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Calorimetric analysis of powder compression: II. The relationship between energy terms measured with a compression calorimeter and tableting behavior

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Abstract

A compression calorimeter was used to study the powder compression behavior of materials exhibiting a wide range of material properties and compactibilities. The calorimetric approach was based on the determination of the heat of compression, the work of compression and the calculation of the internal energy change for the compression phase of the tableting cycle (Lammens, Ph.D Thesis, University of Leiden, Leiden, 1980, pp. 158–259; Coffin-Beach and Hollenbeck, *Int. J. Pharm.*, 17 (1983) 313–324; Wurster et al., *Int. J. Pharm.*, 116 (1995) 179–189). The materials studied were Avicel PH-101, anhydrous lactose, Starch 1500, phenacetin, and polyethylene. Negative compression-induced internal energy changes were observed for all of the materials studied. These results indicated that the compression process lowered the energy states of the powders even though absorption of mechanical energy by the powders is thought to occur during the compression process. Negative ΔE values were also at odds with the measured surface area increases. For Avicel PH-101, anhydrous lactose and Starch 1500, these results did support the previous proposal that a negative internal energy change is indicative of extensive interparticulate bonding (Coffin-Beach and Hollenbeck, *Int. J. Pharm.*, 17 (1983) 313–324). However, in the case of polyethylene and phenacetin, where significant destruction of bonds formed during compression occurred during decompression, the compression energy terms did not reflect the consequences of the complete tableting cycle. For materials with poor compactibility, the compression energy terms were unrelated to the degree of permanent interparticulate bonding. Preliminary attempts were made to address the energetics of decompression so as to make the calculated internal energy change reflective of only the irreversible processes occurring during compression.

Keywords: Compression calorimetry; Heat of compression; Work of compression; Compression-induced internal energy change; Interparticulate bonding

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1. Introduction

A compression calorimeter is an instrument that allows the determination of the mechanical energy expended and the heat evolved during the compression of a powder sample (Lammens, 1980; Coffin-Beach and Hollenbeck, 1983). The First Law of Thermodynamics has been applied to the compression of powders to calculate the compression-induced internal energy change from the heat

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of compression and the work of compression (Coffin-Beach and Hollenbeck, 1983). A negative compression-induced internal energy change has been taken to be a verification of extensive particle-particle interaction (Coffin-Beach and Hollenbeck, 1983). In this work, it was found that the relationship is not so straight-forward and, indeed, no relationship between the internal energy change and the success of tableting can be drawn unless the energetics of the decompression process are also considered. The heat of compression and the work of compression were measured with a compression calorimeter of original design (Wurster et al., 1995). Independently determined material properties, such as the radial tensile strength, work of failure, and the surface area before and after compaction, were measured and relationships between the compression energy terms and the material properties were investigated.

2. Materials and methods

2.1. Materials studied

The compression behaviors of the following materials were studied: Avicel PH-101 (FMC Corp., Philadelphia, PA), anhydrous lactose (Sheffield Products, Norwich, NY), Starch 1500 (Colorcon, West Point, PA), phenacetin (J.T. Baker, Phillipsburg, NJ) and polyethylene (low density, Aldrich Chemical Co., Milwaukee, WI). Avicel PH-101, anhydrous lactose, and Starch 1500 formed intact tablets when compressed under the conditions employed in this study. Phenacetin and polyethylene were selected because they did not form intact tablets when compressed under the same conditions. Phenacetin tablets laminated and polyethylene exhibited virtually no permanent interparticulate bonding. Polyethylene could be poured out of the die as a free-flowing powder after being compressed.

