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Constant compression–decompression stress rate profiles to obtain rate dependence of maltodextrins for direct compression

Mª del Carmen Monedero Perales*, Angel Muñoz Ruiz, Mª Victoria Velasco Antequera, Mª Rosa Jiménez-Castellanos Ballesteros

Dpto. de Farmacia y Tecnología Farmacéutica, Facultad de Farmacia, c/ Tramontana s.n., Universidad de Sevilla, Sevilla 41012, Spain

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Abstract

Compression–decompression fixed stress rate at 0.5 and 5 MPa/s has been used to obtain maltodextrin compacts. Indentation hardness of tablet surfaces has been used to determine the consolidation mechanisms of maltodextrins for direct compression. The compressibility and compactibility of the powders have been determined using an equation previously described. Also, parameters obtained from Heckel tablet-in-die and ejected-tablet methods were calculated. The strain rate sensitivity (SRS) was also calculated for both excipients. Compression rate dependence using the described methods was higher in QDM 500. However, decompression at fixed strain rate close to the instantaneous rate of stress relaxation was observed in profiles at slow speed performed using M 510.

Keywords: Hardness; Heckel; Consolidation mechanisms; Direct compression excipients; Stress relaxation; Maltodextrins

1. Introduction

The increase in density of a powder bed as a pressure is applied forms the basis of the preparation of tablets (Fell and Newton, 1971).

It is well known that some tablet formulations are susceptible to changes in the speed at which they are compressed and this may lead to difficulties when, for example, production is transferred from one type of press to another or when the rate of production is changed (Armstrong and Palfrey, 1987). Armstrong and Blundell (1985) have shown that a powder which consolidates by fragmentation is less susceptible to speed changes than one whose consolidation mechanism is primarily that of deformation.

Since plastic deformation is time-dependent, one parameter in tablet compaction is the time for which the particulate material is held under load (Rees and Rue, 1978).

The most widely used equation relating the relative density of a powder bed during com-

* Corresponding author.

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Table 1
Summary of the results of analysis of variance for the different parameters

		HV	P_y(id)	P_y(0)	SRS(id)	SRS(0)	HV_{max}	γ
Maltodextrins	Excipient	13.9[a]	121.94[a]	3.2	11.73	2.69	0.16	9.2[a]
	Strain rate	58.48[a]	93.28[a]	0.98			10.89[a]	0.05
	Pressure	5588.72[a]						
M 510	Strain rate	0.39	1351.19[a]	1.5			0.07	0.03
	Pressure	2504.01[a]						
QDM 500	Strain rate	110.68[a]	3658.22[a]	3.72			14.33[a]	0.25
	Pressure	3135.69[a]						

[a] $\alpha < 0.01$.

paction to the applied pressure (Roberts and Rowe, 1986) is the Heckel equation (Heckel, 1961). In addition, the density of the compacts has been assessed while under pressure (Cooper and Eaton, 1962) and after the release of pressure (Heckel, 1961).

Solids are known to display time-dependent behaviour which can greatly affect the compressional properties; therefore, Heckel data determined on a hydraulic press may not be a true indicator of powder behaviour in a high speed press (Geoffroy and Carstensen, 1991).

In a previous paper, Monedero Perales et al. (1994) indicated the possibility of using indentation hardness of tablets as an alternative method to study consolidation mechanisms of different substances at a determinate compression rate.

In the present paper two compaction speeds have been applied (0.5 and 5 MPa/s) in a universal testing machine (Instron) in order to study the time-dependent properties of two varieties of maltodextrins. Indentation hardness and Heckel plots have been used as methods to determine strain rate sensitivity.

2. Materials and methods

Two direct compression excipients were used: Maltodextrin Maltrin® M 510, batch A3533 and Maltodextrin Maltrin® QDM 500, batch 083-916V (GPC, Muscatine, Iowa, USA)

The true density of each powder was determined using a helium pycnometer (Model Stereopycnometer, SPY 3 Quantachrome, Syosset, NY, USA). Relative density on precompression (D_0) was measured using techniques described previously by Muñoz-Ruiz et al. (1988).

