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Research paper

Stress relaxation studies of granules as a function of different lubricants

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Abstract

Viscoelastic properties of granules may be studied using stress relaxation. The effect of viscoelastic properties of different lubricants, namely magnesium stearate (Mgst), talc and precirol, on granule compaction properties was examined using texture analyzer TA-XT2i® at low pressure. Normalized compact curves of stress relaxation have been discussed in relation to some parameters (flowability, porosity, viscoelasticity as well as particle size). The literature shows that viscoelasticity is always present and it produces an accompanying plastic deformation.

This study revealed that bonding in compacted granules lubricated with Mgst was higher than those in compacts lubricated with the other two lubricants being studied. When studying the partial porosity of granule beds, we see that this is the result of stored energy, like the tablet case and the problem of its capping. The small stress relaxation due to talc or precirol suggested that these materials deformed principally by energy storage. However, a qualitative characterization of Mgst as tablet lubricant would be that it avoids the accumulation of stress in the compact that causes the problem of capping due to the entrapped air and therefore facilitates the optimization of pharmaceutical manufacturing. It has been possible to normalize stress relaxation using the Wischert model, represented by the sum of several exponentials, according to the nature of the lubricant.

The use of texture analyzer TA-XT2i® was considered to be a good technique for the evaluation of the stress relaxation of solid particles in the compression process at low pressure. It permitted the observation that viscoelasticity is influenced by the lubricant used. The brittle fracture index, like Carr's index values, has been correlated with the viscoelastic characteristics of granules.

Keywords: Granule; Texture analyzer; Lubricant; Stress relaxation; Viscoelasticity; Carr; Capping; Normalization

1. Introduction

Pharmaceutical compacts and powder beds a have complex structure that presents a difficult challenge when measuring their mechanical properties. Furthermore, pharmaceutical compacts are made by uniaxial compression. Prodigious evidence exists to prove that successful compaction requires plastic deformation, though volume reduction, consolidation, during the compaction cycle may include particle fracture, plastic deformation and particle rearrangement. While fine powders may entrap air in pores, they also impede granule flowability.

In practice, physical measurements are used because mechanical properties are not predictable [1]. An important part of formulation is selecting and combining materials to obtain the required mechanical properties, namely flowability of powders, desired bonding and low brittleness for tablets. For flowability, the compressibility index (CI) provides useful criteria and for compact tabletting, indices have been defined.

During tablet formation, pharmaceutical powders are not subjected to an increasing force but undergo a mechanical

Nomenclature

relaxation%	Percentage of relaxation
δ_{max}	Maximum deformation
ΔF	Magnitude of force at time t
ΔF_0	Magnitude of force at $t = 0$
ΔF_∞	Remaining force after relaxation
ε	Partial porosity
ρ_b, ρ_t	Bulk and tapped densities

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[1] Dedicated to Professor Dr J. Joachim on his retirement.

Abbreviations: BFI, brittle fracture index; CI, Carr's compressibility index; Comp. gran., compacted granule; LD, laser diffractometry; Mgst, magnesium stearate; pps, Points per second

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deformation [2]; however, the force observed is a direct consequence of the resistance offered by the material under compaction which, in turn, depends on the physical properties of the substances, which undergo a time-dependent volumetric change [3]. Therefore, the tendency of tablets to cap has been related to many factors, including the storage of elastic energy during compaction, with subsequent elastic recovery after the removal of axial pressure [4]. Several mechanisms have been suggested to explain the consolidation stage. However, the compaction process can be summarized as the packing of different particles by diffusion into void spaces, elastic and plastic deformation of the material; hence characteristic compaction profiles can be expected [5]. Velasco et al. [6] have stated that the formation of an intact compact by compression results from forces present at the particle–particle contact area. As the compression pressure was increased, large true contact areas between particles were established. Plastic materials will permanently deform and create extensive areas of true contact between particles, while elastic materials will store energy under compression, whereas during decompression, the stored elastic energy may disrupt and separate the true contact area that was established by compression forces, resulting in poor bonding.

Shlanta and Milosovich [7] have studied the stress relaxation characteristic of various pharmaceutical materials; they concluded that materials possessing satisfactory compaction properties exhibited an intermediate stress relaxation and that a decrease in the applied force occurs. This phenomenon is known as stress relaxation or creep mechanism and results from deformation of the compressed material into interstitial space; when the stress relaxation was either high or low a suitable compact was not formed under static compression [8]. However, stress relaxation curves have been employed to quantify the energy required for elastic and plastic deformation and hence to interpret the consolidation of different pharmaceutical compacts [9]. In other words, for a given plastic deformation, solids presenting a sufficient degree of relaxation have a great area of contact and consequently, a greater degree of bonding. This makes it possible to reduce the risk of structure failure of compacts, which may result from elastic recovery [9]. In contrast, during relaxation of elastic compacts, the compressed air in such formulations expands and leads to compact fracture if the bonds formed are not strong. This mechanism may prevent the risk of capping or splitting with formulations containing fragmented particles due to entrapped air during the consolidation stage [10]. According to Hiestand [11], "a capped tablet commonly is said to have poor bonding which was overwhelmed by entrapped air" and "very fine powder which does impede the escape of air, but fineness introduces unacceptable flow problems and usually is avoided". Universally, it is recognized that both slower machine speeds and/or using a precompression stage may decrease capping. The viscoelastic character is always present and accompanies plastic deformation for any strain reducing stress concentration [11] and is an aid in bonding and prevention of fracture but imposes strain rate dependency on processing. The viscoelastic properties of compacts can be related to the viscoelastic properties of the compressed particles.

