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A comparative investigation of compression simulators

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Summary

To date 6 high-speed compression simulators operate world-wide and each has been developed, commissioned and validated by a different institution to their own specific standards. A simple comparative test has therefore been developed to investigate the equivalence of data produced by each machine. A common sample of spray-dried lactose (Tablettose, Meggle, F.R.G.) was compressed using the same tooling on each simulator. The force displacement data obtained during compression were analysed using the Heckel equation. Data were compared in terms of mean yield pressure and other Heckel parameters. Within the pressure range attainable by all of the simulators (50–200 MPa), the mean yield pressure was found to differ by up to 10.94%. This was considered acceptable experimental variation between different laboratories. At higher pressures the ICI and Liverpool School of Pharmacy Simulators remained comparable while the Boots Simulator demonstrated a significant difference of up to 16.45%. Differences have been explained in terms of correction for elastic distortion and loading characteristics of the hydraulic systems.

Introduction

Compression behaviour of materials has traditionally been investigated using instrumented tablet presses, mechanical screw feed testing machines or hydraulic presses. Instrumentation of single-punch tableting machines may produce useful comparative data for the formulator but they are limited by their slow single-sided compression which is not representative of the high-speed rotary tabletting machine used in production.

Instrumented rotary tableting machines relate directly to the production situation and produce useful compression, lubrication and powder flow data. However, the instrumentation of such machines has proved difficult, expensive and often inaccurate. Relatively large quantities of a formulation are required which are not normally available for new chemical entities at the stage when the information is most urgently required. Due to the diversity of tableting machine design the results may not be readily transferable to a different model of machine, since the dwell time, magnitude and rate of application of the pre- and main compression can vary from one tablet press to the next.

The mechanical screw feed testing machine provides a more controllable system with which to conduct fundamental investigations. As with single-punch machines, conditions differ from those of a rotary machine with respect to the stress distribution produced in the tablet and friction effects at the die wall. In order to overcome

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these problems Rees et al. (1972) developed a 'simulation device' which produced the double-acting compression effect of a rotary tableting machine.

Screw feed and hydraulic testing machines lack the versatility and high compression rates seen with rotary tableting machines. In 1976, Hunter et al. presented details of the first high-speed compaction simulator. This was a computer-controlled hydraulic press capable of compressing materials according to a programmable displacement/time profile at rates up to 400 mm/s to loads of 40 kN. The formulations to be tested were hand-filled into the die and thus the minimum amount of material was required for each test. Five further high-speed compression simulators have been developed, each with slightly different specifications (see Table 1). Due to the diversity of each system a comparative investigation was undertaken to confirm that results obtained from each machine could be interchanged and that each system produced equivalent quantitative data.

Materials and Methods

α-Monohydrate spray-dried lactose (Tablettose, Meggle Michindustrie GmbH, F.R.G.), was used untreated. The true density was determined using an air comparison pycnometer (Beckmann Model 930); 5 determinations were carried out and the mean was calculated. Material for testing was taken from a common batch which was circulated with a common set of tooling around the participating groups.

Compression

The high-speed compression simulator was fitted with 10-mm flat-faced punches. The elastic deformation of the punches and other parts of the simulator were determined to allow true displacements to be calculated. The punches and die were cleaned and lubricated by painting a suspension of 2% magnesium stearate in carbon tetrachloride, on the inner die surface. The amount of material to give a 3.5 mm thick compact at zero porosity was calculated from the true density. The powder was accurately weighed out and poured into the die cavity. A simple sawtooth displacement/time profile was used to control the compression by the upper punch while the lower punch remained stationary. The material was compressed at a speed of 100 mm/s to a maximum pressure of 500 MPa. Throughout the compression, upper and lower punch displacement and compression force was monitored and stored for subsequent processing. A total of 6 compressions were carried out by each group.

