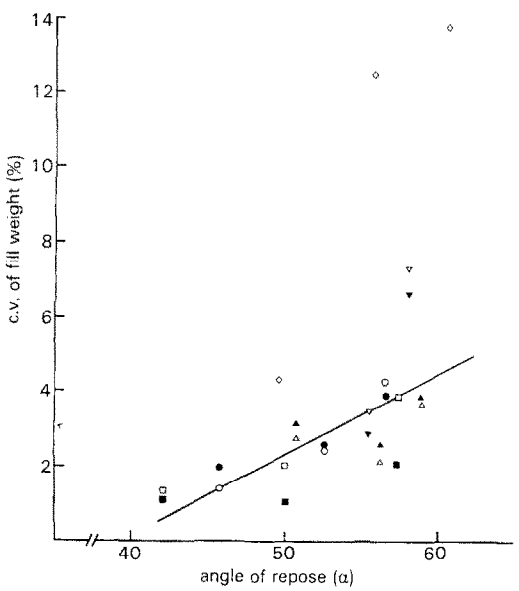

Fig. 4. C.V. of fill weight as a function of angle of repose ('clean' and 'coated' nozzle). Symbols as per Fig. 2.

TABLE 6

Relationship between the coefficient of variation of capsule fill weight (X_{cv}) and the different parameters (P)

Parameter	Including values for lactose ($n = 25$)				Excluding values for lactose ($n = 22$)			
	r	c	m	Comment	r	c	m	Comment
CC	0.632	−2.508	0.257	[b]	0.778	−0.948	0.163	[b]
HR	0.652	−15.656	14.52	[b]	0.793	−9.377	9.283	[b]
α	0.527	−12.05	0.3	[b]	0.664	−6.852	0.186	[b]
FF	0.447	6.555	0.548	[a]	−0.695	5.058	−0.417	[b]
1/FF	0.484	12.24	0.662	[a]	0.818	10.354	0.293	[b]
a	0.627	−0.421	21.127	[b]	0.694	−0.421	11.804	[b]
$1/b$	0.366	2.378	0.056	n.s	0.328	2.331	0.028	n.s
Θ	0.166	2.723	0.03	n.s	0.052	2.83	4.606	n.s
δ	0.303	-4.022	10.75	n.s	0.035	2.551	0.630	n.s
$\gamma_{b,cv}$	0.614	0.436	2.238	[b]	0.819	1.029	1.222	[b]
$C.S._{cv}$	0.728	−0.22	0.246	[b]	0.798	0.088	0.206	[b]

Note: symbols as in Table 5 except: n, number of sets of observations; r, correlation coefficient; c and m, intercept and slope of the best fitting line; [a] significant at 5% level; [b] significant at 1 and 5% levels; n.s, non-significant.

Correlation coefficient (r) The correlations between the flow parameters and their relation to capsule fill weight variations may also be compared by the standard procedures using the correlation coefficient (r).

Figs 2–6 show the graphs of the values of the coefficient of variation of capsule fill weight (X_{cv}) as functions of the various flow parameters which show a significant correlation coefficient. In all cases, values of r are computed for data points, with and without lactose, and the best line of fit obtained by linear regression through the more significant set of results (Table 6). As with the results obtained from Spearman's rank correlation

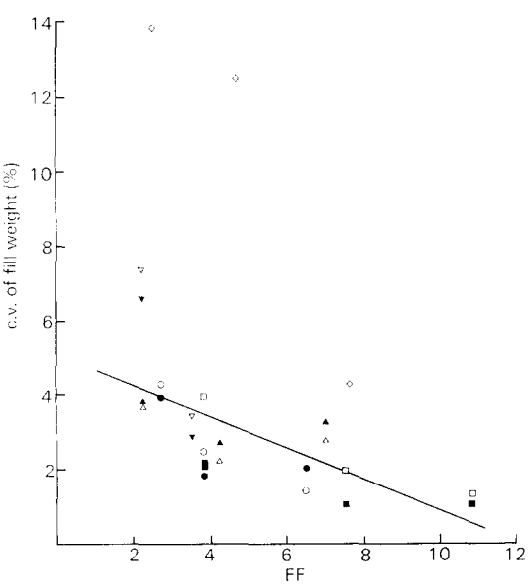

Fig. 5. C.V. of fill weight as a function of FF ('clean' and 'coated' nozzle). Symbols as per Fig. 2.

