DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 21(10), 1235-1243 (1995)

FLOW STUDIES ON MALTODEXTRINS AS DIRECTLY COMPRESSIBLE VEHICLES

M.V. Velasco, A. Muñoz-Ruiz, M.C. Monedero and M. R. Jiménez-Castellanos.
Departamento de Farmacia y Tecnología Farmacéutica,
Facultad de Farmacia, Universidad de Sevilla,
C/ Tramontana S/N.
41012 Sevilla (SPAIN)

ABSTRACT

An evaluation of different methods of investigating the flow properties of bulk solids has been carried out on four new excipients for direct compression: Maltrin® M 150, Maltrin® M 510, Maltrin® QD M 500 and Maltrin® QD M 550.

Rheological properties of the excipients like parameters from shear test, bulk density, compressibility, flow rate, dynamic angle of repose as well as mean weight and variation coefficients are reported.

Although dynamic angle of repose as well as shear cell method provided similar results for the four maltodextrins under study, we observe a different behavior between the Maltrin® M150 and the other excipients under study in the flowmeter, being Maltrin® M150 the only excipient which did not flow through any orifice of the flowmeter.

Therefore, our flowmeter, whose results also shows a good correlation with the coefficient of variation of the weight seems to be the most useful technique in providing a parameter which allows assessing better the difference in flowability for similar excipients, as it is the case of these maltodextrins.

INTRODUCTION

The flowability of a powder (1) is of critical importance in the production of pharmaceutical dosage forms in order to get a uniform feed as well as a reproducible filling of tablet dies, otherwise, high weight dose variations will occur. This parameter is of great importance for direct compression excipients because they must flow without the aid of granulation.

Techniques used to estimate flowability of powders include direct and indirect methods (2). However, there are numerous details and concepts that come into play when discussing flow problems.

This work, as well as a previous one (2), is centered on the evaluation of the different methods of the estimating flowability, using in this case, a similar group of new excipients for direct compression: Maltrin® M 150 , Maltrin® M 510, Maltrin® QD M 500 and Maltrin® QD M 550.

Maltrin® is the registered trademark for a family of Maltodextrins (3). Maltodextrins are composed of water-soluble glucose polymers obtained from the reaction of starch with acid and/or enzymes in presence of water.

Only a few papers have appeared in the literature concerning the use of maltodextrins as direct compression excipients. Li and Peck (4) investigate the influence of the agglomeration process on the micromeritec properties of the granular products. In another paper (5), these authors examine the relationship between the degree of polymerization and the compression properties of some maltodextrins as well as the role of moisture content in the compression. Parrot (6) evaluates a new corn-based maltodextrin, Soludex®, and compares it to nine frequently used commercial maltodextrins. Papadimitriou et al. (7) evaluate maltodextrins as excipients for direct compression tablets and their influence on the rate of dissolution.

More recently, Mollan and Çelik (8), characterize the powder and compact properties of five types of maltodextrins which were manufactured by three different methods and also compare the results with a commonly used soluble filler/binder.

MATERIALS AND METHODS

In this study four new excipients for direct compression were used: Maltrin® M 150 (maltodextrin) batch P1291; Maltrin® M 510 (fine granular maltodextrin) batch A-3533; Maltrin® QD M 500 (quickly dispersible maltodextrin) batch 083-916V and Maltrin® QD M 550 (quickly dispersible maltodextrin) batch 357-96 (Grain Processing Corp., U.S.A.), were used as received. Excipients were stored under controlled temperature (20° C) and humidity conditions (RH= 40%).

Shear cell studies

Mechanical parameters of shear were determined using a ring shear cell (Bromhead Ring Shear, Wykeham Farrance Engineering Ltd, Slough, U.K.) described previously (2). The preconsolidation time was 10 min and the consolidation time was 15 min. The preconsolidation loads used were 300, 260, 220 and 180 g and 5 or 6 reduced loads were used in order to obtain the yield loci.

Flow rates

The flow rate was measured by our data acquisition flowmeter system (9). The vessel used was a stainless-steel cylinder with different hole sizes (6, 9, 12, 20 and 25 mm). A balance with an interface connected to a personal computer (IBM PC compatible) constitute the whole system. A software program for data acquisition, graphics and calculations was used.

