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Comparative study of the lubricant performance of Compritol® HD5 ATO and Compritol® 888 ATO: effect of polyethylene glycol behenate on lubricant capacity

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Abstract

The aim of this paper is to study the lubricant capacity of Compritol HD5 ATO, a glyceryl and polyethylene glycol dibehenate, obtained by atomization. This material is compared to Compritol 888 ATO, constituted only by glyceryl dibehenate. First, this study verifies that Compritol HD5 ATO and Compritol 888 ATO present the same granular characteristics and that their mixes with Lactopress present no structural differences. Secondly, in term of compressibility and cohesiveness, the use of Compritol 888 ATO or Compritol HD5 ATO with Lactopress does not involve any significant modification. Finally, the minor difference of lubricant capacity between Compritol HD5 ATO and Compritol 888 ATO has no consequence in compression practice. The presence of polyethylene glycol behenate does not decrease the glyceryl dibehenate compression functionality. This study concludes that Compritol HD5 ATO could be a very interesting excipient because it associates the glyceryl dibehenate lubricant capacity with the polyethylene glycol behenate-specific capacity in terms of dissolution enhancement.

Keywords: Compritol®; Lubricant capacity; Polyethylene glycol; Glyceryl dibehenate; Powder compression

1. Introduction

In the field of pharmaceutical solid dosage form, solid phase lubricants represent a very important class of excipient. They decrease interparticulate friction during the densification phase and between material and compression die walls during the ejection phase of the compact (Miller and York, 1988). The mechanism of friction decrease is due to the physicochemical properties of the lubricant. These products are often hydrophobic materials in which London interactions dominate. These low energy interactions take the place of more energetic interactions existing in other materials like hydrogen bonds, which create more friction (Zanorwick, 1994).

Unfortunately, the nature of lubricants induces two well-known negative effects due to their hydrophobic characteristics: the decrease of tablet tensile strength and the slowing of drug release (Jarosz and Parrott, 1984; Zanorwick, 1994). These effects are particularly important for magnesium stearate, the most commonly used lubricant. For this reason, several new lubricants that are less hydrophobic are proposed. One of these lubricants is glyceryl dibehenate (Abramovici et al., 1986). Recently, a mix of glyceryl and polyethylene glycol behenate (more than 50% mass fraction

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polyethylene glycol behenate) is proposed on the pharmaceutical excipient market. As the polyethylene glycol behenate is an amphiphilic substance, it can be used to enhance the aqueous solubility or dissolution characteristics of poorly soluble compounds by making solid dispersions (Miralles et al., 1982; Zanorwick, 1994). In this first study, we test the lubricant capacity of this new excipient, commercially named Compritol® HD5 ATO, in order to determine if the presence of polyethylene glycol behenate, in an important mass fraction in the mix, does not decrease the glyceryl dibehenate compression functionality.

2. Materials and methods

2.1. Materials

The present study compares the lubricant capacity of glyceryl dibehenate (Compritol® 888 ATO, named 888 in the following text) and the mix of glyceryl and polyethylene glycol behenate (Compritol® HD5 ATO, named HD5 in the following text) supplied by Gattefossé S.A. (Saint Priest, France). The same atomization process was used to produce the two materials. The particle size distributions of the two materials were investigated by laser light scattering granulometry (Coulter LS 130, Coultronics). These experiments, carried out on air suspensions of the particulate materials, showed that these two materials were powders with quite the same granular distribution.

Lactopress spray dried 202 (α-lactose monohydrous, Lactochem) was chosen as a model for lubricant efficiency tests due to its friction generating properties.

2.2. Methods

Microscopic observations were performed using a scanning electron microscope (SEM; JEOL JSM model 6400F, Japan) at low beam voltage. Samples were sputtered with nickel then observed at a magnification of 200×.

Lactopress and lubricant (HD5 or 888) were mixed in a trembling blender (TURBULA T2C, W. Bachofen, Basel, Switzerland) at different concentrations of lubricant: 0.5, 1, 2 and 3% (w/w). The same mixing process was respected: 150 g sample mixed at 46 rpm for 15 min.