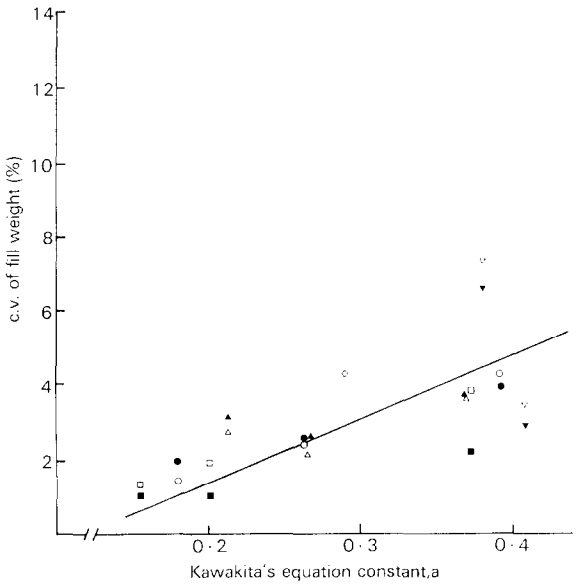

Fig. 6. C.V. of fill weight as a function of Kawakita's equation constant, a ('clean' and 'coated' nozzle). Symbols as per Fig. 2.

coefficient (r_s) significant values of correlation coefficient (r) are obtained between values of X_{cv} and flow parameters such as C.C, H.R, α, FF, 1/FF and 'a'. There is, however, insignificant correlation between the values of X_{cv} and the parameters $1/b$, Θ and δ.

General Discussion

It is apparent from the results presented that parameters such as C.C, H.R, α, a, FF and 1/FF are useful indices of flow which reflect the flow and packing behaviour of powders (on a dosator type capsule machine). Furthermore, these flow parameters may also be used to predict capsule fill weight uniformity. Better flowability tends to yield more uniform fill weights. Since values of Θ and δ do not correlate with either the above flow parameters or the fill weight variation, their use in flow assessments and for predicting capsule fill weight uniformity should be discouraged.

Generally, both Spearman's rank correlation (r_s) and the correlation coefficient (r) yield comparable results with respect to the correlation between fill weight uniformity and the powder flow parameters. Spearman's method is particularly useful when direct measurements are not feasible and only rankings are available. In addition no assumption that sampling from a normal distribution is necessary. A notable difference is, however, observed for the r_s and r values for the correlation between X_{cv} and $1/b$ (Tables 5 and 6, respectively). Whilst a significant correlation is indicated when the r_s value (0.686) is considered, computation of r (0.328) suggests non-significant correlation between X_{cv} and $1/b$. Hence, the use of $1/b$ in flow assessment and the prediction of capsule fill weight variation should be approached with caution. A more reliable index may be the use of the constant, a.

It is also apparent from Table 6 that the flow parameter 1/FF may be better correlated to fill weight variation than the use of FF. As the term 1/FF represents the unconfined yield strength (f_c) of the powder per unit major consolidating stress (σm), this is a direct measure of the tendency of the powder to arch or bridge during packing and consolidation resulting in variation of the capsule fill weight. A similar relationship between 1/FF and tablet weight variation of directly compressible vehicles has been reported by Ho et al. (1977). York (1975b) has also suggested that 1/FF might be a theoretically more correct parameter than FF for the evaluation of flow properties.

The fact that there is good correlation between the values of X_{cv} and the values of C.C and H.R but poor correlation between X_{cv} and values of the minimum and maximum bulk density suggests that it is not the initial or the final value of the powder bulk density per se that is important but the rate of packing down and the extent of the bulk density changes during consolidation that affect fill weight variation (Tan, 1987).

Examination of the results presented (Figs 2–6) also shows some scatter of the data points. This is not unexpected as the present study involves different size fractions of five dissimilar excipients. In addition to the major influence exerted by the flowability of the powders, fill weight uniformity may also be affected by other factors such as powder coating on the nozzle wall and its loss