Hiestand believes that the problem of tablet capping is due to the entrapped air. Also, it has been demonstrated that a soft binder or more precisely, one with a glass transition temperature less than the room temperature, results in better dimensional reproducibility than that observed for a hard binder (i.e. $T_g >$ room temperature), and this in fact may decrease the problem of capping.

De Blaey and Polderman [12] have suggested that in tablet manufacturing, the addition of lubricant implies a decrease in friction together with an increase of the expansion work, which is consistent with the concept that lubricants increase the viscoelastic nature of the materials and therefore avoid the accumulation of stress in the compact that causes the problem of capping. However, lubricant particles coat the granule particles and interrupt interparticulate bonding with plastic deformation. In contrast, fragmentation of brittle particles results in large areas of new surfaces, reducing the detrimental effect of a lubricant [13].

The aim of this study was to relate granule viscoelastic characteristics to lubricant properties by measuring granule relaxation. This was accomplished by measuring some parameters such as relaxation%, packing properties (i.e. Carr index) and relaxation curve modelization. We attempted, during this study, to illustrate some factors that affect the expression of stress relaxation.

2. Materials and methods

2.1. Materials

Corn starch (batch 970616, Roquette, France), fine lactose powder (100 mesh, batch 9470618, HMS Holland), monohydrate theophyllin (batch G 7641/2, Cooper Melun, France), Calipharm BP (dicalcium phosphate dihydrate, batch PHR 08L, Albright and Wilson Ltd, West Midlands) and Natrosol (Hydroxyethylcellulose, batch R 1254, 250 mesh provided by SPCI, France) were used. All ingredients were used as received. They were only sieved using a 500-μm sieve. The tested lubricants were talc P3 (batch 3952 SPCI, St. Denis, France), magnesium stearate (Mgst, batch 112392, Cooper Melun, France) and precirol Ato 2155 wl (glycerol palmito-stearic ester, batch A 16223, Gattefossé St. Priest, France). Lubricant specific surface areas as measured with a gas adsorption Nova 2000 apparatus (RHEO, France) were 16.00 (Mgst), 12.00 (talc) and 1.02 m^2/g (precirol).

2.2. Procedure

2.2.1. Wet granulation technique

Two formulae were used for the study: mixture A – lactose fine powder and corn starch, 80 and 15%, respectively; and mixture B – lactose fine powder, natrosol and

calipharm, 45, 10 and 40%, respectively. Taking 5% theophyllin monohydrate as tracer, mixing and wet granulation (with distilled water) steps were performed using the lodïge mixer (type TM 20, GmbH Germany) at 250 rpm. After granulation, granules were dried at 60°C in a ventilated oven. The granule calibration was performed with an oscillating granulator (Erweka type FGS, Germany) fitted out with a 1000-μm screen. Two kilograms of each mixture were obtained.

The moisture content was measured with an infra red moisture analyzer (Mettler LP16, Deltarange, type LP16 M, Switzerland) during 15 min at 120°C. The values of moisture content measured were 1.5 and 2.8% for mixtures A and B, respectively.

Powdered lubricants were screened on a 125-μm sieve (Analysensieb Retsch, 5657 Haan Germany) then mixed with the granules of A and B using a tumbler mixer (Turbula T2C, W.A. Bachofen AG Basel, Switzerland) for 5 min at 42 rpm in a plastic vessel. The prepared granules were mixed with increasing lubricant percentages: 0.5, 1, 1.5, 2, 2.5 and 3% (w/w).

2.2.2. Stress relaxation test

The compression characteristics of prepared granules (mixtures A and B) in the absence and presence of different lubricants were studied; the instrumental method was developed to measure stress relaxation of compacted bed granules under constant deformation. Texture analyzer TA-XT2i®, as a well-controlled compaction device, was installed (RHEO Champlan, France); it was supplied with an aluminium flat probe. A weight of granules, equivalent to a volume of 30 cm^3 was mounted between the platens. The beaker filling was done manually, delicately with the help of a spatula. The texture analyzer was calibrated by fixing the following parameters: type of graph (compression force measure), test type (force relaxation), probe displacement speed (1 mm/s), maintained time (60 s, 200 pps). When the compression pressure reached a fixed value (49 N), the probe cylinder displacement was kept stationary and the decay of the force was measured without changing the other parameters. In this way, the sample reaches the maximum deformation. According to the nature of the sample, which is more or less brittle, the material may continue to fracture in the same way after it reaches constant deformation (subsequent fractures).

Stress relaxation of the compact was monitored for 60 s and the deformation was measured through probe displacement recording, three compacts being repeated for each measurement. However, the stiffness of granules (Young's modulus, E) was determined as a function of maximum stress (σ_{max}) to the maximum deformation ratio (δ_{max}) [14].

$$E = \frac{\sigma_{max}}{\delta_{max}} \quad (1)$$

The relaxation curves were normalized and the decaying parameter $F(t)$ was calculated as follows.