Angle of repose

Dynamic angle of repose was measured according to the revolving cylinder method (10). A sealed hollow stainless-steel cylinder having an internal diameter of 80 mm with one end transparent is made to revolve horizontally. It is half-filled with the powder, so that the free surface of the powder forms a diametrical plane. The maximum angle that this plane makes with the horizontal on rotation of the container is taken as the angle of repose. The data given are the means of 10 measurements.

Bulk density and compressibility on tamping

Bulk density was determined from the weight of powder filling a 250 mL graduated cylinder. The powder was then tamped 10 and 500 times, the occupied volumes are determined, V_{10} and V_{500}, respectively. The data given are the means of 10 measurements. Compressibility (11) was then determined from the equation:

$$\%Compressibility = \left(\frac{tamped\ density - bulk\ density}{tamped\ density}\right) x100$$

Tablet Compression

Tablets were compressed on an instrumented single-punch tablet machine (Bonals, model AMT 300, Barcelona, Spain) running at 30cycles/min, equipped with a forced feeding system and using 12 mm punches. The weight (mg) of each of 60 individual tablets was determined by dusting each tablet with a camel-hair brush, and placing it on an electronic balance (Mettler AE 50, Mettler Instrumentate, Geneva, Switzerland). The weight data from the tablets were analyzed for sample mean, and coefficient variation (C.V.).

RESULTS AND DISCUSSION

The parameters obtained from the yield loci and the plots of Mohr semicircles at different pre-consolidation loads for the excipients are listed in Table 1.

Table 2 shows the values of rheological properties of Maltodextrins, as well as the mean and the coefficient of variation (C.V) of weight of the tablets made.

It is known that flow properties are influenced by cohesion and, at the same time, by friction between particles. In our case, although the values of both

TABLE 1

Results for maltodextrins of the parameters corresponding to pre-consolidation loads (σ_{max}), cohesion (C), correlation coefficient (r), friction coefficient (μ), traction (T), maximum principal stress (σ_{1max}), angle of friction (Ø) and unconfined yield stress (f_c).

excipient	σ_{max}	C	r	μ	T	σ_{1max}	Ø	f_c
M150	75	26.09	0.993	0.590	44.22	197.36	30.54	91.42
	65	22.70	0.984	0.615	36.91	184.92	31.60	81.23
	55	15.89	0.979	0.673	23.60	161.01	33.96	59.72
	45	19.96	0.979	0.530	37.64	122.88	27.94	66.38
QD M500	75	30.17	0.993	0.826	36.54	280.07	39.54	128.1
	65	20.01	0.990	0.782	25.60	199.68	38.01	82.06
	55	25.66	0.989	0.717	35.77	173.84	35.66	100.0
	45	22.10	0.993	0.803	27.52	161.99	38.77	92.20
QD M550	75	27.92	0.992	0.689	40.54	225.49	34.55	106.3
	65	27.93	0.991	0.631	44.24	187.15	32.26	101.3
	55	23.55	0.994	0.562	41.86	150.32	29.36	80.53
	45	23.41	0.957	0.639	36.62	133.49	32.59	85.52
M510	75	31.21	0.959	0.711	43.93	255.75	35.4	120.9
	65	30.99	0.974	0.598	51.81	183.65	30.89	109.3
	55	24.65	0.970	0.654	37.68	166.61	33.19	91.14
	45	24.75	0.972	0.659	37.51	142.34	33.41	91.95

TABLE 2

Data for bulk density (d_{500}), friction coefficient (μ), compressibility (C), flow rate using 12 mm aperture setting (average flowrate) (Flow), dynamic angle of repose (DAR), flow factor (ff), mean weight (W) and variation coefficients (C.V.).