Manipulation of the data

The force/displacement data were calibrated and corrected for elastic deformation using the standard procedures for each group. The data were then analysed using the Heckel equation (1) (Heckel, 1961a and b).

$$\ln \frac{1}{1-D} = KP + A \tag{1}$$

Where D is the relatively density of the compact at pressure P, K is a material constant which is the slope of the straight line region of the plot, the reciprocal of which is the mean yield pressure P_y. A is the value of the intercept of the straight line and is a function of the initial bulk volume. The relative density D_A can be calculated using Eqn 2.

$$D_A = 1 - e^{-A} \tag{2}$$

The relative density of the powder bed at the point when a measurable force is applied, was determined and recorded as D_0.

Regression analyses were carried out on the Heckel plots over the ranges 50–200 MPa, 50–300 MPa, 50–350 MPa and 50–400 MPa. The mean ± S.D. of the mean yield pressure, A and D_A from the 6 compressions were then determined.

The Liverpool School of Pharmacy produced two data sets one year apart in order to act as a control for the material.

Results and Discussion

Table 1 details the specifications of the machines used in this investigation.

TABLE 1

Compression simulator specifications

Institution	Maximum load (kN)	Maximum compression rate (mm/s)	Displacement LVDT stroke range (mm)		Controlling computer	Manufacturer
			Upper	Lower		
ICI	50	400	±50	±25	Commodore PET	Keelavite
Boots	50	1 000	±50	±50	Hewlett Packard Mini	Mand
Wellcome	22.5	400	±12.5	–	Commodore PET	Mand
Smith, Kline & French	50	1 000	±5	±5	Apple IIe	Mand
Glaxo	50	3 000	±10	±10	Olivetti	ESH
Liverpool School of Pharmacy	50	3 000	±10	±10	Apple IIe	ESH

The mechanisms of compaction of lactose under the conditions used in this investigation have been reported previously by Roberts and Rowe (1985). Densification was predominantly by fragmentation but some strain rate sensitivity indicated that a certain amount of plastic deformation could be taking place.

Fig. 1 and Table 2 depict results obtained from the Liverpool School of Pharmacy simulator. It can be seen that minimal change in the material occurred during the year long investigation. The reduction in standard deviation between the two data sets was due to improvements made to the displacement measuring system after results had been collected initially.

Considering the mean yield pressures (Table 2). In the range 50–200 all the simulators produced values within 10.94% of the mean. This was considered an acceptable level of experimental variation between the different laboratories. At higher pressures the ICI and Liverpool School of Pharmacy simulators remained within 8.21% of the mean. The Boots simulator demonstrated a significant difference at higher pressures, producing yield pressure values of up to 16.54% of the mean. These differences are most probably due to the methods employed to correct for elastic distortion of the simulator and punches. The general method used was to bring the punches into contact and then increase the load to the maximum. The distortion was measured during loading using Linear Variable Differential Transformers (LVDTs) or dial gauges. The Boots Co. Ltd. derived independent upper and lower punch distortion values. The method used by the Wellcome Foundation in correcting punch distortion was as described by Ho (1986).

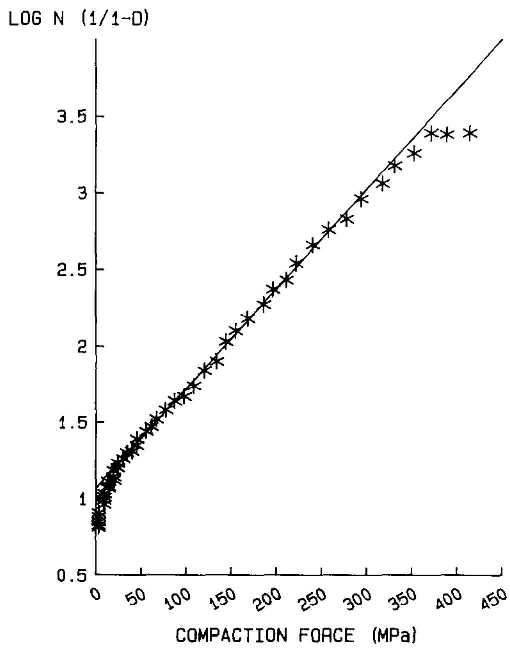

Fig. 1. Heckel plot for Tablettose made by the Liverpool Polytechnic compaction simulator. Tablettose density = 1.53 g/ml, regression = 50–200 MPa.