The analysis of relaxation curves in brute raw data is difficult because the applied force or deformation rate is never absolutely attained; the relaxation curves were normalized, in the form of percentage of relaxation, and this permitted us to minimize the errors.

$$\text{relaxation}\% = \frac{[F_0 - F(t)]}{F_0} \times 100 \quad (2)$$

where F_0 and $F(t)$ were the forces recorded initially and after 1 min of relaxation, respectively.

2.2.3. Particle size analysis

Particle size distributions of both lubricants and granules with their mixtures were analyzed before and after compaction using Laser diffractometry Mastersizer (Type S long bed version 2.15 Malvern Instruments, UK). The Malvern software is Windows® based and controls all the functions of the Mastersizer during measurement and then uses the collected data to calculate the results. Laser diffractometry (LD) measurements were performed in a dry powder module.

After compaction, the granule is just tapped, because the force is not enough to create bonding. For this reason, we studied the particle size distribution of granules while using the LD for the dry module. This analysis was performed just after the compression on 3/4 of the beaker content that was deposited in the hopper.

The dry powder sample is manually placed into the sample hopper with the air supply and vacuum extraction system connected. When the sample hopper is vibrated, the sample travels down the hopper until it eventually falls into the main feed mechanism. The rate at which the sample was fed was controlled by the feed rate (1.2 g) control and also by the gap between the feed gates on the sample hopper. The jet pressure controls the airflow pressure through the air cell (0.8 bar). Very low values are chosen in order to prevent further granule fragmentation or breaking because if the sample is fragile this could modify the analysis results. As the sample falls through the sieve (which is not filled with ball bearings), its fall is accelerated by compressed air and passes through the tubing to be analyzed. The mean diameter of particles was determined, $d(V, 0.5)$.

2.2.4. Microscopy

The last 1/4 of the beaker granules were used for the microscopical study. These granules to be analyzed were delicately displayed on a microscopical slide with a spatula (magnification 40×). The measurement of particle sizes of granules after compression was performed using a Nikon optical microscope (Nikon Eclipse E 600, provided by Roucaire, France) fitted with a calibrated micrometric eyepiece and connected to a video computer system. Archivex software was used for taking photos and for photographic treatment.

2.2.5. Rheological tests

The flow and packing properties of the powders were determined using an automatic tap volumeter (Stampflvolumeter Stav volumeter 2003, J. Engelsmann, Ludwigshafen a. Rh.) with 100 g of powder filled into a mounted measuring cylinder (250 ± 1.0 ml).

The powder bed was levelled with a spatula and the maximum volume was read (bulk volume). Then the samples were tapped 500 times to obtain constant volume (250 taps/min), then the powder volume was read again (tapped volume). The bulk (ρ_b) and tapped density (ρ_t) of samples were determined. The different densities of the powders were evaluated as a function of the number of taps. The study of particle packing arrangement during tapping was proposed as the CI [16]. All experiments were performed in triplicate. The CI% is a measure of the propensity of a powder to consolidate. Changes occurring in packing arrangement during the tapping procedure are expressed as the CI (Eq. (3)).

$$\text{Compressibility index} = \frac{[\rho_t - \rho_b]}{\rho_t} \times 100 \tag{3}$$

2.2.6. Granule partial porosity

Castel's empirical formula was utilized for the determination of granule partial porosity [17].

$$\varepsilon\% = \frac{\text{partial void volume}}{\text{granule volume}} \times 100 \tag{4}$$

However, partial void volume could be evaluated as a function of maximum probe displacement when relaxation took place.

2.2.7. Data treatment

All results and model evaluations were analyzed with the SigmaPlot® program for Windows version 2.0 (SPSS Inc, Germany).

Rees and Rues [18] studied stress relaxation behaviour for 360 s and observed that data plots behave as a true Maxwell model 30 s after application of the maximal force. This model is composed of a spring and a shock absorber grouped in series, the spring translating the linear elasticity, E, of material, and the shock absorber its viscosity, η. The behaviour of such a model is as follows:

$$F(t) = F_{max} \times \exp(t/t_0) \tag{5}$$

However, partial loss of compression energy in the form of decreasing exponential type could be calculated according to the following equation [8]. This model is valid for all studied material types. The change in the $\Delta F_\infty \geq 0$ value depends on the mechanical properties of the compact.

$$\Delta F = \Delta F_0 \, e^{(-kt)} + \Delta F_\infty \tag{6}$$

where ΔF is the amount of force left in the viscoelastic region at time t; ΔF_0 is the total magnitude of this force at $t = 0$; ΔF_∞ is the elastic value remaining after relaxation; and k is the viscoelastic constant.

Casahoursat et al. [9] had demonstrated that $\Delta F_0 \exp(-kt)$ is a sum of two, three or four exponentials, whereas the exponential decay functional number is a function of material plasticity. Moreover, the author had stated that three or more exponentials may be calculated easily for materials with a high degree of plasticity.

$$\Delta F = \Delta F_\infty + [A \times \exp(\alpha t) + B \times \exp(\beta t) + C \times \exp(\gamma t) + \cdots + D \times \exp(\delta t)] \tag{7}$$

$$\Delta F = \Delta F_\infty + \sum_{i=1}^{n} F_i \times \exp(-\frac{t}{\eta_i}) \tag{8}$$

where η_i is the shock absorber viscosity of Maxwell body. *A–D* are multiplication coefficients and α, β, γ and δ (s^{-1}) are time constants of each relaxation phenomenon. This model is similar to the Wischert model, where a spring and two or three Maxwell bodies are grouped in parallel.