2.2. Calorimetric studies

Single component compressions of the five materials were performed using the previously described compression calorimeter (Rowlings, 1989; Wurster et al., 1995). Compressions were performed with a hydraulic laboratory press (Carver, Model C press and Model 2735 pneumatic-hydraulic activation system, Wabash, IN) and a plexiglass punch and die assembly. A compression pressure of approx. 4000 $lb/inch^2$, a dwell time of 40 s, and a sample weight of 5.0 g were used in all of the compression studies. Upper and lower punch force (Piezotronics Model 200A05, Depew, NY) and upper punch displacement (Lucas Schaevitz Model GCA-121-1000, Pennsauken, NJ) transducers were used for the purpose of determining the mechanical energy expended during the one-sided compression process. The heats of compression were determined with two independent temperature sensors: a tungsten wire temperature sensor positioned within the powder sample and a two-thermistor (Yellow Springs Instrument, no. UUa35J3, 5000 Ω at 25°C) system positioned behind thin metal plates in the lower surface of the upper punch. Determination of the heat of compression involved the following steps for both the in-sample and in-punch temperature sensors: measurement of the compression-induced temperature rise, determination of the effective heat capacity of the material when contained in the punch and die assembly and correction for the background heat effects. Typically, 5-10 compressions were performed to determine the mean temperature rise. The two temperature sensors could be operated simultaneously. However, the two temperature sensors were not developed at the same time and the data in this paper were obtained using separate compressions for the in-sample and in-punch temperature sensors. Simultaneous heating and compression experiments were performed in order to determine the effective heat capacities of the materials in the system and thereby allow calculation of the heats of compression. A nichrome wire heater and a special upper punch were used to allow known amounts of heat to be released within the die cavity coincident with the compression of a powder sample. The temperature rises observed in the simultaneous heating and compression experiments were found to be a linear function of the heater energy over the range of inputs studied. Linear regression was performed on the data consisting of mean temperature rise vs heater energy input. The reciprocal of the slope of the regression line yielded the effective heat capacity. A correction for background heat effects was performed based on an energy correction method which has been described in detail in the accompanying paper (Wurster et al., 1995).

2.3. Recompression studies

Recompression studies were performed using the compression calorimeter for each of the materials studied. Three samples of each material were employed and the in-punch temperature, the upper and lower punch forces, and the upper punch displacement were measured during each recompression. The in-punch heat of compression and the upper punch work were calculated for the recompression data. The in-punch temperature sensor was used for these studies because it exhibited somewhat better reproducibility than the in-sample temperature sensor (Wurster et al., 1995).

2.4. Surface area studies

Gas adsorption surface area measurements (Quantasorb, Quantachrome Corp., Syosset, NY) were made on the materials before and after the compression experiments. The surface area measurements were performed at 77 K using nitrogen as the adsorbate. The powder samples were studied after pretreatment in a vacuum oven at 50°C for 12 h. The tablet samples were ejected, pretreated as above and then analyzed. A five-point BET analysis was performed within the relative pressure range of 0.10–0.30 (Brunauer et al., 1938). Duplicate samples were used for each determination. True density measurements (Micropycnometer, Quantachrome Corp., Syosset, NY) were also performed before and after compression and the true density was found to be unchanged by compression (Rowlings, 1989). This indicated that occluded pores were not formed during compression and that the nitrogen gas in the gas adsorption studies had access to the internal structure of the tablets.

2.5. Breaking strength and work of failure studies

A tablet hardness tester with pneumatic actuation (Vankel Industries, Model H-800-2, Edison, NJ) was instrumented with a force transducer (PCB Piezotronics, Model A00202, Depew, NY) and a displacement transducer (Schaevitz Engineering, Model GCA-121-250, Pennsauken, NJ) in order to determine the breaking strength and work of failure of tablet specimens (Rees and Rue, 1978). A solenoid valve and electric switch were installed to reproducibly open the air line and initiate the test. The loading rate was set via

Table 1
Results obtained from the single component compressions using the in-sample temperature sensor

Material	ΔT [a] (°C)	$C_{p,\text{effective}}$ (cal/°C per tablet)	Q_c (cal/g)	UPW (cal/g)	LPW (cal/g)	FW (cal/g)
Avicel PH-101	5.10 (0.18)	5.11	−4.66	2.52 (0.02)	2.25 (0.03)	0.27 (0.04)
Anhydrous lactose	3.04 (0.35)	4.50	−2.30	0.80 (0.04)	0.70 (0.04)	0.10 (0.02)
Starch 1500	2.13 (0.15)	5.28	−1.72	0.90 (0.03)	0.81 (0.02)	0.10 (0.01)
Phenacetin	3.48 (0.12)	5.14	−3.15	0.64 (0.02)	0.56 (0.02)	0.08 (0.01)
Polyethylene	3.80 (0.26)	5.76	−4.02	0.98 (0.03)	0.80 (0.04)	0.18 (0.01)

[a] Symbols are defined in the text.
Standard deviations are in parentheses.

a flow control valve to 25 lb/s. The tablets were evaluated 1 h after ejection and 10 measurements were made for each material.

