Drug Development and Industrial Pharmacy, 24(1), 37–44 (1998)

RESEARCH PAPER

The Effect of Wax on Compaction of Microcrystalline Cellulose Beads Made by Extrusion and Spheronization

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ABSTRACT

The effect of wax on the deformation behavior and compression characteristics of microcrystalline cellulose (Avicel® PH-101) and acetaminophen (APAP) beads is described. Beads of Avicel PH-101 and APAP formulations were prepared using extrusion and spheronization technology. A waxy material, glyceryl behenate, N.F. (Compritol®), was added to the formulations in amounts ranging from 10% to 70% of total solid weight. Beads with a selected particle size range of 16–30 mesh were compressed with an instrumented single punch Manesty F press utilizing a 7/16-in. flat-faced tooling set. Compaction profiles were generated for the tablets to evaluate the effect of wax on the densification of beads containing wax. Beads made without wax (the control formulation) required greater compression forces to form cohesive tablets. As the amount of wax in the bead formulation was increased, the beads become more plastic and compressible. The Heckel equation which relates densification to compression pressure was used to evaluate the deformation mechanisms of the bead formulations. The analysis shows that as the level of wax in the bead formulation is increased, the yield pressure decreases, indicating that the beads densify by a plastic deformation mechanism.

INTRODUCTION

Beads have been used extensively in the formulation of sustained release dosage forms or delivery systems. Recent attention has shifted to formulating these beads into tablets by mixing the beads with powder or other additives and lubricants to improve tablet consolidation (1–5). Previous work done in this laboratory to characterize the compaction parameters of beads containing microcrystalline cellulose (MCC) concluded that MCC beads are relatively noncompressible, but will form soft intact tablets (4). To improve the compressibility of the

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beads, a waxy material was added to the bead formulation, which formed harder tablets, without any external additives or additional lubrication.

The aim of this work was to prepare beads with wax by extrusion and spheronization technology, to compact the beads into tablets using an instrumented Manesty F single stroke tablet press, and to evaluate the effect of wax on the consolidation of beads compared to beads made without wax.

MATERIALS AND METHODS

Materials

Acetaminophen (APAP, Penco of Lyndhurst Inc., Lyndhurst, NJ), Avicel PH-101® (microcrystalline cellulose [MCC], FMC Corporation, Princeton, NJ), and Compritol® (glyceryl behenate, N.F., Gattefossè, France) were used to prepare the beads. Table 1 summarizes the composition of the formulations used in this study.

Bead Preparation

The beads were manufactured by extrusion and spheronization technology (6). A 1.0-kg batch of dry powder mixture was blended in a 12-qt Hobart mixer bowl (Hobart model A200T, Hobart Corporation, Hobart, NY) for 10 min at shaft speed of 50 rpm. The granulating liquid, purified water, was added over 8 min; water was added slowly over 3 min, then the mixer was stopped, the sides and the bottom of the bowl were scraped to ensure uniform mixing, and the compound was mixed for an additional 5 min.

The wet granulation was passed through a Luwa extruder operating at 50 rpm, using 1.5 mm screens (model EXDS-60 Luwa Corporation, Charlotte, NC). The extrudate was spheronized in the marumerizer (model Q-230, Luwa Corporation) operating at 1000 rpm and fitted with a 2-mm scored friction plate. The spheres were collected after 60 sec residence time and dried in a hot-air oven for 24 hr (Stokes model 38C, Pennwalt Corporation, Warminster, PA) at 45°C. Beads in the 16/30 mesh size range were used for the compaction studies.

Compaction

The beads were compressed using an instrumented single punch Manesty F press using a 7/16-in. flat-faced tooling set. For all formulations, a constant fill volume of 0.80 cm^3 was used and the speed of the press was 67 tablets per min. Five tablets were used to determine the tablet weight, ejected tablet thickness, ejected tablet diameter, and crushing strength (Schleuniger, model 2E, Germany) after ejection. Tablet tensile strength was calculated to compare tablets of different sizes (5), using the equation

$$Ts = \frac{2Fc}{\pi DH}$$

where Ts is tensile strength, Fc is the force required to break the tablet (crushing strength), D is tablet diameter, and H is tablet thickness. During testing, all tablets

Table 1

Composition of Formulations

Formulation	APAP (g)	Avicel (g)	Compritol (g)
100% Avicel PH-101 (F-I)	0	1000	0
0% Wax (F-II)	100	900	0
10% Wax (F-III)	100	800	100
30% Wax (F-IV)	100	600	300
50% Wax (F-V)	100	400	500
70% Wax (F-VI)	100	200	700

broke diametrically. Compaction profiles, tensile strength versus pressure, were compared for the materials.

