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International Journal of Pharmaceutics 262 (2003) 39–45
international journal of pharmaceutics
www.elsevier.com/locate/ijpharm

Comparative study of the lubricant performance of Compritol® 888 ATO either used by blending or by hot melt coating

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Received 27 February 2003; received in revised form 16 May 2003; accepted 23 May 2003

Abstract

Compritol® 888 ATO is used as a lubricant in oral solid dosage formulations. It can also be used as a hot melt coating agent sprayed onto a powder. In this study, we compare the lubricant performance of Compritol® 888 ATO either used by classical blending or by hot melt coating onto Lactopress by compression tests. In physical mix, the Compritol concentration does not affect the compressibility. The same compressibility is obtained with lactose coated by 0.5 or 1% of Compritol, but a higher compressibility can be observed with 2 and 3%. Cohesiveness of lactose depends on the process: hot melt coating induces a decrease of tablet tensile strength. In terms of forces transmission during compression phase and axial ejection pressures, Compritol used by hot melt coating allows for a concentration of 0.5% to directly obtain the lubricant performance of 3% of Compritol used by blending. These results suggest that the hot melt coating process induces an homogenous repartition of the lubricant on the lactose surface, contrary to classical blending procedure. Thus, lubrication by hot melt coating seems to be a very efficient procedure. It could be used specifically for large surface area particulate systems producing a lot of friction.

Keywords: Compritol; Lubricant capacity; Glyceryl dibehenate; Powder compression; Hot melt coating

1. Introduction

During tablet formulation, solid phase lubricants are always added. They decrease interparticulate frictions during the densification phase and between material and compression die walls during the ejection phase of the compact (Zanorwick, 1994; Miller and York, 1988). Lubricants are classically added by blending. Lubricant performance depends on the lubricant capacity of the material as well as its capacity to be mixed with the other components of the formula and to cover their surfaces. That capacity depends on the granular characteristics of the solid phase lubricant. These characteristics are not always easily handled either by producers or by users. Solid phase lubricants are used at low concentrations in compression blends, and classically from 0.5 to 2% up to 3% (w/w) of the total mix. At the industrial scale, greater concentrations of lubricant can be used, up to 5%. But a perfect lubrication corresponds to a thin lubricant film on the surface of the solid, often equivalent to the specific surface area of the particulate system to lubricate, at a lower concentration. These comments clearly show a problem of spreading the lubricant at the surface.

Among many lubricants available, some possess low melting points and can be easily used as a hot melt

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0378-5173/$ – see front matter © 2003 Elsevier B.V. All rights reserved.
doi:10.1016/S0378-5173(03)00316-8

coating agent sprayed onto a powder. One of these is glyceryl dibehenate, name as Compritol® 888 ATO (Gattefossé S.A.). That product is already used as a coating agent by hot melt coating for taste masking or controlled release (Barthelemy et al., 1999; Faham et al., 2000a,b; Griffin and Niebergall, 1999).

In this study we test the lubricant performance of Compritol® 888 ATO either used by classical blending or by hot melt coating.

2. Materials and methods

2.1. Materials

The present study compares the lubricant capacity of glyceryl dibehenate (Compritol® 888 ATO, named Compritol in the following text) either used by blending or by hot melt coating. That lubricant is produced by atomization and supplied by Gattefossé S.A. (Saint-Priest, France).

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

2.2. Methods

2.2.1. Preparation of coated lactose

A pre-weighted quantity of lactose was heated in a top-spray fluid bed coater (GPCG 1.1, Glatt, Germany). Compritol was melted with microwaves and then kept in its liquid form in a stirred-beaker. The coating agent was then sprayed on the lactose. Compritol was added at four different concentrations to the lactose: 0.5, 1, 2 and 3% (w/w). Coated products were cooled in the fluid bed system to room temperature.

2.2.2. Preparation of blends of lactose and Compritol

Lactose and Compritol 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 is respected: 150 g sample mixed at 46 rpm for 15 min.

2.2.3. SEM observation

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× and 5000×.

2.2.4. Compression analysis

The friction parameters of the mixture were investigated using an eccentric 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 min^{-1}. During the compression phase, the forces applied on the upper and the lower punches were recorded by 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) were measured with a tablet testing instrument (PHARMA TEST PTB511-E, Siemensstrass, Hainburg, Germany).