TABLE 2

Heckel analysis results

	P_y(MPa) $\bar{x}$	P_y(MPa) σn^{-1}	% Error from mean	D_A $\bar{x}$	D_A σn^{-1}	D_0 $\bar{x}$	D_0 σn^{-1}	A $\bar{x}$	A σn^{-1}
ICI									
50–200	172.95	8.67	−3.25	0.677	0.00997	0.557	0.0126	1.132	0.0304
50–300	185.26	3.80	+1.87	0.690	0.00379			1.171	0.0114
50–350	181.18	7.08	−4.62	0.685	0.00817			1.155	0.0254
50–400	174.24	6.15	−8.21	10.676	0.00797			1.126	0.0246
Boots									
50–200	198.30	7.23	+10.94	0.681	0.00446	0.544	0.00288	1.144	0.0134
50–300	208.93	5.41	+10.66	0.689	0.00763			1.170	0.0254
50–350	216.75	6.08	+14.09	0.696	0.01017			1.190	0.0347
50–400	221.23	7.92	+16.54	0.699	0.01188			1.202	0.0407
LSP I									
50–200	171.32	11.15	−4.16	0.677	0.01260	0.568	0.00194	1.130	0.0387
50–300	171.44	15.30	−6.01	0.683	0.01889			1.149	0.0604
50–350	177.58	13.76	−6.52	0.683	0.01838			1.151	0.0600
50–400	180.06	15.86	−5.15	0.685	0.02142			1.160	0.0718
Control									
LSP II									
50–200	181.93	4.96	+1.78	0.687	0.00410	0.460	0.00665	1.162	0.0131
50–300	183.55	2.26	−2.93	0.689	0.00098			1.168	0.0031
50–350	184.36	3.28	−2.95	0.690	0.00258			1.171	0.0083
50–400	183.80	4.25	−3.18	0.689	0.00414			1.168	0.0132
Wellcome									
50–200	169.26	5.40	−5.31	0.642	0.00379	0.466	0.00675	1.024	0.0106
50–250	159.52	6.34	*	0.629	0.00330			0.992	0.0089

LSP, Liverpool School of Pharmacy.
* Maximum load range attainable by the Wellcome simulator.

It should be noted that all corrections for distortion used were approximate, since the true distortion would be compression speed-dependent. The intercept values A are similar as would be expected since the same material was used.

The differences between each group's results emphasise the importance of proper measurements of distortion during displacement measurements under load. Differences could also be due to variations in loading characteristics of the hydraulic systems which have not been accounted for in this study.

A degree of caution should therefore be exercised when comparing data produced by different research groups.

References

Heckel, R.W., Density-pressure relationships in powder compaction. *Trans. Metall. Soc. A.I.M.E.*, 221 (1961a) 671–675.

Heckel. R.W. An analysis of powder compaction phenomena. *Trans. Metall. Soc. A.I.M.E.*, 221 (1961b) 1001–1008.

Ho, A.Y.K., *Time Dependent Characteristics in Tablet Compaction*. Ph.D. Thesis, University of London, 1986.

Hunter, B.M., Fisher, D.G., Pratt, R.M. and Rowe, R.C., A high speed compression simulator. *J. Pharm. Pharmacol.*, 28 (1976) 65P.

Rees, J.E., Hersey, J.A. and Cole, E.T., Simulation device for preliminary tablet compression studies. *J. Pharm. Sci.*, 61 (1972) 1313–1315.

Roberts, R.J. and Rowe, R.J., The effect of punch velocity on the compaction of a variety of materials. *J. Pharm. Pharmacol.*, 37 (1985) 377–384.