The friction parameters of the mixture were investigated using an alternative press (EK0, Korsch Pressen, Berlin, Germany) equipped with 10 mm diameter, round flat-faced punches and 10 mm high die walls during the filling phase. For all samples, eight different pressure levels were applied. For each pressure, five tablets were produced with a cadence of 10 cycles per minute. During the compression phase, the forces applied on the upper and the lower punches were recorded on a numerical recorder (Windograph 900, Gould).

After compression, the tablets were weighted (precision of 0.1 mg; METTLER TOLEDO AB 204, Switzerland) and the diameter (precision of 0.01 mm), the thickness (precision of 0.01 mm), and the tensile strength (precision of 0.01 N) measured with a tablet testing instrument (PHARMA TEST PTB511-E, Hainburg, Germany).

Specific software for uniaxial compression (ADOC, Technological Group of Pharmaceutical Powders, Université de Bourgogne, France) was used for treatment of compression cycle data.

The following compaction parameters were obtained (Doelker, 1994):

- The consolidation pressure, mean of the maximum pressure applied on the two punches.
- The bulk density of tablets for compressibility evaluation. These data were chosen in preference to the bulk density of the powder bed under pressure, because they are not influenced by the deformation of the mechanical axes of the press.
- The tensile strength of tablets for tablet cohesion evaluation. The crushing force (F) can been converted to diametrical tensile strength (σ) using $\sigma = (2F)/(\pi dt)$, where d and t are respectively the tablet diameter and the tablet thickness (Fell and Newton, 1970).
- The transmission, ratio of maximum pressures applied on lower and upper punches, indicative of friction between particles during compression phase.
- The axial ejection pressure ($P_{\mathrm{ej\,ax}}$), for the friction evaluation during tablet ejection phase, calculated using $P_{\mathrm{ej\,ax}} = F_{\mathrm{ej}}/S_{\mathrm{lat}}$, where F_{ej} is the maximum force applied on the lower punch during ejection phase and S_{lat} is the lateral surface of compact before ejection phase. The use of S_{lat} in ejection

pressure calculation, rather than the lower punch surfaces, permits us to take into account the surface where the friction between compact and die are really applied.

3. Results and discussion

Particle shapes of HD5 (Fig. 1A) and 888 (Fig. 1B) are essentially spherical. This is a typical particle shape for atomized powder. Particle diameters range from 10 to 200 μm for the two powders. Some fibres are visible on particle surfaces for the two materials and seem to be created during the atomization process independently of chemical composition. It is impossible to identify the two lubricants in terms of particle size distribution and morphology based on SEM observations. Fig. 1C presents a SEM observation of Lactopress: lactose particles are from acicular shape to large agglomerate (around 200 μm). The morphology difference between lactose particles and HD5 or 888 particles allows clearly their identification in mixes. The comparison of HD5–Lactopress mix (Fig. 2A) and 888–Lactopress mix (Fig. 2B) at a concentration of 3% of lubricant shows no difference in terms of mixes structure: some spherical lubricant particles (encircled in Fig. 2) appear free between the lactose particles. There is no particle size, nor shape differences between HD5 and 888 and mix structures are equivalent. In this study, only the lubricant chemical composition changes.

Fig. 3 presents the evolution of tablet density with the applied consolidation pressure for all mixes HD5–Lactopress and 888–Lactopress. First, the powder-bed compressibility is not modified with the lubricant concentration from 0.5 to 3%. Secondly, the use of HD5, in place of 888, has no repercussion on lactose compressibility.