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

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

- the consolidation pressure, mean of the maximal pressure applied on the two punches.
- the bulk density of tablets for compressibility evaluation. These data are 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 the tablet diameter and the tablet thickness, respectively (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 ($P_{\mathrm{ej\cdot ax}}$), for the friction evaluation during tablets ejection phase, calculated using $P_{\mathrm{ej\cdot ax}} = F_{\mathrm{ej}}/S_{\mathrm{lat}}$, where F_{ej} is the maximal

force applied to the lower punch during ejection phase and S_{lat} is the lateral surface of compact before the ejection phase. The use of S_{lat} in ejection pressure calculation, rather than the lower punch surfaces, permit one to take into account the surface where the frictions between compact and die are really applied.

3. Results and discussion

Fig. 1A presents a SEM observation of Lactopress: lactose particles are from acicular shape to large agglomerate (around 200 μm). The observation of 888-Lactopress mix (Fig. 1B) at a concentration of 3% of lubricant shows some spherical lubricant particles (encircled on Fig. 1B) appearing free between the lactose particles. No free Compritol 888 particle appear on Fig. 1C and the morphology of coated Lactopress particle is the very same than lactose particle (Fig. 1A). In the same way, the observations at higher magnification (5000×) present similar surface details between Lactopress coated (Fig. 2B) and not (Fig. 2A).

When Compritol is mixed with lactose, its concentration (from 0.5 to 3%) does not affect the lactose compressibility (Fig. 3). In the same way, when 0.5 or 1% of Compritol is sprayed by hot melt coating onto the lactose, the powder-bed compressibility is not significantly changed. On the other hand, for higher concentrations (from 2 to 3%), a slight increase of compressibility can be observed. There is no explanation for this phenomenon.

An empiric function such as $\rho_c = ae^{bP} + c$, where ρ_c is tablet density, P is consolidation pressure, and a–c are three constants, was numerically adjusted to the two groups of data in order to show these compressibility differences (Fig. 3).

Cohesiveness of lactose is not significantly affected by the lubricant concentration (Fig. 4). But, its cohesiveness depends on the process: hot melt coating induces a decrease of tablet tensile strength.

Fig. 4 presents an empiric function such as $\sigma = ae^{b\rho_c} + c$, where σ is tablet tensile strength, ρ_c is tablet

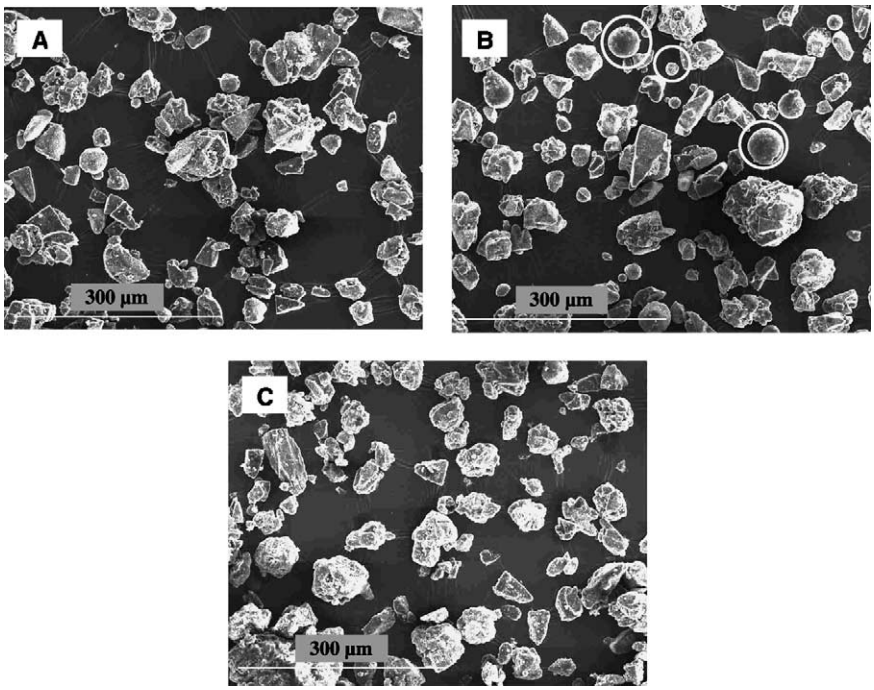

Fig. 1. SEM images (200×), (A) Lactopress. (B) Physical mix of Lactopress and Compritol 888 ATO. (C) Compritol 888 ATO spray on the lactose by hot melt coating surface.