With regard to the number of points per second (200 pps) and duration of the relaxation test, it was difficult to normalize beyond 1 min because of the software possibilities.

3. Results and discussion

The powder flow properties obtained from tap density measurements are summarized in Table 1 as a function of lubricant rate used. Carr's CI indicates no changes in Mgst beyond 1.5% compared to precirol. On the contrary, talc appears not to affect powder flow (mixture A). With regard to mixture B, Mgst always improves the flow properties of granules unlike precirol and talc, which reach their limiting values at 1.5 and 2%, respectively.

Several mechanisms have been suggested to explain the consolidation stage [18]. The use of texture analyzer TA-XT2i® was considered to be a good technique for the evaluation of the stress relaxation of solid particles in the compression process. Fig. 1 illustrates a stress relaxation curve of compacted granules, which characterizes the viscoelastic behaviour of the compacts in the presence of different lubricants. For reasons of legibility, we represent only the curves that correspond to 1% of lubricant, as relaxation curves depend on the chemical nature, particle size and moisture content [18]. However, in the first section of the curves, the force increases (F_0). Then, when deformation is constant, the recorded force $F(t)$ in relation to time decreases quickly and tends towards a more or less asymptotic value, which depends on material characteristics [9]. Hence, $F(t)$ represents the resistance encountered by the elastic part of the compacted material [3]. It may be noticed that the structure relaxation of compacts lubricated with Mgst slowed down more quickly than that of compacts lubricated with talc and precirol.

Table 1
Results of Carr index (CI), granule bed porosity (ε) and Young's modulus according to lubricant rate[a]

	Mixture A			Mixture B		
	CI (%)	Porosity, ε (%)	Young's modulus (*N*/mm)	CI (%)	Porosity, ε (%)	Young's modulus (*N*/mm)
Mgst (%)						
0	18.40 ± 1.32	36.45 ± 0.53	68.49 ± 3.75	16.98 ± 0.95	23.54 ± 1.56	79.52 ± 4.21
0.5	9.52 ± 1.30	18.26 ± 0.20	92.20 ± 1.04	12.86 ± 1.30	19.23 ± 1.27	103.75 ± 2.65
1	7.64 ± 0.70	17.50 ± 0.21	94.73 ± 2.90	11.11 ± 0.36	19.80 ± 0.57	101.39 ± 1.95
1.5	6.38 ± 1.40	16.59 ± 0.30	100.70 ± 2.97	11.60 ± 0.79	18.77 ± 0.25	99.87 ± 2.85
2	6.83 ± 1.00	16.04 ± 1.96	89.98 ± 1.70	11.60 ± 2.52	17.75 ± 0.32	105.32 ± 6.10
2.5	6.60 ± 0.73	15.67 ± 0.75	93.31 ± 0.50	10.48 ± 0.29	17.87 ± 2.37	96.35 ± 2.04
3	7.99 ± 2.32	15.12 ± 1.84	85.36 ± 2.92	10.49 ± 1.15	17.44 ± 0.15	100.94 ± 3.95
Precirol (%)						
0	18.40 ± 1.32	36.45 ± 0.53	68.49 ± 3.75	16.98 ± 0.95	23.54 ± 1.56	79.52 ± 4.21
0.5	18.20 ± 2.43	33.64 ± 0.75	59.83 ± 1.90	16.68 ± 0.45	19.29 ± 1.58	85.32 ± 3.95
1	15.47 ± 2.49	39.10 ± 0.17	68.19 ± 2.58	14.97 ± 0.71	21.35 ± 0.07	80.27 ± 5.32
1.5	12.36 ± 0.32	26.06 ± 1.23	74.40 ± 4.21	14.56 ± 0.19	23.72 ± 0.74	88.26 ± 7.21
2	11.11 ± 1.43	26.91 ± 1.03	72.58 ± 2.03	15.07 ± 0.35	20.19 ± 0.11	83.45 ± 5.89
2.5	9.40 ± 0.31	28.44 ± 0.40	68.96 ± 1.42	15.34 ± 0.22	19.94 ± 0.63	76.40 ± 4.25
3	9.28 ± 3.71	28.23 ± 0.24	69.16 ± 0.98	15.20 ± 0.13	20.34 ± 1.38	70.04 ± 3.95
Talc (%)						
0	18.40 ± 1.32	36.45 ± 0.53	68.49 ± 3.75	16.98 ± 0.95	23.54 ± 1.56	79.52 ± 4.21
0.5	15.34 ± 0.31	31.72 ± 2.60	60.75 ± 1.90	17.92 ± 1.12	20.19 ± 3.39	75.34 ± 1.98
1	15.34 ± 2.40	31.31 ± 0.01	61.66 ± 3.20	13.92 ± 0.27	19.94 ± 0.25	78.69 ± 2.53
1.5	16.55 ± 0.41	32.94 ± 0.07	56.98 ± 5.29	13.50 ± 2.12	20.34 ± 0.11	77.21 ± 2.85
2	16.27 ± 0.13	32.62 ± 0.15	60.23 ± 3.52	13.50 ± 0.14	21.13 ± 2.51	74.01 ± 0.99
2.5	18.20 ± 0.42	32.30 ± 1.82	61.18 ± 1.93	12.48 ± 0.19	21.79 ± 0.20	70.85 ± 4.56
3	16.68 ± 5.18	31.22 ± 1.67	63.01 ± 2.97	13.25 ± 1.22	20.80 ± 1.81	74.14 ± 7.2

[a] Values are the arithmetic mean and standard deviation of three replicates.