The instrumentation of the tablet press monitored the upper punch force and the upper punch movement in the die. An AT computer system collected the data using Unkelscope® data acquisition software at a sampling rate of 2048 points per channel. Three data files were collected at each maximum punch stroke. Densification of the beads during compression was determined using a conversion program written in Microsoft QuickBASIC® language (7). The materials were compared using densification plots, $\ln(1/E)$ versus P, the upper punch pressure. The deformation mechanism of the beads was interpreted from the densification and pressure data generated in the die using the Heckel model (8,9),

$$\ln\left(\frac{1}{E}\right) = KP + A$$

where E is tablet porosity in die, P is upper punch pressure in die, while K and A are regression parameters. Regression analysis was applied to compression cycle phase I (the linear portion only), pressure greater than baseline to maximum upper punch pressure. In all cases, F ratios for regression were significant and R^2 greater than 96%. A, the regression intercept, less the initial fill densification, is defined as B, which represents the degree of initial particle packing, particle rearrangement, and initial particle fragmentation. K is related to the yield pressure (inverse slope) of the material and was used to characterize the pressure at which significant permanent deformation occurs for the material (7). The magnitude of the yield pressure was used to differentiate plastic deformation and brittle fracture mechanisms. The elastic recovery (ER) was calculated using the following equation, which is applicable only for the cylindrical compacts made by using flat-faced tooling sets (5).

$$\mathrm{ER}(\%) = \frac{de^2He - dc^2Hc}{dc^2HC} \times 100$$

where de and dc are the diameters of the compacts after ejection and at maximum load in the die, respectively, and He and Hc are the thickness of the compacts after ejection and at maximum load in the die, respectively.

RESULTS

Compaction

The compaction of a material involves both the compressibility, which is defined as the ability of a material to decrease in volume under pressure, and its consolidation, which is the ability to form a compact of a certain strength. Figure 1 shows the compaction profiles for all the formulations, where the 100% MCC beads (F-I) and the 10% APAP/90% MCC beads (F-II) are the controls for the study. The extrusion and spheronization process produces smooth spherical pellets (10), which have low surface-to-volume ratio. In the absence of wax in the formulation a higher pressure is required to deform (or fracture) the beads, forming more contact areas to produce cohesive compacts. This is probably due to the strong bond strength formed by water granulated MCC pellet systems prepared by extrusion and spheronization technology (10,11). When APAP is added to the formulation, there is a dramatic decrease in tablet strength and it requires even greater pressure to produce intact compacts (Table 2). The drop in tablet strength may be due to the disruption of bond formation between MCC particles, by APAP, a poorly compressible material by itself; hence even at high pressure (and possible fracturing), APAP/MCC bead formulation produces weak tablets.

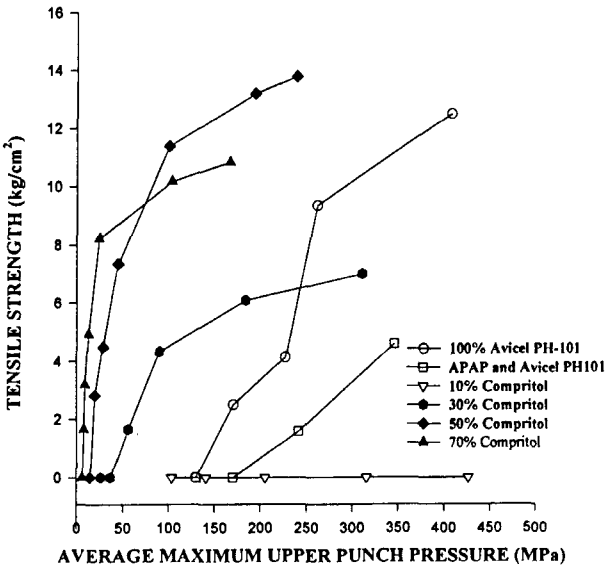

Figure 1. Compaction profile for 10% APAP, Compritol, and Avicel PH-101 beads.