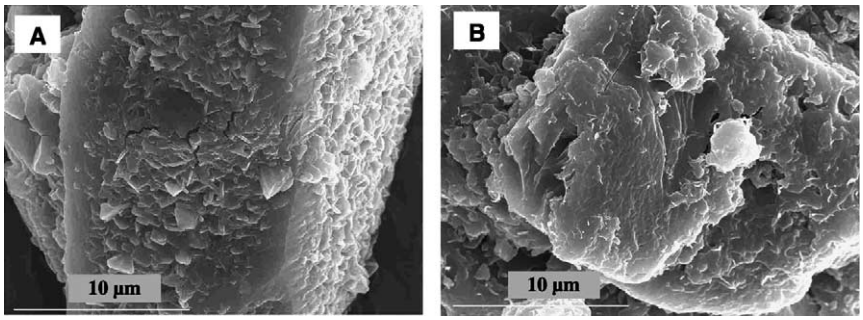

Fig. 2. SEM images (5000×). (A) Lactopress surface. (B) Lactopress coated by Compritol 888 ATO.

density, and *a*, *b*, and *c* are three constants, that was numerically adjusted to the data relative to blending and hot melt coating. Thanks to these adjustments, we can calculate for a density of 1.25 g cm^{-3}, that the tablet tensile strength would be 0.83 MPa for blending and 0.50 MPa for hot melt coating. Tablet tensile strength is decreased by nearly 40% with hot melt coating. Such a dramatic decrease suggests that the hot melt coating process allows an homogenous repartition of the lubricant on the lactose, contrary to classical blending procedure.

Fig. 5 presents the evolution of pressure transmission during the densification phase. For samples prepared by blending, transmission greatly depends on the lubricant concentration. For a concentration of 0.5% of Compritol, transmission ranges from 45 to 70% depending on the consolidation pressure. These results show an incomplete lubrication of lactose.

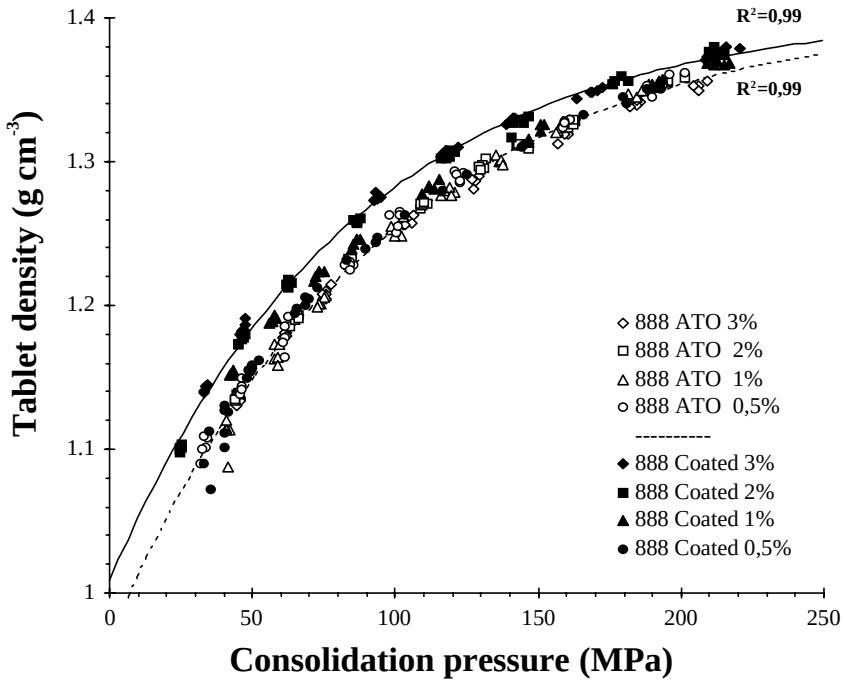

Fig. 3. Compressibility comparison of different mixes of Lactopress and Compritol. 888 ATO: Compritol 888 ATO blend with lactose. 888 Coated: Compritol 888 ATO spray on the lactose by hot melt coating. Compritol ranges from 0.5 to 3%.