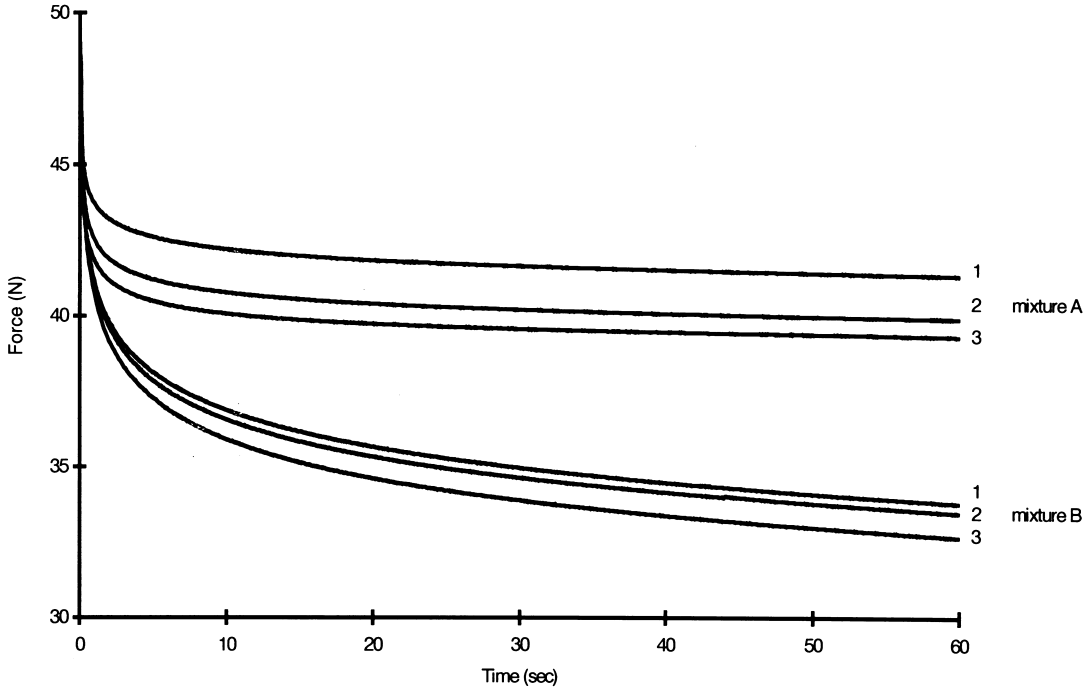

Fig. 1. Effect of different lubricants (1%) on the stress relaxation curves of prepared granules (mixtures A and B): 1, precirol, 2, talc and 3, Mg stearate.

This curve can give an idea of the contribution of these lubricants to the viscoelastic behaviour of granules. We note again that mixture B presents more pronounced viscoelastic character than mixture A.

Moreover, according to Maarschalk's equation [14], Table 1 illustrates that a material with high elasticity with increasing deformation rate has the lowest Young's modulus as indicated by talc and precirol. These values are nearly similar with regard to the standard deviation (SD), even if precirol tends to isolate itself from talc in mixture B. In contrast, Mgst shows the highest Young's modulus, which reflects high plasticity.

Because the deformation or stress is never reached in the absolute, we expressed the relaxation% in Fig. 2; this shows the effect of different lubricants on the percentage of relaxation model, as proposed by Peleg [15], of the prepared granules (mixtures A and B). The viscoelastic profiles distinguish that granules lubricated with Mgst exhibited the greatest stress relaxation followed by talc and precirol; the results characterize the relaxation% behaviour of Mgst. However, Hiestand et al. [19] have demonstrated that materials that tend to cap exhibit slower stress relaxation. Cole et al. [20] previously explained the phenomenon of stress relaxation; when a particulate system as granules lubricated with Mgst having high relaxation% is compacted and held under load, stress relaxation in the compressing device occurs as a result of reduction in the compact volume due to the plastic deformation of compacted material into void spaces. This causes increased bonding and sliding between particles. However, the compact behaved as a set of spring and shock absorber [21]. The consolidation behaviour of different granules (mixtures A and B) has been demonstrated in Fig. 2, where mixture B with the highest moisture content exhibited an increment in relaxation% values compared to those of mixture A. In 1990, Li and Peck [22] stated that the method of granulation had an influence on the physical properties of granules and that the moisture content of the material exerted an effect on its compaction behaviour.