Fig. 4 presents the evolution of tablet tensile strength with tablet density. The use of either one of

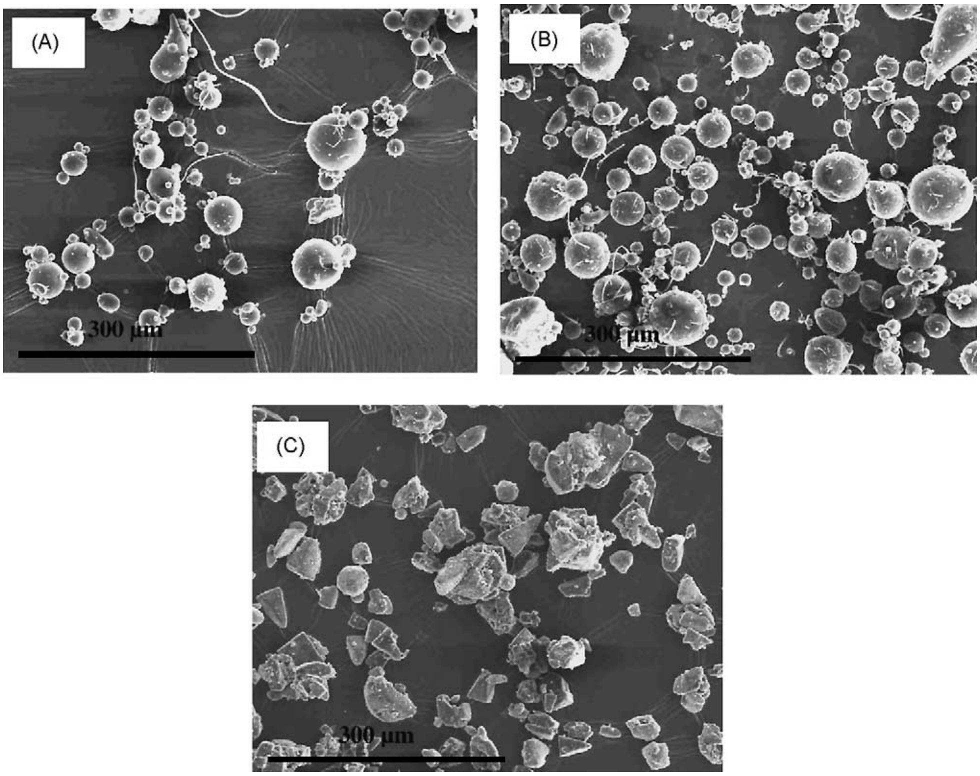

Fig. 1. SEM images (200×): (A) HD5, (B) 888, (C) Lactopress.

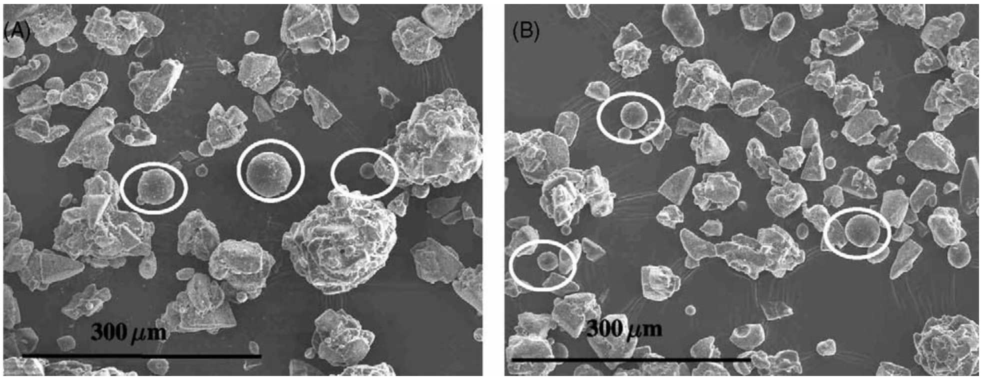

Fig. 2. SEM images (200×) of Lactopress and lubricant mixes at the concentration of 3%: (A) HD5, (B) 888.

these two Compritol® does not show any significant modification of tensile strength. These results also demonstrate that HD5 or 888 concentration variation does not influence Lactopress cohesion. It seems that the two lubricants do not possess negative effects on cohesion of lactose during the powder densification phase.