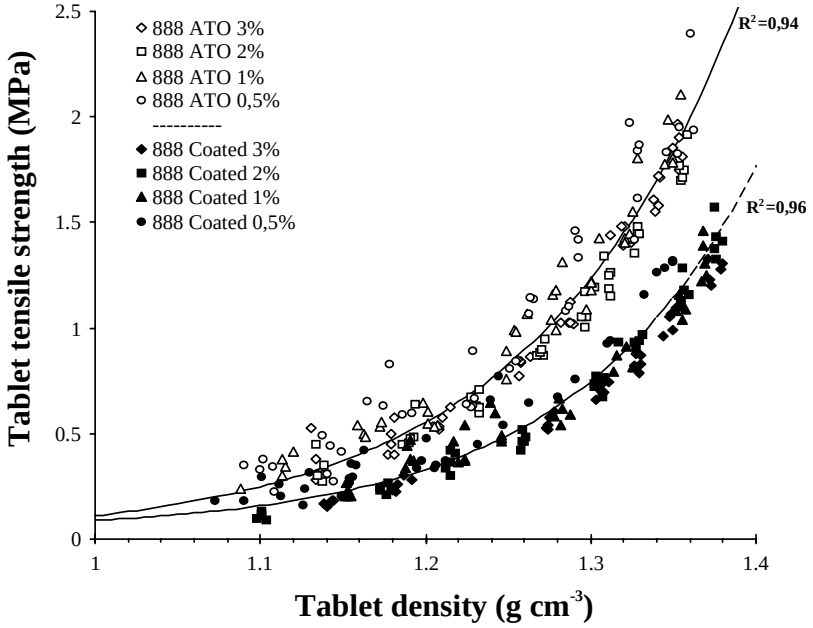

Fig. 4. Cohesiveness comparison of different mixes of Lactopress and Compritol. 888 ATO: Compritol 888 ATO blend with lactose. 888 Coated: Compritol 888 ATO spray on the lactose by hot melt coating. Compritol ranges from 0.5 to 3%.

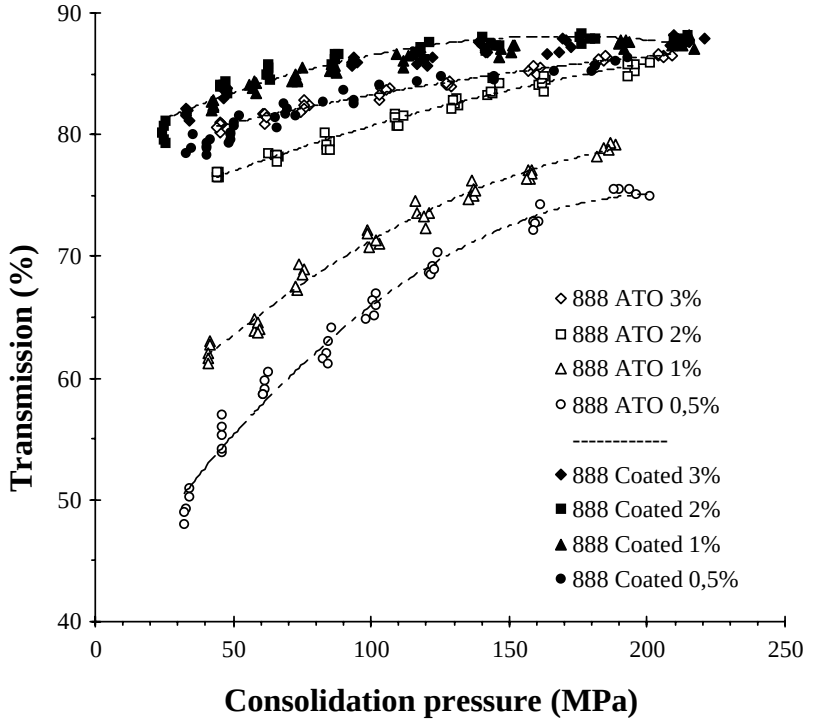

Fig. 5. Force transmission comparison during the densification phase of different mixes of Lactopress and Compritol. 888 ATO: Compritol 888 ATO blend with lactose. 888 Coated: Compritol 888 ATO spray on the lactose by hot melt coating. Compritol ranges from 0.5 to 3%.