Table 2

Comparison of the Maximum Upper Punch Pressure Obtained from Compression to the Same Maximum Punch Stroke (4.23 mm)

Formulation	Maximum Upper Punch Pressure (MPa)	Tensile Strength (kg/cm^2)
100% Avicel PH-101 (F-I)	261	9.32
0% Wax (F-II)	241	1.57
10% Wax (F-III)	206	0
30% Wax (F-IV)	89.8	4.31
50% Wax (F-V)	44.8	7.34
70% Wax (F-VI)	12.6	4.91

The addition of 10% wax to the APAP/MCC formulation causes further decrease in tablet strength. Compritol has been used primarily as a lubricant at a level of 1.5%–3% alone, or 1% in association with 0.2%–0.3% of magnesium stearate (12). At 10% level, the wax has an effect seen with an over-lubricated formulation, in which the binding sites are coated, resulting in a weak tablet (13). This formulation, though more compressible than control formulations, produced tablets with zero tensile strength at all compression pressures tested, probably due to less MCC, less MCC–MCC bonding, disruptive APAP, and insufficient wax to compensate for the loss of MCC in the binder system. This is in agreement with the literature finding that the ability of a material to deform (being more compressible) does not ensure the formation of a stronger compact (5).

As wax level is increased to 30%, (one-third of the bead formulation), consolidation is dramatically improved and less upper punch pressure is required to improve tablet strength. The formulation contains less MCC, but the loss was compensated with wax and now the bonding mechanism depends on wax level. At 50% wax level, there is further increase in consolidation at lower pressure range, leading to greater tablet strength compared to the control formulations. However, when the wax level was increased to 70%, the formulation required less upper punch pressure to form tablets with strengths up to 8 kg/cm^2, but upon further increase in pressure, its tensile strength does not reach the strength of the 50% wax formulation.

Figure 1 shows that as the component of the bead formulation changes, the consolidation dramatically changes as well. The MCC formulation has a similar plot to the 50% wax formulation, but shifted to higher pressure range. The addition of APAP to MCC reduced consolidation and bonding due to the poorly compressible nature of APAP. As the level of wax in the formulation increases, the wax becomes more dominant in terms of tablet strength.

Deformation Mechanism

The relationship between densification and pressure during compression was compared for the formulations at one maximum upper punch stroke with Heckel plots. Heckel plots have been classified into three types based on the dominant deformation mechanism (14). Type A plots are exhibited by materials that consolidate by plastic flow, such as MCC powder and sodium chloride. Type B plots are exhibited by materials that consolidate by particle fragmentation, represented by lactose. Type C plots, represented by fatty acids, are characterized by the absence of a particle rearrangement stage, and densification is by plastic deformation and possible asperity melting.

Figure 2 represents the densification cycle to form one tablet in the die. The differences in magnitude of pressure and densification are more apparent when the first compression phase is isolated, as shown in Fig. 3.

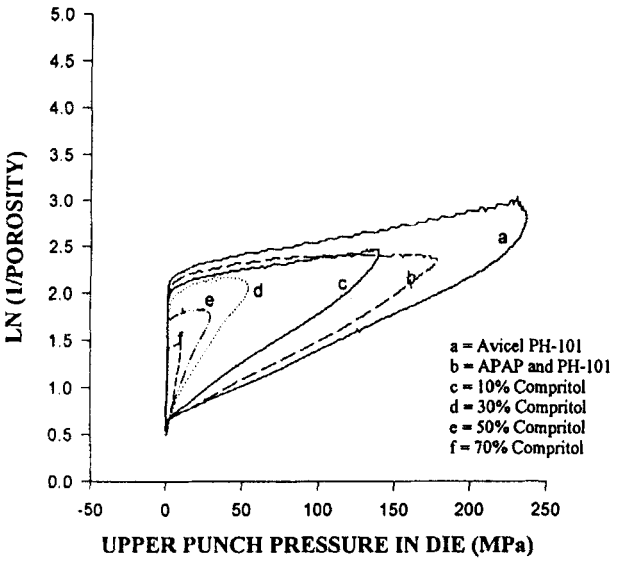

Figure 2. The densification vs. upper punch pressure in the die for 10% APAP, Compritol, and Avicel PH-101 beads compressed to the same maximum punch stroke.