Transmission is influenced by lubricant concentration (Fig. 5). At the concentration of 0.5%, transmission varies from 45 to 70% in function of the consolidation pressure. This concentration of lubricant is too low to assure the adequate lubrication of Lactopress. Transmission increases progressively when the lubricant concentration increases and is

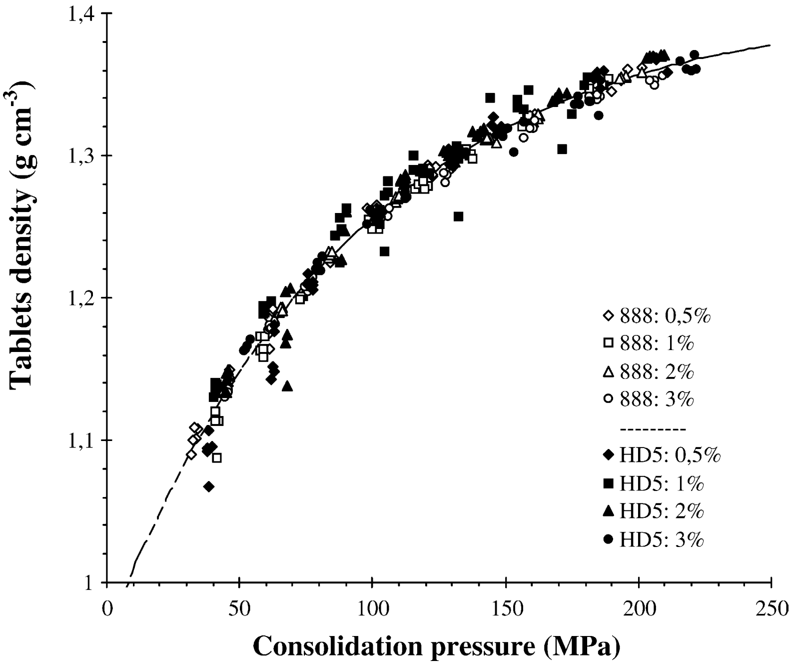

Fig. 3. Compressibility comparison of the different mixes: Lactopress–HD5 and Lactopress–888. Range of lubricant concentrations from 0.5 to 3%.

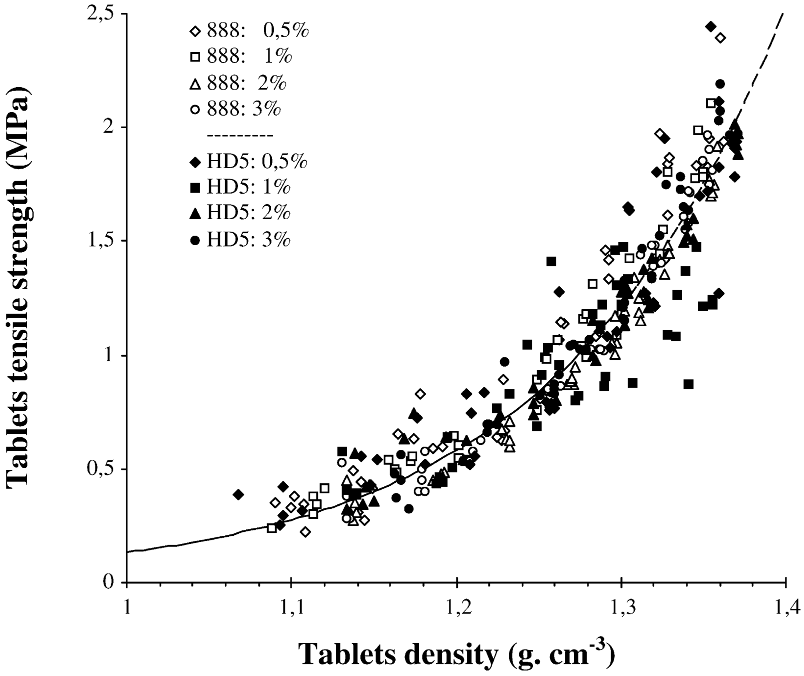

Fig. 4. Cohesiveness comparison of the different mixes: Lactopress–HD5 and Lactopress–888. Range of lubricant concentrations from 0.5 to 3%.