Table 2
Indentation diameters and Vickers hardness of upper, lower and side surfaces of tablets of Maltrin® M 510

			30 MPa	60 MPa	90 MPa	120 MPa	150 MPa
Slow	U	D	0.785 ± 0.000	0.576 ± 0.009	0.487 ± 0.002	0.424 ± 0.009	0.377 ± 0.003
		HV	15.88 ± 0.01	29.50 ± 0.95	41.18 ± 0.42	54.31 ± 2.34	68.84 ± 1.18
	L	D	0.769 ± 0.006	0.582 ± 0.001	0.511 ± 0.004	0.429 ± 0.004	0.380 ± 0.000
		HV	16.76 ± 0.27	28.85 ± 0.11	37.46 ± 0.68	53.08 ± 1.15	53.08 ± 1.15
	S	D	0.877 ± 0.016	0.608 ± 0.006	0.512 ± 0.019	0.438 ± 0.008	0.391 ± 0.008
		HV	12.74 ± 0.47	26.49 ± 0.52	37.46 ± 2.79	50.99 ± 1.97	63.89 ± 2.65
Fast	U	D	0.788 ± 0.001	0.591 ± 0.001	0.503 ± 0.014	0.430 ± 0.002	0.383 ± 0.002
		HV	15.75 ± 0.09	28.05 ± 1.04	38.73 ± 2.19	52.78 ± 0.58	66.56 ± 0.73
	L	D	0.771 ± 0.003	0.604 ± 0.002	0.502 ± 0.009	0.426 ± 0.005	0.388 ± 0.005
		HV	16.48 ± 0.13	26.83 ± 0.21	38.84 ± 1.39	53.86 ± 0.35	64.91 ± 1.88
	S	D	0.938 ± 0.066	0.640 ± 0.001	0.503 ± 0.023	0.415 ± 0.004	0.378 ± 0.002
		HV	11.20 ± 1.57	23.92 ± 0.10	38.74 ± 3.63	56.77 ± 1.15	68.40 ± 0.76

A quantity of powder sufficient to produce tablets of known thickness at zero theoretical porosity was weighed separately and filled manually into the die. Flat compacts were prepared at five different pressures between 0 and 150 MPa. Tablets were made after lubricating the die with a 5% w/v chloroformic solution of stearic acid (Humbert-Droz et al., 1982). The compaction was performed using a universal testing machine (Instron, Model 8033); a general control program was used to obtain the compression–decompression fixed strain rate, 0.5 and 5 MPa/s.

The diameter of the Vickers indentation was measured using a Zwick 3212 hardness testing machine (Norma UNE, 1986). Preliminary tests were performed to select an applied force that ensured a permanent indentation in the tablet surface. The force selected was 9.8 N. Contact time was fixed at 10 s.

Five indentations were made in the upper and lower surfaces, and two indentations in the side of two tablets.

3. Results and discussion

Table 1 shows the ANOVA values of the different parameters under study (*HV*, Vickers hardness; P_y(id), tablet-in-die yield pressure; P_y(0), ejected-tablet yield pressure; SRS, strain rate sensitivity; HV_{max}, compactibility; γ, compressibility).

Table 2 and Table 3 show indentation diameters and Vickers hardness values (average of two tablets) of the upper, lower (average of five indentations) and side surfaces (average of two indentations) of different tablet batches of Maltodextrin Maltrin® M 510 and QDM 500.

As expected, the diameter of the indentation decreases and Vickers hardness increases as applied pressure was increased (from batches 1 to 5) (Romano Moreno and Vázquez López, 1988). The effect of strain rate on Vickers hardness was significant in the case of QDM 500, and non-existent in the case of M 510. A similar effect was observed previously (David and Augsburger, 1977) on the crushing strength values of plastic materials.

The location of the indentation (upper, lower and side of the compacts) was a significant factor for both maltodextrins (M 510, $F = 11.29$, $P < 0.01$; QDM 500, $F = 16.62$, $P < 0.01$). It can be observed that these values are very similar in Maltodextrin QDM 500 and M 510, indicating an inefficient transmission of the compression stresses through the mass during compaction (Aulton, 1981).

The most frequently used relationship between relative density and applied pressure is the Heckel equation (Ilkka and Paronen, 1993), which is based on the assumption that efficient transmission of compression stress densification of the bulk powder column follows first-order kinetics (Heckel, 1961).

