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STUDY OF FLOWABILITY OF POWDERS. EFFECT OF THE ADDITION OF LUBRICANTS

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ABSTRACT

In early paper we have studied the flow parameters of powders using a ring shear. Also, we have evaluated an adequate method to estimating flowability according to powder characteristics. The goal of this article is the study of the action of three lubricants, magnesium stearate, PRUV® and PRECIROL®, on the flowability of an excipient for direct compression, Maltrin® M510. Flow characteristics are evaluated with flowrate, repose angle and compressibility. The influence of concentration and mixing time is also evaluated. Compressibility did not discriminate the lubricant effect. The maximum correlation coefficient flowrate and the repose angle showed the best flowability for magnesium stearate mixtures.

INTRODUCTION

Most of the pharmaceutical industry processes require powder movements. For this reason, flowability is of critical importance in obtaining the target weight of solid dosage forms (1).

The factors which influence the flow characteristics of powders are diverse, particles properties (shape, size, size distribution and density), environment, for instance humidity and the test method used to evaluate it (2,3). The simplest method of determining powder flowability directly is to measure the time required for a specific weight of material to pass through an orifice. This method does not allow the evaluation of fluctuations in the flow during the test, so it can not distinguish between different materials (4,5).

In the light of the above, we proposed a new method described previously (6), based in a data-acquisition system constituted by a balance with an interface connected to a personal computer (IBM PC Compatible).

Also, we have studied the flow parameters of excipients for direct compression determined using a ring shear (7) and we have evaluated an adequate method to estimating flowability according to powder characteristics (8).

Like most of the lubricants used in direct compression, beside lubricant and antiadherent actions, often possess glidant properties (9) due to a reduction or alteration of electrostatic interactions (10) and a filing up of the unevenness of the particles (11), in the present study, modification of the flow properties of a Maltrin® M510 due to the addition of three lubricants is evaluated. This direct compression excipient was chosen because it showed the best flowabality properties among a family of maltodextrins (M510, M150, QD M 500, QD M 550) (12).

MATERIALS AND METHODS

Maltrin® M510 -batch G0705- (Grain Processing Corporation, Iowa, Muscatine, U.S.A.) as directly compressible vehicle model, magnesium stearate -batch 920844- (Lab. Dr. Esteve, Barcelona, Spain), PRUV® -sodium stearyl fumarate - batch 139-01 (Juliá - Parrera, Barcelona, Spain) and PRECIROL® (glyceryl palmitostearate) -batch 18832- (Gattefossé, Saint-Priest, Cedex, France) as lubricants were used.

The excipient was mixed for two mixing times, 2 and 10 minutes, with three different concentrations (0.5%, 1% y 2%) of magnesium stearate, PRUV® and PRECIROL®, in a plastic vessel in an asymmetric double-cone mixer (Retsch, D-Haan) at 50 rev.min^{-1}.

The flowrate of the different mixtures was determined with the technique developed by us (6). Due to the available quantity of mixtures, a glass funnel was selected as vessel (13).

Static angle of repose was measured according to the fixed funnel and free standing cone method (14). A funnel with the end of the stem cut perpendicular to the axis of symmetry is secured with its tip 2 cm height, H, above graph paper placed on a flat horizontal surface. Powder is carefully poured through the funnel until the apex of the conical pile so formed just reaches the tip of the funnel. The mean diameter, 2R, of the base of the powder cone is determined and the tangent of the angle of repose is given by:

$$\tan\alpha = \frac{H}{R}$$

where α is the repose angle.

Compressibility on tamping is described in detail in earlier studies (15). The weight variation of tablets was made in an instrumented single-punch tablet machine Bonals Mod. AMT 300 (Bonals, Barcelona, Spain). Weight uniformity was determined according to European Pharmacopeia II.

Data were analyzed using an analysis of the variance with the design of the experimental conditions chosen.

RESULTS AND DISCUSSION

Figures 1 and 2 show two examples of flowrate graphics corresponding to Maltrin® M510 with 0.5% of magnesium stearate and PRECIROL ® respectively, at 10 minutes of mixing time.