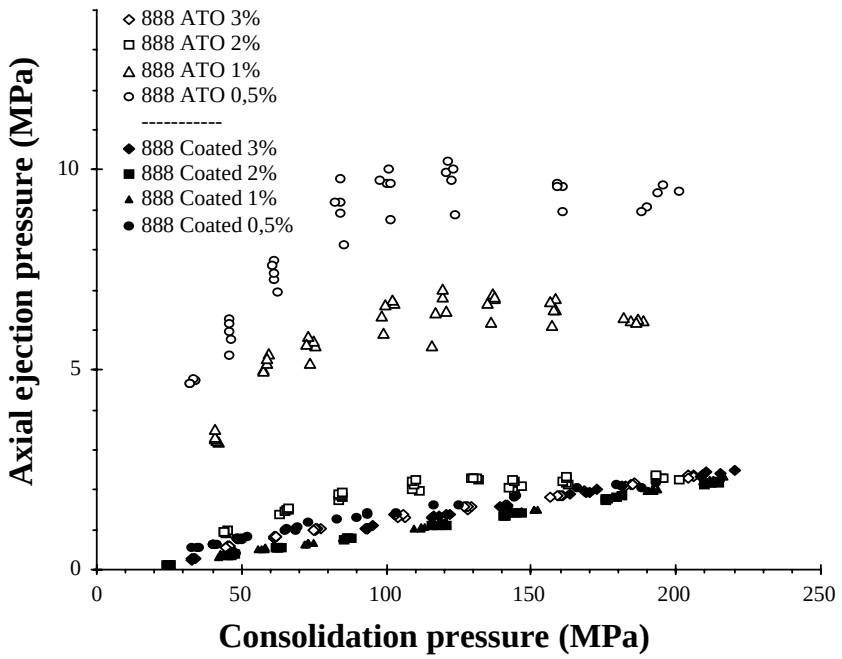

Fig. 6. Friction comparison during the ejection phase of different mixes of Lactopress and Compritol. 888 ATO: Compritol 888 ATO blend with lactose. 888 Coated: Compritol 888 ATO spray on the lactose by hot melt coating. Compritol ranges from 0.5 to 3%.

Transmission increases steadily with the lubricant concentration and exceeds 75% with 2% of Compritol, even for the lowest consolidation pressures. With 3% of Compritol, transmission reaches about 80–85% depending on the consolidation pressure applied.

Samples prepared by hot melt coating present a very different behavior. Even for the lowest concentration of lubricant (0.5%), transmission reaches values obtained by blending only with 3% of Compritol. With 1% of Compritol, we can observe an increase of transmission, then for 2 or 3% of lubricant transmission stays the same. Hot melt coating greatly increases the efficiency of lubrication when compared with blending. Lubricant performance stays the same from 1 to 3%, it seems that with these concentrations of lubricant, all the surface of lactose is lubricated.

Fig. 6 presents the evolution of axial ejection pressure during the ejection phase. Comments made for transmission also apply to axial ejection pressure. Compritol used by blending possesses a progressive lubricant effect in function of its concentration. On the other hand, Compritol used by hot melt coating allows for a concentration of 0.5% to directly obtain the lubricant performance of 3% of Compritol used by blending. With a lubricant concentration ranging from 1 to 3%, axial ejection pressures are slightly lower, thus lubrication is better. But there is no significant gain in term of lubrication, showing again a possible saturation of the lactose surface by Compritol.

4. Conclusion

This study points out that the use of Compritol by hot melt coating greatly increases its performance as a lubricant. A concentration of 0.5% of Compritol allows us to reach the same lubrication compare to blending with 3% of lubricant. The decrease of cohesiveness observed for samples prepared by hot melt coating, even at low concentrations, shows that the process permits us to cover the surface of lactose particles efficiently. Thus, lubrication by hot melt coating seems to be a very efficient procedure. It could be used specifically for large surface area particulate systems producing a lot of friction.

Acknowledgements

The authors thank A. Genevois-Malmazet, Gattefossé S.A., for her kind help and expertise in hot melt coating, and C. Pillien and S. Mielcarek, Université de Bourgogne, for their kind help in the compression experiments.

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