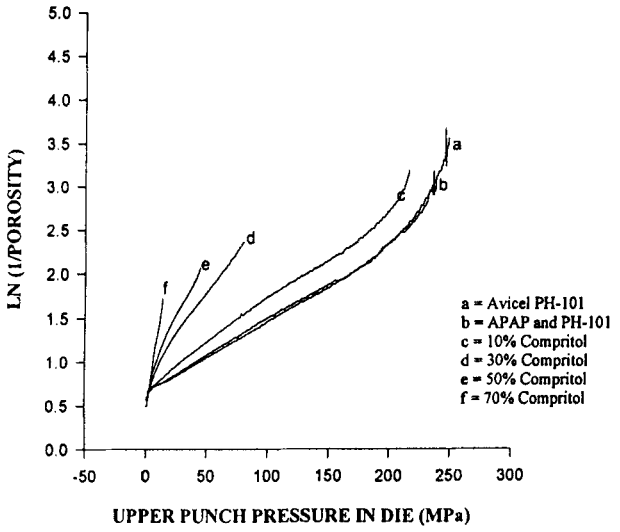

Figure 3. The first phase of compression in the densification vs. upper punch pressure in the die for 10% APAP, Compritol, and Avicel PH-101 beads compressed to the same maximum punch stroke.

York and Pilpel (14) studied the relationship between the mixture of lactose and four fatty acids powders and their tableting, and concluded that waxes, like fatty acids, are typical plastic materials that exhibit type C powder characteristics of Heckel plot—they show steep linear slopes, indicating little or no evidence of particle rearrangement. They also reported that mixtures of the fatty acids with lactose powder show a change in consolidation behavior from type B to type C as the level of fatty acid in the mixture is increased. Figure 3 shows that incorporating a wax in a bead formulation has similar effect on the beads' consolidation behavior as the fatty acids had on a powder mixture. As the level of wax added to the bead formulation was increased, the steepness of the densification plot increased (Fig. 2), and the yield pressure decreased (Table 3). This indicates that increasing the wax level in the beads increases the plasticity of the formulation which makes densification by plastic deformation the probable dominant deformation mechanism. The formulations without wax (F-I and F-II) overlap (Fig. 3), indicating that the addition of 10% APAP causes little effect on the deformation characteristics of Avicel PH-101 beads. Figure 3 also shows that the beads made with less than 10% wax fracture at higher compression pressures and the fractured particles may undergo further plastic deformation. This is evident by a second linear region in this phase, especially in the formulations that contain no wax in the bead formulation. The pressure at which this transition takes place seems to be material dependent.

Densification plots were compared for each formulation to evaluate the effect of maximum punch penetration (and therefore different forces) on the material's deformation behavior. At low compression pressures, the formulations have similar regions, but at higher pressures (deeper upper punch penetration) they differentiate into different yielding areas (yield pressure of each cycle) (Figs. 4–9). The plots also show that at low compression pressures (below 10 MPa), there is a period of increased pressure without a corresponding increase in densification. This unique characteristic (com-

Table 3

Comparison of the Yield Pressure (1/K) of Compacts Compressed to the Same Maximum Punch Stroke (4.23 mm)

Formulation	Intercept (A)	Slope (K)	Yield Pressure (MPa)	R^2	F Value
100% Avicel PH-101 (F-I)	0.539	0.00994	101	96.3	8488
0% Wax (F-II)	0.610	0.00915	109	98.5	21807
10% Wax (F-III)	0.677	0.0104	96.2	99.2	41962
30% Wax (F-IV)	0.703	0.0216	46.3	98.2	16486
50% Wax (F-V)	0.669	0.0328	30.5	97.7	13558
70% Wax (F-VI)	0.446	0.0934	10.7	99.6	82484

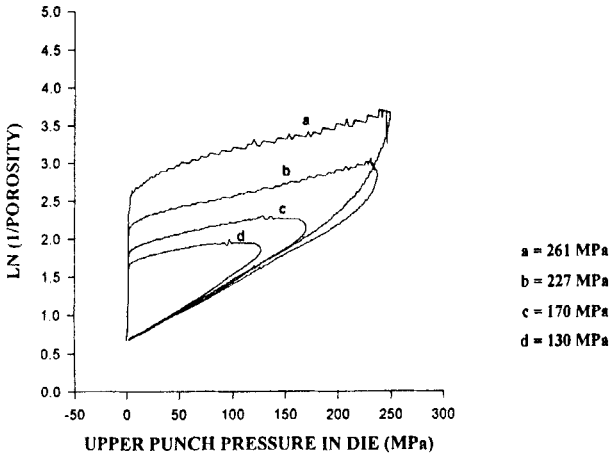

Figure 4. The densification vs. upper punch pressure in the die for Avicel PH-101 beads compressed to different maximum punch penetrations.

pared to densification plot of a typical powder) seems to be more noticeable as the level of wax in the bead formulation is increased. This may be due to the fact that beads, being spherical, form a dense, rigid packing upon being poured into the die and undergo little or no particle rearrangement as the pressure is applied (5,9).