In general, it can be observed two behaviors according to two different slopes. In the phase a (Figure 1), the powder flows slowly because it has to overcome the wall effect, the static friction and the delay of the operator (6). This fact may be aggravated by the stickness of the material as well as for its low density (1.371 g/cm^3 for Maltrin® M510, and values between 1.278 and 1.338 g/cm^3 for its mixtures) in comparison with other materials (6,15). In the phase b (Figure 2), with a higher slope, the material has overcome all the friction force from the wall and starts to flow according to its own characteristics. For this reason, three different flow parameters can be obtained. At the beginning, the first phase (phase a) flowrate (FP), the maximum correlation coefficient flowrate (MCC) (phase b) and the average flowrate (AV) (phase a + b) using all data except first instantaneous flowrate, that are due to the operator delay.

Table 1 shows the average of the results of the flow parameters of the mixtures of Maltrin® M510 with the three lubricants at different concentrations and mixing times. The angle of repose and compressibility index are listed in Table 2.

Coefficient of tablet weight variation (C.V.) was a sensitive parameter to assess the interaction between the excipient and the lubricants in flow properties ($F=6.206$; $\alpha<0.01$, LSD). The lower variations were found for magnesium stearate and PRUV® mixtures, while tablets elaborated with PRECIROL® mixtures showed a higher variation.

Magnesium stearate and PRUV® mixtures with Maltrin® M510 showed a significant lower first phase and average flowrate (Table 1) than PRECIROL® mixtures ($F=8.94$, $\alpha<0.01$, LSD) and ($F=9.68$, $\alpha<0.01$, LSD) respectively. However, the maximum correlation coefficient (Table 1) increased in the following order: PRECIROL®, PRUV® and magnesium stearate, with a statistically significant difference ($F=28.29$, $\alpha<0.01$, LSD). Repose angle (Table 2) showed statistical difference ($F=39.71$, $\alpha<0.01$, LSD) between the three mixtures of lubricants. A linear relation ($r=0.98$) was found between maximum correlation coefficient flowrate and the repose angle values. These results are in agreement with other works (17), where we indicated that the maximum correlation coefficient flowrate is the most representative parameter of flow characteristics of a material. In relation to the compressibility index (Table 2), there was no statistically difference between the three lubricants, so we agree with Lubner and Ricciardiello (2) who stated that the measure of this parameter become useless in the evaluation of the characteristics of this kind of powders.

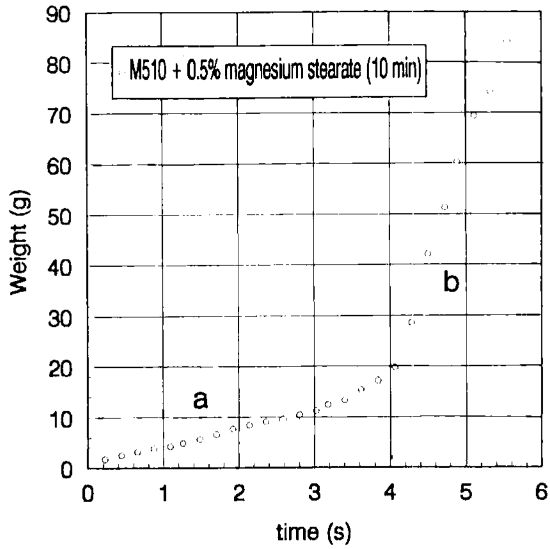

FIGURE 1
Flowrate of Maltrin® M510 with 0.5% of magnesium stearate mixed for 10 minutes.

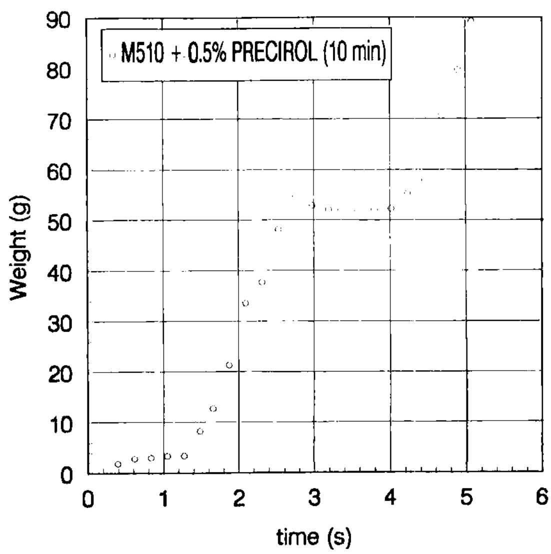

FIGURE 2
Flowrate of Maltrin® M510 with 0.5% of PRECIROL® mixed for 10 minutes.