Table 3
Indentation diameters and Vickers hardness of upper, lower and side surfaces of tablets of Maltrin® QDM 550

			30 MPa	60 MPa	90 MPa	120 MPa	150 MPa
Slow	U	*D*	0.845 ± 0.014	0.616 ± 0.000	0.480 ± 0.001	0.412 ± 0.002	0.377 ± 0.008
		HV	13.71 ± 0.45	25.82 ± 0.04	42.50 ± 0.35	57.48 ± 0.82	66.89 ± 3.04
	L	*D*	0.863 ± 0.003	0.617 ± 0.005	0.486 ± 0.004	0.412 ± 0.005	0.372 ± 0.006
		HV	13.14 ± 0.10	25.67 ± 0.44	41.41 ± 0.84	57.49 ± 1.53	70.81 ± 2.52
	S	*D*	0.939 ± 0.002	0.649 ± 0.000	0.486 ± 0.022	0.415 ± 0.000	0.382 ± 0.001
		HV	11.10 ± 0.05	23.26 ± 0.05	41.58 ± 3.92	56.90 ± 0.19	66.89 ± 0.61
Fast	U	*D*	0.820 ± 0.002	0.647 ± 0.002	0.492 ± 0.002	0.443 ± 0.000	0.386 ± 0.010
		HV	14.55 ± 0.10	23.38 ± 0.18	40.37 ± 0.48	49.93 ± 0.19	65.71 ± 3.65
	L	*D*	0.826 ± 0.002	0.634 ± 0.006	0.515 ± 0.001	0.447 ± 0.006	0.390 ± 0.001
		HV	14.36 ± 0.08	24.36 ± 0.51	36.90 ± 0.22	48.95 ± 1.33	64.26 ± 0.51
	S	*D*	0.969 ± 0.020	0.682 ± 0.018	0.514 ± 0.000	0.447 ± 0.001	0.397 ± 0.000
		HV	10.43 ± 0.43	21.07 ± 1.57	37.05 ± 0.03	48.88 ± 0.38	62.02 ± 0.22

Table 4
Results derived from experimental data obtained using Heckel tablet-in-die and ejected-tablet methods: intercept density of the linear regression (D_a), density contribution to movement and rearrangement (D_b), relative density of precompression (D_0), yield pressure (P_y), correlation coefficient (r) and values of F-test (F)

			D_a (g/cc)	D_b (g/cc)	D_0 (g/cc)	P_y	r	F
M 510	Slow	Ejected	0.513	0.032	0.481	59.08	0.998	9.591
		In-die	0.493	0.093	0.399	41.99	0.999	0.662
	Fast	Ejected	0.449	0.032	0.481	54.00	0.997	10.86
		In-die	0.503	0.116	0.387	46.58	0.999	0.403
QDM 500	Slow	Ejected	0.407	0.105	0.304	43.10	0.997	13.51
		In-die	0.487	0.174	0.312	32.89	0.999	1.448
	Fast	Ejected	0.502	0.198	0.304	55.95	0.996	9.633
		In-die	0.523	0.250	0.273	41.25	0.998	0.445

Parameters derived from Heckel in-die and Heckel ejected-tablet methods are shown in Table 4 and Heckel tablet-in-die plots are shown in Fig. 1 for both maltodextrins.

P_y values for both excipients show a strain rate dependence, indicating a consolidation mechanism primarily by plastic deformation (Armstrong and Blundell, 1985).

Heckel parameters will be more dependent on the compression–decompression cycle than the size of the die (Danjo et al., 1989).

During decompression of tablets at fixed stress rate postcompressional compaction behaviour can be observed, as indicated by the lower value of P_y obtained in tablet–in-die Heckel plots than in the ejected-tablet method. This may be due to the fact that during decompression the stress rate is controlled, and the plastic flow of the material occurs at this moment of the cycle (David and Augsburger, 1977).

Tablet-ejected Heckel plots are shown in Fig. 2. The P_y values of both excipients, calculated using this method, demonstrate no strain rate dependence.

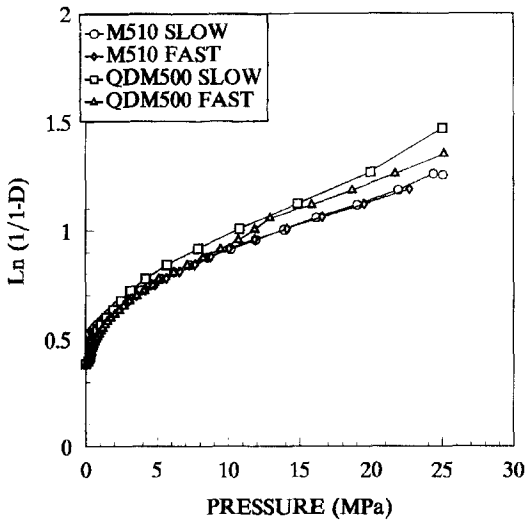

Fig. 1. Tablet-in-die Heckel plots.