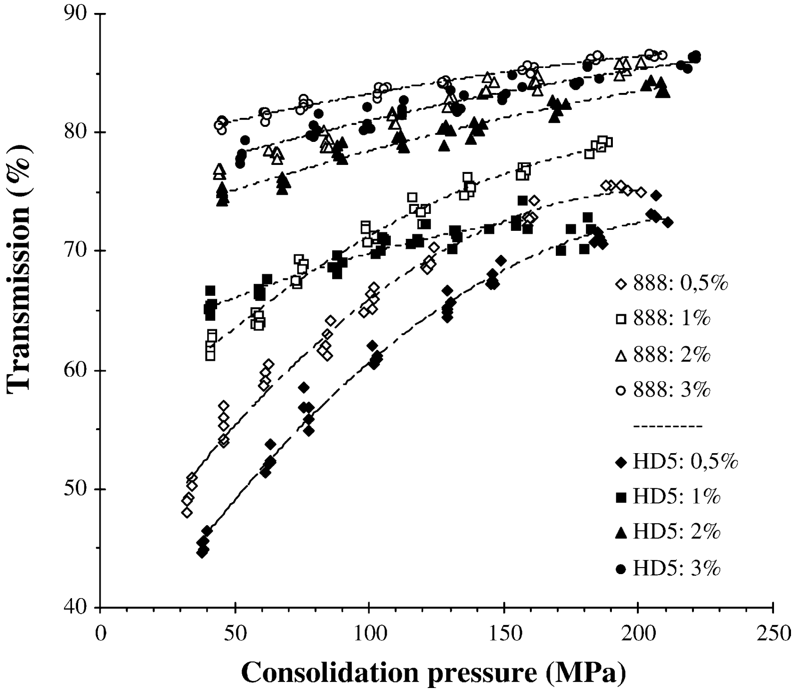

Fig. 5. Interparticulate frictions comparison of the different mixes: Lactopress–HD5 and Lactopress–888. Range of lubricant concentrations from 0.5 to 3%.

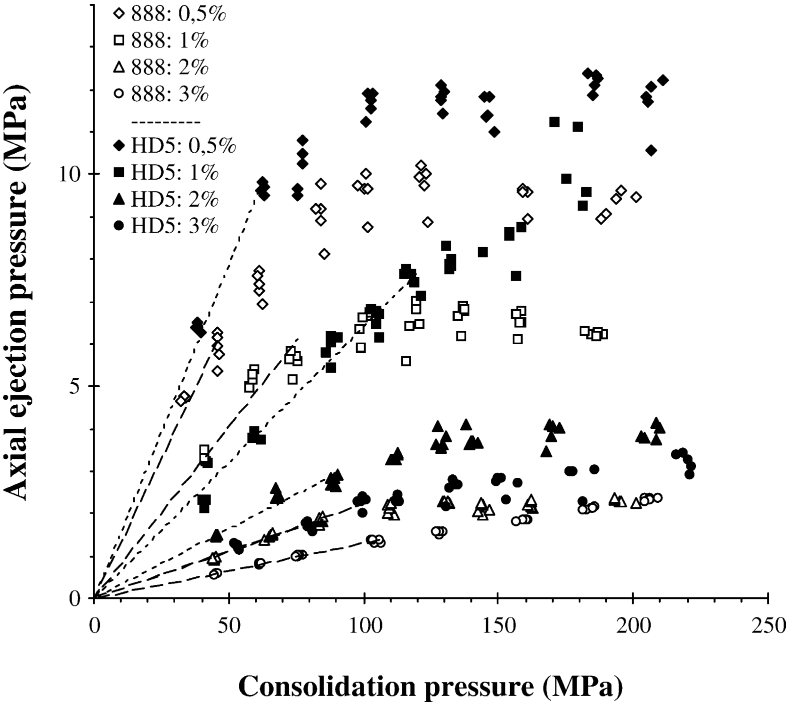

Fig. 6. Interparticulate frictions comparison of the different mixes: Lactopress–HD5 and Lactopress–888. Range of lubricant concentrations from 0.5 to 3%.