In recent work, it has been demonstrated that compact relaxation depends to a large extent on the amount of energy stored in the compact during compression, as well as on the interparticle bonding [23]. Since particle size is known to affect compact properties, where the degree of relaxation depends upon particle size [7], Fig. 3 implies that granules lubricated with talc and precirol have the highest fragmentation propensity during compaction, while in the case of granules lubricated with Mgst, the lack of fragments in the compacts causes a more or less coherent lubricant matrix to be formed [24]. Fig. 3 shows that the particle size distribution of granules lubricated with Mgst after compaction was higher than that of original granules before compaction (592.19 and 423.04 μm), respectively. This may be due to the lubricant film formed around the granule particles [25],

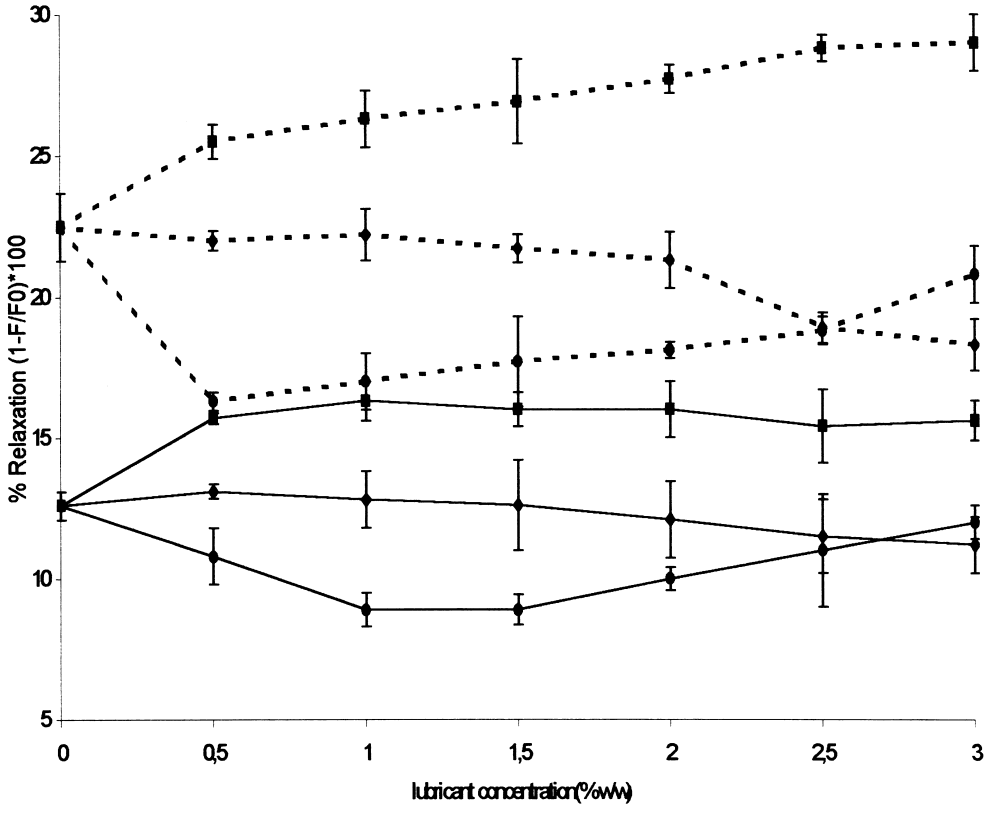

Fig. 2. Viscoelastic characterization of prepared granules as a function of lubricants; (●) precirol; (◆) talc, (■) Mg stearate; (—) mixture A; (- - -) mixture B.

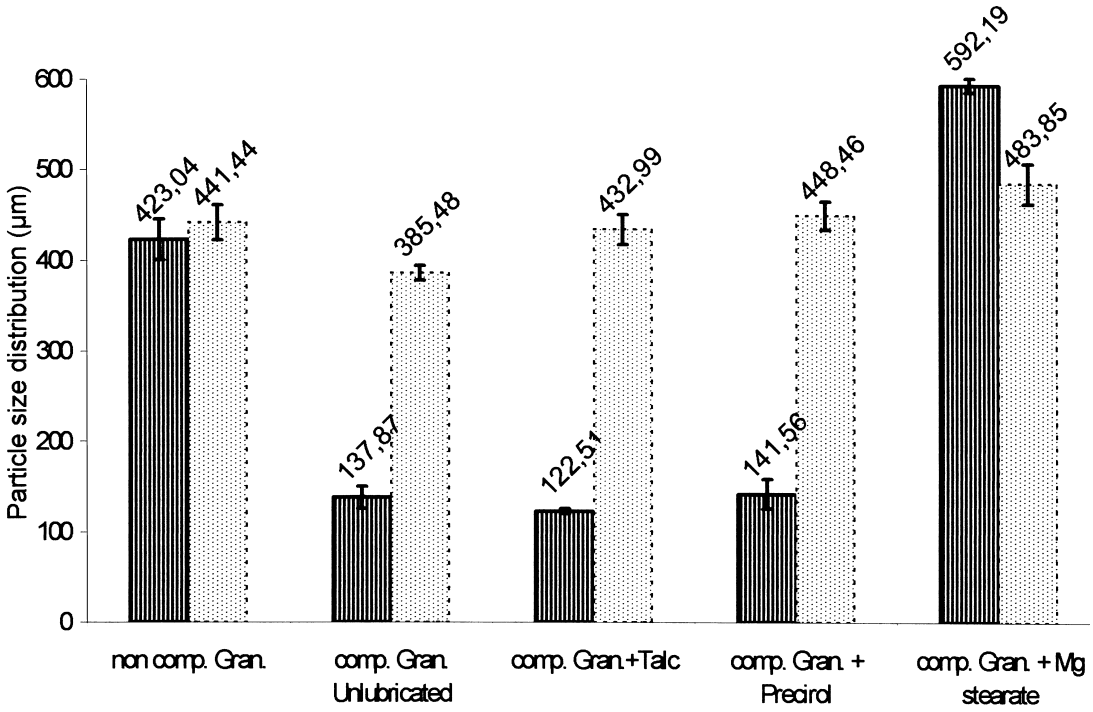

Fig. 3. Effect of 3% lubricants on particle size distribution of different granules on compression under 49 N: (—) mixture A; and (- - -) mixture B.