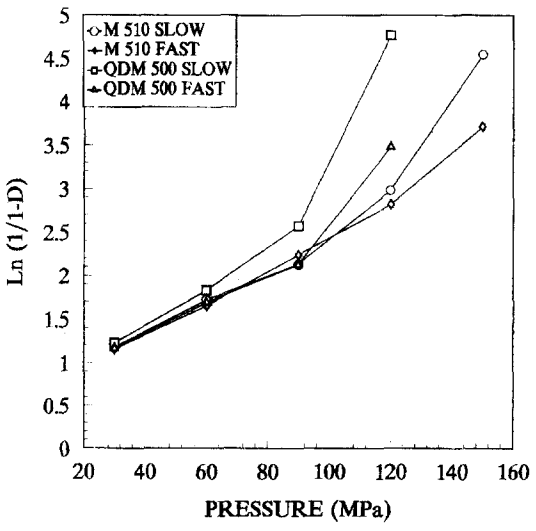

Fig. 2. Ejected-tablet Heckel plots.

Table 5
Values of compactibility (HV_{max}, MPa) and compressibility (γ, MPa^{-1}), correlation coefficient (r), values of F-test (F) and probability level (P)

			HV_{max}	γ	r	F	P
M 510	Slow	U	68.849	0.0107	0.999	6.56	>0.999
		L	67.831	0.0085	0.999	5.25	>0.999
		S	63.898	0.0109	0.999	6.65	>0.999
	Fast	U	66.567	0.0097	0.999	6.19	>0.999
		L	64.917	0.0100	0.996	6.43	>0.999
		S	68.408	0.0107	0.995	6.83	>0.999
QDM 500	Slow	U	68.892	0.0116	0.988	8.06	>0.999
		L	70.813	0.0106	0.992	7.29	>0.999
		S	66.897	0.0124	0.983	8.73	>0.999
	Fast	U	65.713	0.0117	0.971	7.50	>0.999
		L	64.267	0.0100	0.991	6.14	>0.999
		S	62.023	0.0120	0.982	7.57	>0.999

Roberts and Rowe (1985) propose an additional study of the effect of punch velocity to understand the compression process. In this sense SRS (strain rate sensitivity) was measured according to the relation proposed by these authors.

$$\mathrm{SRS} = \frac{P_{y_2} - P_{y_1}}{P_{y_2}} \times 100$$

where SRS is the strain rate sensitivity, P_{y_1} is the yield pressure at low speed and P_{y_2} is the yield pressure at high speed. The parameter SRS has been calculated in absolute values.

The SRS calculated using Heckel tablet-in-die and ejected-tablet methods demonstrated no statistical differences between both excipients (0.097 and 0.233 for M 510 and QDM 500, respectively). However, it can be observed that the difference between P_y values for both excipients obtained at the two strain rates are different, but not in the same way.

The P_y values from Heckel ejected-tablet and Heckel tablet-in-die methods are very dissimilar for M 510 but not for QDM 500. This can be explained by the 'instantaneous rate of stress relaxation' described by Rees and Tsardaka (1993). These authors obtained instantaneous rate of stress relaxation values for Starch 1500 (0.8 MPa/s) and Avicel® PH 102 (0.5 MPa/s).

When a material is compressed, stress relaxation occurs during the decompression phase. If the instantaneous rate of stress relaxation is higher than the decompression stress rate, compactional behaviour of the material during decompression can be observed. This occurs later in the case of M 510.

Based on the equation described in previous work (Monedero Perales et al., 1994):

$$\ln\left(1 - \frac{HV}{HV_{max}}\right) = \gamma P_a D_r$$

where HV is the deformation resistance or Vickers hardness, HV_{max} is the compactibility, P_a is the applied pressure or compression stress to make the tablet and D_r is the relative density. This equation allows a logarithmic-regression adjustment.