Excipient	d_{500} (g/ml)	μ	C (%)	Flow (g/s)	DAR (°)	ff	W (mg)	C.V.
M 150	0.592	2.19	20.5	--	50.3	2.98	304.6	3.36
QD 500	0.369	1.03	6.79	5.90	44.3	3.34	299.3	1.06
QD 550	0.454	1.18	6.77	6.63	38.6	3.62	300.6	1.65
M 150	0.581	1.16	4.76	8.97	32.6	3.66	331.4	0.9

parameters are rather similar for the four excipients under study, it seems that there are no correlation in the sequence that follows the mean values of both parameters. In this sense, while the cohesion is from minor to maximum: M150, QD M500, QD M550 and M510; for friction coefficients is M150, QD M550, M510 and QD M500. However, the latest parameter agrees completely with the data of specific surface area performed by adsorption multi-point BET-method (Sorptomatic 1900, Micromeritis) for the four excipients, whose values vary from 1.468 to 4.857 m^2/g for M150 and QD M500 respectively. We can state that, the more specific surface the excipients have, the more friction between particles is evaluated (1).

Flow function, being defined as the unconfined yield stress versus the maximum consolidation stress, is illustrated in Figure 1 for the four maltodextrins. This function can be used to evaluate the behavior in response to stress. As Provent et al.(12), we found low variability in the response of maltodextrins to stress. However, the cohesion under zero stress (ordinate at the origin) showed a good correlation with coefficient of variation (C.V.) (0.92).

Plots of C.V. against flow factor (ff) (reciprocal of the slope of the flow function) did not show high linearity, like Ho et al (13) stated. York (14) has suggested that 1/ff may have more theoretical value because it represents the unconfined yield stress of powder per unit maximum consolidation stress. Therefore, C.V. was plotted against 1/ff, but we found again, that in our case, there was poor linearity (0.85).

As Ho et al (13), when plotting mean tablet weights versus bulk density, no linearity was found, observing a different behavior between M150 and the other

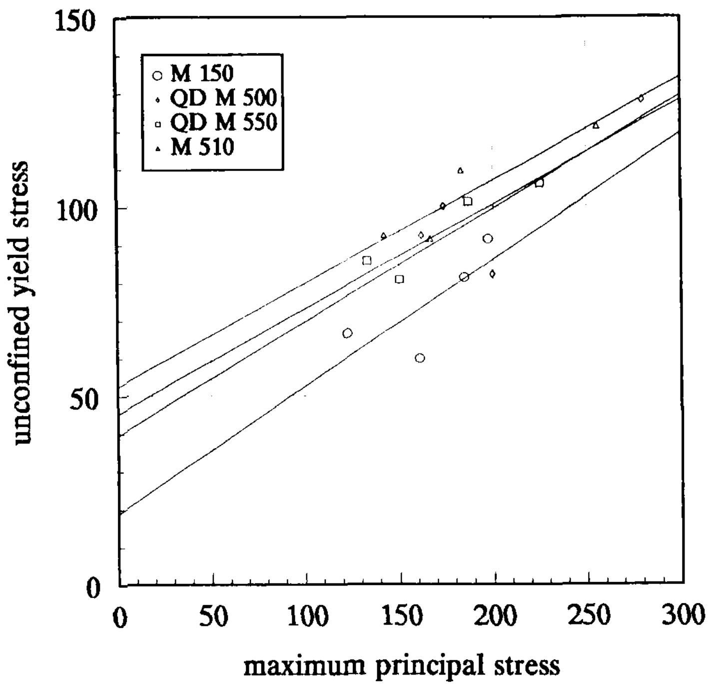

FIGURE 1.-
Flow function for the four maltodextrins.

excipients under study. This fact is similar in the flow rate method, where Maltrin® M 150 was the only one which did not flow (Table 2).

It has been suggested that materials exhibiting angles of repose greater than 45° (15) and compressibility greater than 20% (16-17) are cohesive and would present problems during tabletting. Again, Maltrin® M150 exhibited values above limits, coinciding in no passing the test for weight uniformity and showing the highest value of C.V. of weight (Table 2).

On the other hand, while we can found high correlation between percentage of compressibility and C.V. (0.97), the correlation between the dynamic angle of repose and the C.V. was low (0.78). This suggests that, at least in our case, the dynamic angle of repose has little use in predicting flowability during tabletting.