TABLE 1

Average of the results of the flow parameters of the mixtures of Maltrin® M510 with the lubricants (first phase flowrate FP, average flowrate n-2 AV and maximum correlation coefficient flowrate MCC).

lubricant	concentration (%)	time (min)	FP (g/s)	AV (g/s)	MCC (g/s)	C.V. (%)
Magnesium stearate	0.5	2	7.322	17.14	38.15	0.7300
		10	4.455	16.62	43.94	0.9067
	1	2	7.064	19.60	38.92	0.5133
		10	3.863	13.39	41.92	0.5300
	2	2	4.715	16.61	40.05	0.7633
		10	3.488	10.99	43.34	0.9567
PRUV®	0.5	2	6.479	15.60	38.13	0.6000
		10	4.978	16.67	36.25	1.227
	1	2	2.823	10.17	34.53	0.6867
		10	2.682	13.46	35.70	0.9167
	2	2	14.546	22.57	30.57	0.7330
		10	6.742	14.98	35.12	0.6600
PRECIROL®	0.5	2	15.19	28.18	30.41	1.090
		10	10.189	17.96	27.97	1.300
	1	2	24.129	25.53	23.11	0.9966
		10	6.646	18.18	20.57	0.7700
	2	2	25.36	23.90	28.00	0.8300
		10	7.517	17.58	17.45	0.9400

The effect of concentration was neither significant for flow parameters (FP, AV and MCC) (Table 1), nor repose angle (Table 2) in magnesium stearate mixtures. For this reason, the adequate concentration will be the slowest because above this limit, the phenomena of loss of cohesion in tablets begins to be noted (2,13). On the contrary, mixing time was a significant variable for all the parameters cited above. Increasing mixing time demonstrated a diminishing in FP y de AV values (Table 1), while, in agreement with other authors (13), the MCC values (Table 1) increased.

The concentration and the mixing time did neither affect significatively the flowability parameters (FP, AV and MCC) (Table 1) nor the compressibility index (Table 2) of PRUV® mixtures. The concentration was slightly significative in angle of repose ($F=9.25$, $\alpha<0.01$) (Table 2). These results lighten the lubrication phase as it does not need to control any variable, such as concentration or mixing time, that can modify negatively the material and tablets properties (18,19).

TABLE 2

Average of the results of repose angle and compressibility index of the mixtures of Maltrin® M510 with the three lubricants.

lubricant	concentration (%)	time (min)	repose angle (°)	Compressibility index (%)
Magnesium stearate	0.5	2	35.17	1.411
		10	37.06	2.166
	1	2	36.20	3.060
		10	37.05	2.264
	2	2	35.15	4.149
		10	35.97	3.949
PRUV®	0.5	2	36.07	3.538
		10	36.30	2.875
	1	2	36.72	2.525
		10	38.85	2.737
	2	2	38.21	1.808
		10	38.39	3.970
PRECIROL®	0.5	2	36.30	3.916
		10	38.30	2.182
	1	2	38.12	2.517
		10	40.20	2.214
	2	2	40.92	1.489
		10	40.75	1.912

The results obtained in PRECIROL® mixtures showed an irregular behavior (Figure 2). The concentration did not have significant effect on the flow parameters (FP, AV and MCC) (Table 1), while a significant difference was found in CV values ($F=3.96$, $\alpha<0.05$) (Table 1) and repose angle ($F=14.99$, $\alpha<0.01$) (Table 2). The mixing time modified negatively VP, VN2 (Table 1) as well as repose angle (Table 2), while it did not modify MCC and CV (Table 1). The increase in mixing time meant a deleterious effect in flow as Sekulovic et al. (20) observed in an excipient for direct compression (Elcema G-250).

In conclusion all the parameters, except compressibility index, showed statistical difference between the lubricants, however, repose angle and the maximum correlation coefficient flowrate distinguish better the interactions. Also, a linear relation between them was found.

In general, mixtures of PRUV® and magnesium stearate did not modify significatively the flowability of the excipient under study. In the manufacture of tablets with Maltrin® M510, magnesium stearate and PRUV® can be used as lubricants. The addition of PRECIROL® means an erratic flow.

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