The densification plots can also be used to describe the extent of elastic recovery of the material in the die.

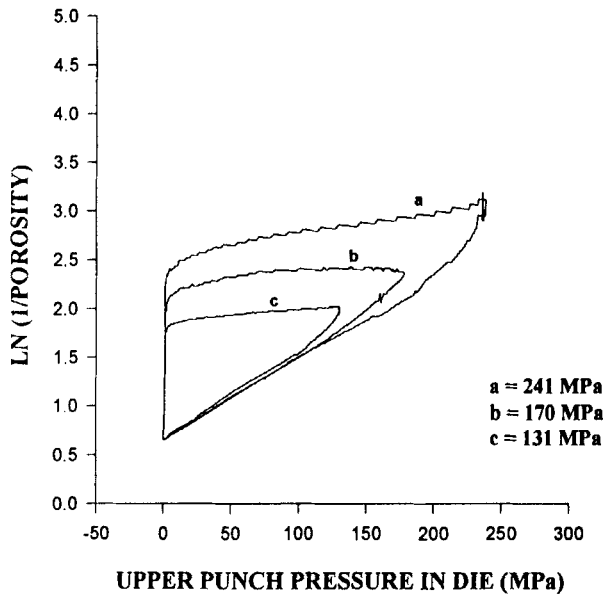

Figure 5. The densification vs. upper punch pressure in the die for 10% APAP and Avicel PH-101 beads compressed to different maximum punch penetrations.

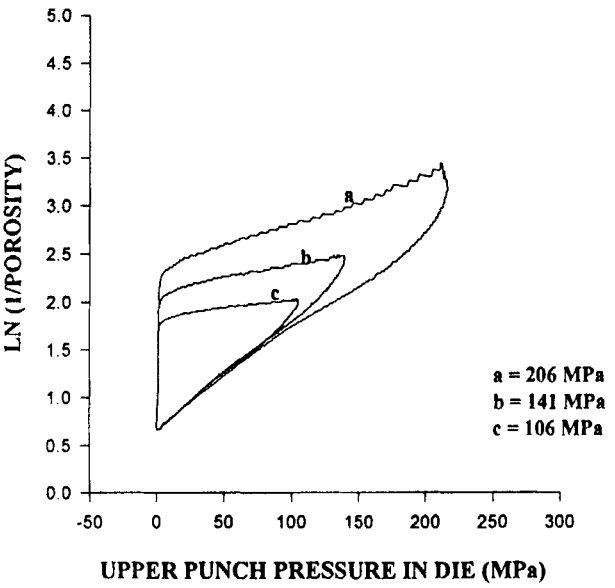

Figure 6. The densification vs. upper punch pressure in the die for 10% APAP, 10% Compritol, and Avicel PH-101 beads compressed to different maximum punch penetrations.

The apparent consolidation behavior of a mixture of a plastic material and a nonplastic material is governed by the extent of deformation of the major component or the maximum punch stroke selected (14). Formulations

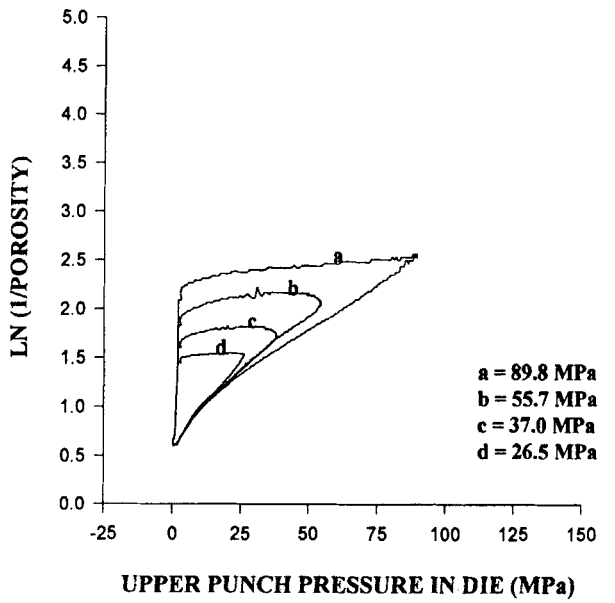

Figure 7. The densification vs. upper punch pressure in the die for 10% APAP, 30% Compritol, and Avicel PH-101 beads compressed to different maximum punch penetrations.