In relation to friction, it can be observed in tables 1 and 2, two different friction coefficients for the four excipients under study, being always the lowest values the ones obtained from shear test. This can be explained because they have been obtained with different methods and therefore, they have different physical meaning. The coefficient of friction obtained in the shear cell method correspond

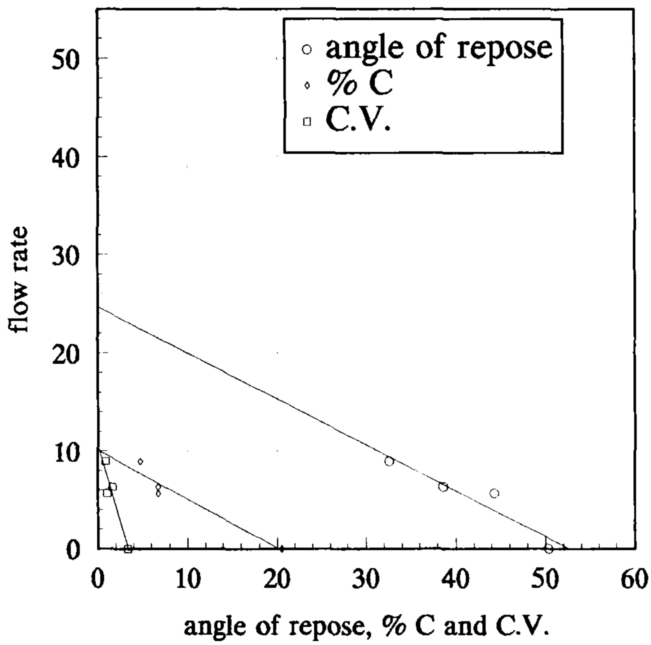

FIGURE 2.-
Flow rate versus dynamic angle of repose, percentage of compressibility and coefficient of variation.

to the friction between particles when the powder is under a consolidation load and we impart a rotation that causes the sample to shear. We calculate it as the arctangent of the slope of the yield loci. On the other hand, the friction coefficient from the dynamic angle comes from tangent the angle that forms the powder after a rotation given when it stays freely in a cylinder.

A good relationship was observed between flow rate and variation in flow rate, because while M150 did not flow through any orifice of the flowmeter (6, 9, 12, 20 and 25 mm), QD M500 only from 12 mm, QD M550 from 9 mm and Maltrin® M510 did flow, through all the orifices, being also the one that showed the highest flow (8.97g/s). Also flow rate values showed good correlation with the dynamic angle of repose (0.94) and compressibility index (0.97) (Figure 2), as well as with the C.V. (0.94), so it can be used directly to predict tablet weight variation. These results are in disagreement with Cole et al (18) that found poor correlation between these flow rate and C.V. .

Although several authors point out that the shear cell is well-suited for evaluating the flow properties of some pharmaceutical powders (13, 19, 20, 21, 22), the shear cell method is tedious and rather operator-dependent (19). In this method is very important the selection of normal consolidating stress as well as the consolidation time, because can cause significant differences in ff values (2, 19, 23, 24). Also, it is recognized that shear cell measurements of unconfined yield stress have poor precision (25).

The above reasons can justify why in our study, the shear cell method to evaluate flowability did not allow to distinguish clearly between the different flowability of our four excipients. The flow factor (Table 2) obtained for the maltodextrins are rather similar so it can not be concluded on their basis the behavior of these excipients. Under our experience, the main application of shear test may be found only for those excipients that can not flow through the flowmeter. In the same sense, Li and Peck (4) found problems to choose the compressibility percentage as an adequate system to distinguish the different flow behaviour of two maltodextrins (M 150 and QD M500).

All these results agree with an early paper (2) where we used different excipients for direct compression. Again, our flowmeter appears to be a more useful technique than shear test in providing a parameter which allows assessing better the difference in flowability, now in this work, for similar excipients. This fact can be explained on the basis that although some flowmeters have been constructed with vibrators attached to facilitate flow of materials which will not flow under gravitational forces alone, our system is completely automatic and let it use from a funnel to the hopper of a tablet machine, and even a cylinder with such features that the static friction, the operator delay and the decrease of the weight of the powder are eliminated.

ACKNOWLEDGMENT

The authors want to acknowledge the support from Grain Processing Corporation.

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