which facilitates particle sliding. Unfortunately, it has been pointed out that the particle size of granules lubricated with talc as well as precirol was reduced after compaction to 122.5 and 141.5 μm, respectively, which in turn reduces the possibility of forming a strong bond [26]. This result has been confirmed by photographic pictures (Fig. 4). The morphological characteristics of the used lubricants (Mgst, talc and precirol) justify the obtained results. Mgst has the highest projected specific surface area (16 m^2/g) as measured by RHEO Company and the lowest particle size diameter (5.66 μm). The specific surface area presented by talc and precirol were 12 and 1.02 m^2/g, respectively, while their mean diameter values were 18.68 and 46.41 μm, respectively. However, the small particles of Mgst can occupy the space between granules, forming a lubricant film on the particle surface showing a significantly high cohesive index [13]. Precirol, due to its morphological properties, has small flakes with high cohesion forming agglomerates which may not delaminate [6]. This hypothesis can explain the consolidation behaviour of granules lubricated with precirol at different rates.

At low concentration, lubricant particles are distributed between granules during consolidation, resulting in low relaxation of the compact, while at concentrations higher than 1%, precirol particles agglomerate with an increment in the compact relaxation. This presents an anti-friction character of its lipidic composition at the time of compression. Nevertheless, talc is not an anti-friction lubricant [25,27] and presents a high elastic behaviour [9]. However, film formation is unlikely to become complete when dealing with poorly flowing powder like talc [28]. Relaxation depends upon particle size [9]; hence, for talc and precirol, structure relaxation is slowed down by the entrapped air as soon as constant deformation is applied, which is responsible for the capping tendency during the consolidation phase. One could not have the same result for precirol in normal compression mode due to the lipidic melting matrix that coats the granules. This phenomenon was previously seen with paracetamol granules [9]. These results could indicate different consolidation mechanisms; granules lubricated with Mgst are consolidated initially by particle sliding and then subsequently by plastic deformation [29]. Thus, for proper bonding force, plasticity is necessary to reduce sufficiently the distance between adjacent particles [30], because the compaction cycle may include particle plastic deformation and particle rearrangement [31], whereby plasticity plays the dominant role during densification [7].

The evidence is changed for both talc and precirol, which consolidate by fragmentation and display a small amount of stress relaxation. Plastic deformation is not the principle mechanism of consolidation in these cases, whereas the interparticle bonding of compacted granules decreases quite drastically upon mixing with materials which fragment and consolidate extensively under load. Moreover, the influence of moisture content on the degree of plasticity of different granules was previously studied [9]. The authors have reported that degree of plasticity is increased with moisture content. Accordingly, Fig. 2 illustrated that granules of mixture B with high moisture content have higher plasticity than those of mixture A; as previously indicated, compaction is facilitated by viscoelastic character. Mixture B presents high residual humidity value (rH%) because of

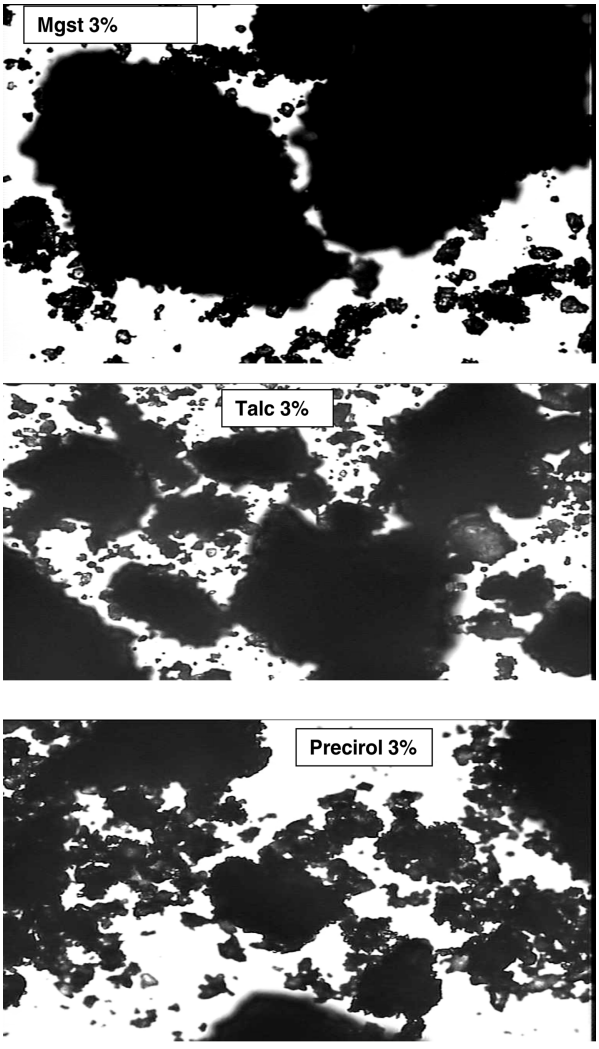

Fig. 4. Scanning micrograph of compacted granules with different lubricants at 40× magnification (mixture B).

the presence of Natrosol (cellulose derivative), which increases the viscoelastic character and bonding between particles [11].