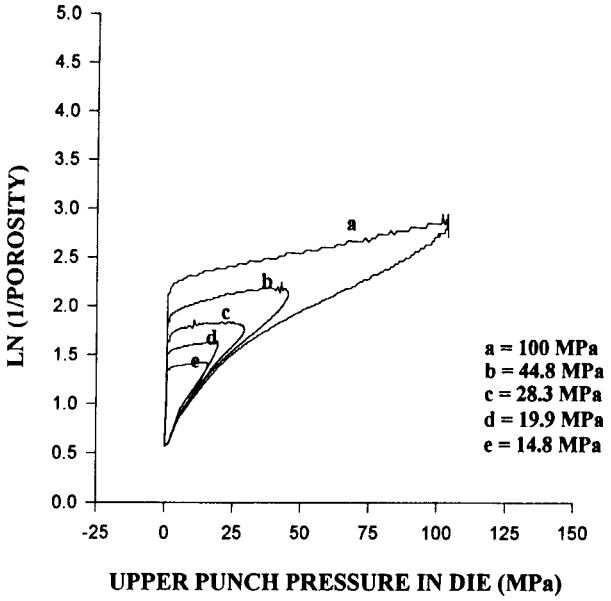

Figure 8. The densification vs. upper punch pressure in the die for 10% APAP, 50% Compritol, and Avicel PH-101 beads compressed to different maximum punch penetrations.

containing less than 10% wax have less consolidation or higher yield pressures and exhibit more elastic recovery upon ejection than those with 30% or more wax (Figs. 4–9). The elastic behavior is indicated on the plots by

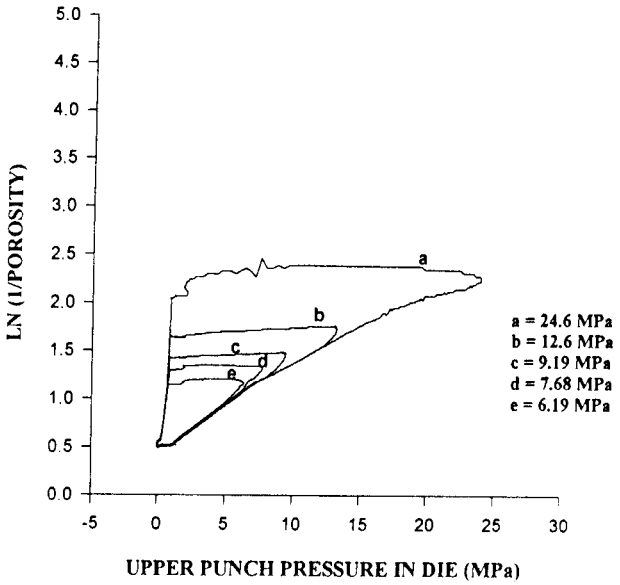

Figure 9. The densification vs. upper punch pressure in the die for 10% APAP, 70% Compritol, and Avicel PH-101 beads compressed to different punch penetrations.

Table 4

Comparison of ER (%) Values Obtained from Compaction to the Same Maximum Punch Penetration (4.23 cm)

Formulation	Elastic Recovery (%) Values	Tensile Strength (kg/cm^2)
100% Avicel PH-101 (F-I)	11.9	9.32
0% Wax (F-11)	9.54	1.57
10% Wax (F-III)	10.8	0
30% Wax (F-IV)	7.12	4.31
50% Wax (F-V)	4.06	7.34
70% Wax (F-VI)	4.00	4.91

steeper slopes during decompression and can be correlated to the larger values of the elastic recovery indices (Table 4). These high elastic recovery values may explain the weaker tablet strengths for bead formulations that have no wax. Without wax in the bead formulation, the beads do not have a large extent of deformation, thereby requiring higher pressures to yield. Plastic materials easily deform to readily increase bonding surface area, whereas the harder materials (control formulations) need greater pressures in order to fracture to increase surface area for bonding. The effect of elasticity depends on the original amount of deformation and bonding that occurred. Figures 4–6 show that the higher the compression pressure, the greater the elastic recovery in the die.

CONCLUSIONS

Consolidation is affected by the properties of the material being added or subtracted from the bead formulation. Bead formulations containing greater than 10% wax were more compressible than those made with less or without wax. As the level of wax increases in the bead formulation, plastic deformation becomes the more dominant deformation mechanism. Compacts made from beads without wax undergo higher elastic recovery, especially at greater compression pressures. The densification plot shows transition in the extent of plastic deformation, elastic mechanism, and fracture of the bead formulation at different maximum punch strokes.

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