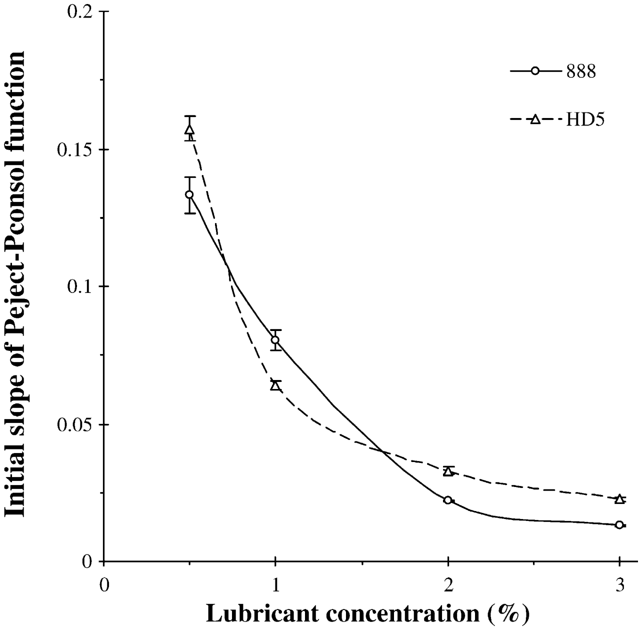

Fig. 7. Interparticulate frictions comparison: initial slope of axial ejection pressure-consolidation pressure function vs. lubricant concentration.

higher than 75% at 2% of Compritol® even with the lowest consolidation pressures. Above 2% of lubricant, Lactopress is adequately lubricated. The comparison of all transmission data from HD5 and 888 shows that HD5 is slightly less lubricating than 888. An empirical second-order polynomial function was numerically adjusted to the different groups of data (Fig. 5) to show these transmission differences. Those are too low to have practical repercussions on tablet feasibility. For example, with a consolidation pressure of 100 MPa, using HD5 instead of 888 decreases the transmission value from 65 to 61% for a concentration at 0.5% and from 82 to 81% for a concentration at 3%. In practice, this effect is not significant.

Fig. 6 presents the evolution of the axial ejection pressure versus consolidation pressure for all mixes. During the ejection phase, frictions existing between the powder and the die walls depend also on the lubricant concentration. The axial ejection pressure decreases progressively when the lubricant concentration increases from 0.5 to 3%. This effect is significant enough for a concentration of 3%. The lubrication of Lactopress particle surface is not necessarily achieved at this concentration.

HD5 seems less lubricating than 888. For each concentration, the axial ejection pressure versus consolidation function is fitted to a straight line, for the initial pressure values. The different slopes are calculated with linear regression and represented in dotted line in Fig. 6.

Fig. 7 presents the evolution of these initial slopes versus lubricant concentration for the two materials. This figure shows that the lubricant capacity difference between HD5 and 888 is much smaller than it would appear in Fig. 6. In every case, as above-mentioned about transmission, this difference between HD5 and 888 seems too low to have practical consequences on tablet feasibility.

4. Conclusion

First, this study verifies that HD5 and 888 present the same granular characteristics and their mixes with Lactopress present no structural difference. In terms of compressibility and cohesiveness, the use of 888 or HD5 with Lactopress does not involve any significant modification. In addition, the two materials offer quite the same lubricant capacity; the minor difference between HD5 and 888 has no consequence in compression practice. This fact is surprising: even though HD5 contains glyceryl behenate, as 888, more than 50% of its composition is polyethylene glycol behenate. The presence of polyethylene glycol behenate does not decrease the glyceryl behenate compression functionality. This conclusion could be due to the exact nature of HD5 mix structure, obtained by atomization. It remains to be seen if HD5 keeps the polyethylene glycol behenate-specific properties in terms of dissolution enhancement.

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