Thus, to optimize compact formation, attention should be paid to porosity. Partial porosity of different compacts has been shown in Table 1; this parameter reflects the bonding characteristics of granules and statistically significant differences have been distinguished between the porosity values of compacted granules lubricated with Mgst and those lubricated with talc or precirol. The order of porosity values obtained (Mgst < precirol < talc) with the stress relaxation data shows that relaxation% increases with decreasing bed granule porosity. Thus, final compact porosity depends on powder consolidation during compression and compact relaxation after punch release. However, for a predominantly plastic material, there appears to be a direct relationship between the amount of elastically stored energy and the minimum porosity that can be reached [30].

In this study, we do not compress to obtain tablets as the compression force is weak, that is to say we do not obtain a tablet at the end, but we compress the granules and thus the notion of interparticle friction should be introduced as it will affect the relaxation phenomenon. The anti-friction lubricants will facilitate particle sliding until the maximum relaxation. We note that flowability characteristics on the Carr's index measures were correlated with viscoelastic characteristics of granules.

This circumstance could explain the compact porosity of granules lubricated with Mgst, which is completely dependent on the relaxation behaviour. Brittle materials, therefore, cannot store large amount of elastic energy and consequently, their change in porosity after compression is generally low [30].

Usually, brittleness causes capping and the measure of the degree of compact brittleness is evaluated using the brittle fracture index (BFI) [31]. This is defined as $BFI = 0.5(\sigma/\sigma_0 - 1)$, and is obtained by performing a transverse compression test on a compact with and without a small hole in it, the tensile strengths being σ and σ_0, respectively. The BFI is a quantification of the stress relaxation by plastic deformation of the compact at the hole [8].

Its expression is similar to that of relaxation%, and permits us to correlate the latter to the degree of particle fracture. The value of BFI is lower when relaxation% is high and therefore the tendency to fracture is minimized. Fragments resulting from the breaking of compacts can form fines which by the effect of entrapment of air, present a major obstacle during the pharmaceutical process. These fines can impede particle sliding during flowing and compression tests; in fact, the relaxation% of bed powder is lower. This can cause particle fracture during compression.

Table 2
Exponential function number given by modelling of relaxation curves using SigmaPlot® for Windows version 2.0 according to Eq. (7)

Mixture A		α (s^{-1})
Precirol 3%	$44.78 + 2.28\exp(-6.359t) + 1.073\exp(-0.632t)$	6.359 ± 0.168
Talc 3%	$44.08 + 1.014\exp(-0.0767t) + 3.384\exp(-2.752t)$	2.752 ± 0.096
Mgst 3%	$41.87 + 3.12\exp(-4.919t) + 0.903\exp(-0.0567t) + 1.359\exp(-1.497t) + 1.238\exp(-0.423t)$	4.919 ± 1.156
Mixture B		
Precirol 3%	$32.21 + 6.211\exp(-0.0586t) + 9.927\exp(-2.091t)$	2.091 ± 0.052
Talc 3%	$31.89 + 9.821\exp(-1.649t) + 6.184\exp(-0.0583t)$	1.649 ± 0.123
Mgst 3%	$32.56 + 4.23\exp(-1.76t) + 3.8\exp(-0.253t) + 3.807\exp(-9.46t)$	9.460 ± 0.763

It has been verified that the preliminary relaxation curves obtained using tested lubricated granules could be the sum of three exponentials, particle size, porosity and plasticity of particles in compacts [9].

Table 2 illustrates that the recorded force obtained for compacted granules lubricated with Mgst behaved as the sum of four exponentials, while those lubricated with talc or precirol behaved as the sum of two exponentials. According to Casahoursat [9], the first exponential term corresponds to the largest value of the time constant ($\alpha\ s^{-1}$); this permits us to judge material compressibility. The obtained values, combined with the relaxation% results, tend to agree. For example, Mgst, which presents the highest degree of viscoelasticity, has the largest value of α.

We note that the number of exponential terms is not directly related to the viscoelastic character of the material, because for the Mgst 3% (mixture B) we have only three exponential functions compared to mixture A; nevertheless, the viscoelastic character of mixture B is greater.

4. Conclusions

To characterize the flow and compaction behaviour of granules, the effect of different lubricants on the compression properties of granules was studied. Studies of the consolidation mechanisms could correlate stress relaxation behaviour with flow properties, particle size, viscoelasticity and porosity data, in order to assess the extent to which bonding has occurred during compaction.

The literature shows that viscoelasticity is always present and it produces accompanying plastic deformation; this study revealed that lubricants used exert an influence on granule relaxation. Generally, Mgst can be expected to be the lubricant of choice in preventing capping risks due to the entrapment of air during compression.

Particle size analysis permits us to see that relaxation is equally influenced by particle size. The linear equation of the Wischert model to describe material relaxation should be used with precaution because the exponential function number is not directly correlated with material viscoelastic character. The problem complexity permits us to discuss a constant value of α, which according to some authors estimates the material comprimability.

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