To calculate the compressibility parameter (γ) using this method, a maximum HV was obtained for each excipient using high applied pressure. These results are showed in Table 5. The value of HV_{max}, which represents the maximum hardness which would be attained at infinite applied pressure, was not very different for both excipients. Based on these parameters ($< 10^2$), the consolidation mechanism was mainly by plastic deformation (Jetzer, 1982). In the same way compressibility values ($> 10^{-2}$) exhibited the same result, which means that these excipients show a consolidation mechanism by plastic deformation.

The parameter HV_{max} showed strain rate dependence, but the compressibility parameter γ did not.

It can be seen that the methods to elucidate the consolidation mechanisms and the compression rate dependence in pharmaceutical compression showed that Maltrin® QDM 500 is a more stress dependent material than M 510; however, M 510 on the basis of differences of P_y values between Heckel tablet-in-die and Heckel ejected-tablet methods showed an instantaneous rate of stress relaxation close to the rate of the slow decompression stress–time profile performed, thus compaction of the materials occurs during decompression.

References

Armstrong, N.A. and Blundell, L.P., The effect of machine speed on the compaction of some directly compressible tablet diluents. *J. Pharm. Pharmacol.*, 37 (1985) 28.

Armstrong, N.A. and Palfrey, L.P., Punch velocities during the compaction process. *J. Pharm. Pharmacol.*, 39 (1987) 497–501.

Aulton, M.E., Indentation hardness profile across the face of some compressed tablets. *Pharm. Acta Helv.*, 56 (1981) 133–137.

Cooper, A.R. and Eaton, I.E., Compaction behaviour of several ceramic powders. *J. Am. Ceramic Soc.*, 45 (1962) 97–101.

Danjo, K., Ertell, C. and Carstensen, J.T., Effect of compaction speed and die diameter on Athy–Heckel and hardness parameters of compressed tablets. *Drug Dev. Ind. Pharm.*, 15(1) (1989) 1–10.

David, S.T. and Augsburger, L.L., Plastic flow during compression of directly compressible fillers and its effect on tablet strength. *J. Pharm. Sci.*, 66(2) (1977) 155–159.

Fell, J.T. and Newton, J.M., Effect of particle size and speed compaction on density changes in tablets of crystalline and spray-dried lactose. *J. Pharm. Sci.*, 60(12) (1971) 1866–1869.

Geoffroy, J.M. and Carstensen, J.T., Effects of measurement methods on the properties of materials. *Powder Technol.*, 68 (1991) 91–96.

Heckel, R.W., Density–pressure relationship in powder compaction. *Trans. Metall. Soc. AIME*, 221 (1961) 671–675.

Humbert-Droz, P., Mordier, D. and Doelker, E., Methode rapide de détermination du comportament à la compression pour études de préformulation. *Pharm. Acta Helv.*, 57 (1982) 136–143.

Ilkka, I. and Paronen, P., Prediction of the compression behaviour of powder mixtures by the Heckel equation. *Int. J. Pharm.*, 94 (1993) 181–187.

Jetzer, W.E., Measurement of hardness and strength of tablets and their relation to compaction performance of powders. *J. Pharm. Pharmacol.*, 38 (1982) 254–258.

Monedero Perales, M.C., Muñoz-Ruiz, A., Velasco Antequera, M.V. and Jiménez-Castellanos, M.R., Study of the compaction mechanisms of lactose-based direct compression excipients using indentation hardness and Heckel plots. *J. Pharm. Pharmacol.*, 46 (1994) 177–181.

Muñoz-Ruiz, A., Borrero, J.M., García, M.A. and Jiménez-Castellanos, R., Un programa de ordenador para el estudio reológico de los polvos. *Ciencia e Industria Farmacéutica*, 7 (1988) 321–325.

Norma española UNE 7-423-86/2.

Rees, J.E. and Rue, P.J., Time-dependent deformation of some direct compression excipients. *J. Pharm. Pharmacol.*, 30 (1978) 601–607.

Rees, J.E. and Tsardaka, K.D., Compaction stress relaxation interpreted using a hyperbolic relation. *Int. J. Pharm.*, 92 (1993) 137–141.

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

Roberts, R.J. and Rowe, R.C., The effect of the realtionship between punch velocity and particle size on the compaction behaviour of materials with varying deformation mechanisms. *J. Pharm. Pharmacol.*, 38 (1986) 567–571.

Romano Moreno, S. and Vázquez López, F., Determinación de la resistencia mecánica de comprimidos II. Estudio en comprimidos de excipientes de compression directa. *CIF*, 7(2ª ep.) (1988) 285–292