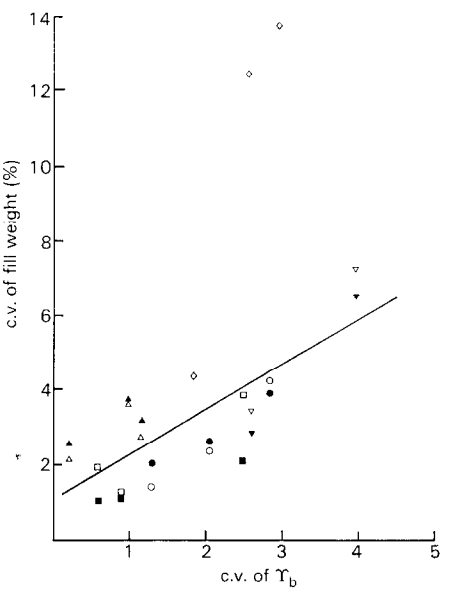

Fig. 7. C.V. of fill weight as a function of c.v. of initial powder bed bulk density, γ_b ('clean' and 'coated' nozzle). Symbols as per Fig. 2.

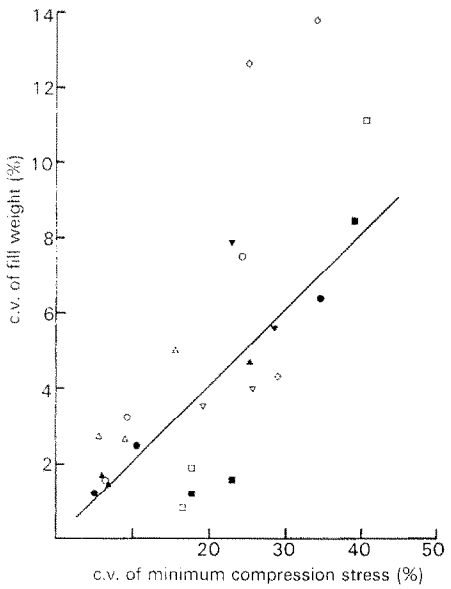

Fig. 8. C.V. of fill weight as a function of c.v. of minimum compression stress ('clean' and 'coated' nozzle). Symbols as per Fig. 2.

behind the piston tip (Tan, 1987) which would undoubtedly lead to more variable fill weights. Generally better correlations are obtained when data points for lactose powders are excluded from the computation of results. For lactose powders, the problems associated with powder binding on the nozzle wall and piston jamming during capsule filling (Tan 1987) result in anomalously high values of X_{cv} and prevent any meaningful correlation with the flow parameters from being drawn. The use of lubricated lactose powders or a lubricated dosator nozzle and piston system would help to resolve the capsule filling problems but it would also mean that flow assessments need be carried out with lubricated powders. Correlations between the values of X_{cv} and powder flowability then apply to lubricated systems only. Another potential disadvantage of using a lubricated lactose system is the modification of the nozzle wall surface by the lubricant film, thus preventing a fundamental study of the effect of wall surface texture on powder-wall friction.

In addition to the influence of flow parameters on capsule fill weight variation, the latter is also affected by the uniformity of the powder feed bed ($\gamma_{b.cv}$) and the uniformity of the compression stress (CS_{cv}) (Tan, 1987). This is confirmed by the results presented in Tables 5 and 6 and Figs 7 and 8 where significant r_s and r values are observed between values of X_{cv} and $\gamma_{b.cv}$ and between X_{cv} and CS_{cv}. These results indicate that more uniform fill weights are attained with less variable initial powder feed bed bulk density (supporting the findings of Woodhead, 1980) and constant compression stress. With regard to the latter, it is not the magnitude per se but the uniformity of the stress transmission that affects fill weight variation. This may have important implications for the automatic control of capsule fill weight by monitoring the variation in the compression stress transmission. Further work is, however, required to confirm this relationship and explore the feasibility of instrumenting a capsule filling machine for such a use under production environment.

Conclusions

(1) The values of CC, HR, α, FF and 1/FF rank the flowability of the powders in a significantly constant manner. This implies that they are measuring a similar property of the powders. Hence, all these parameters are useful indices of flow which may be applied to predict capsule fill weight variation. In contrast, values of Θ and δ do not exhibit a similar rank order and appear to be providing a different measure of the flow properties of the powders.

(ii) The values of X_{cv} are also dependent on the values $\gamma_{b.cv}$ and CS_{cv}. More uniform fill weights are obtained with lower values of $\gamma_{b.cv}$ and CS_{cv}.

(iii) Capsule fill weight uniformity is material and particle size dependent. High weight variation seen for lactose powders may be associated with powder binding and piston jamming during filling. Hence better correlations are obtained when data points for lactose are excluded. For a particular excipient, the fine size fraction exhibits higher weight variation.

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