3. Results and discussion

Tables 1 and 2 list the compression-induced temperature rise (ΔT), the effective heat capacity ($C_{\text{p,effective}}$), the heat of compression (Q_c), the upper punch work (UPW), the lower punch work (LPW), and the frictional work (FW) for each of the five materials studied. Tables 1 and 2 present data obtained using the in-sample and in-punch temperature sensors, respectively. Phenacetin was not studied with the in-punch temperature sensor. Fig. 1 and 2 show typical in-sample and in-punch temperature rise vs time profiles. Fig. 3 shows typical punch force vs displacement profiles in which the upper curve reflects the upper punch force and the lower curve represents the lower punch force. Fig. 4 and 5 show the temperature rise vs corrected heater energy input plots obtained from the determinations of effective heat capacity for the in-sample and in-punch temperature sensors, respectively. The correlation coefficients for the linear fits were greater than 0.99 in all cases. Table 3 lists the tablet breaking force (F) and the work of failure (W_f) obtained from radial tensile strength measurements for those materials where intact compacts were formed on compression. The gas adsorption surface area

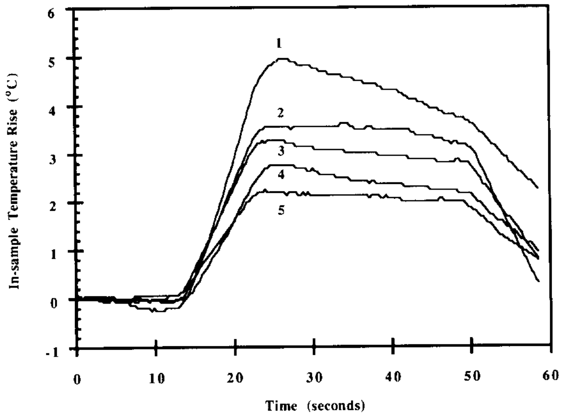

Fig. 1. Typical in-sample temperature rise vs time profiles for (1) Avicel PH-101, (2) polyethylene, (3) phenacetin, (4) anhydrous lactose, and (5) Starch 1500.

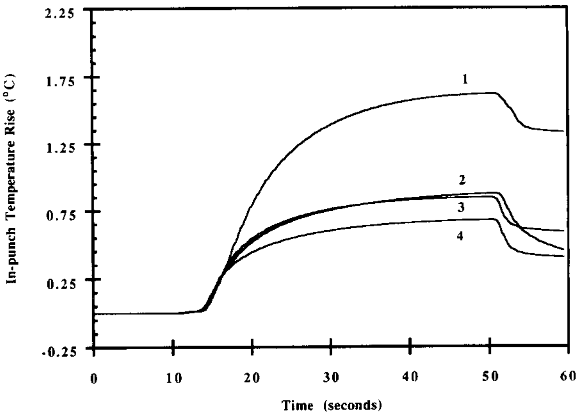

Fig. 2. Typical in-punch temperature rise vs time profiles for (1) Avicel PH-101, (2) polyethylene, (3) anhydrous lactose, and (4) Starch 1500.

Table 2

Results obtained from the single component compressions using the in-punch temperature sensor

Material	ΔT [a] (°C)	$C_{\text{p,effective}}$ (cal/°C per tablet)	Q_c (cal/g)	UPW (cal/g)	LPW (cal/g)	FW (cal/g)
Avicel PH-101	1.62 (0.06)	11.06	−2.87	2.51 (0.04)	2.26 (0.06)	0.25 (0.05)
Anhydrous lactose	0.86 (0.06)	9.30	−1.04	0.84 (0.02)	0.74 (0.02)	0.09 (0.01)
Starch 1500	0.68 (0.03)	13.26	−0.97	0.91 (0.03)	0.82 (0.03)	0.09 (0.01)
Polyethylene	0.88 (0.02)	18.75	−2.20	1.01 (0.03)	0.86 (0.03)	0.15 (0.01)

[a] Symbols are defined in the text.

Standard deviations are in parentheses.

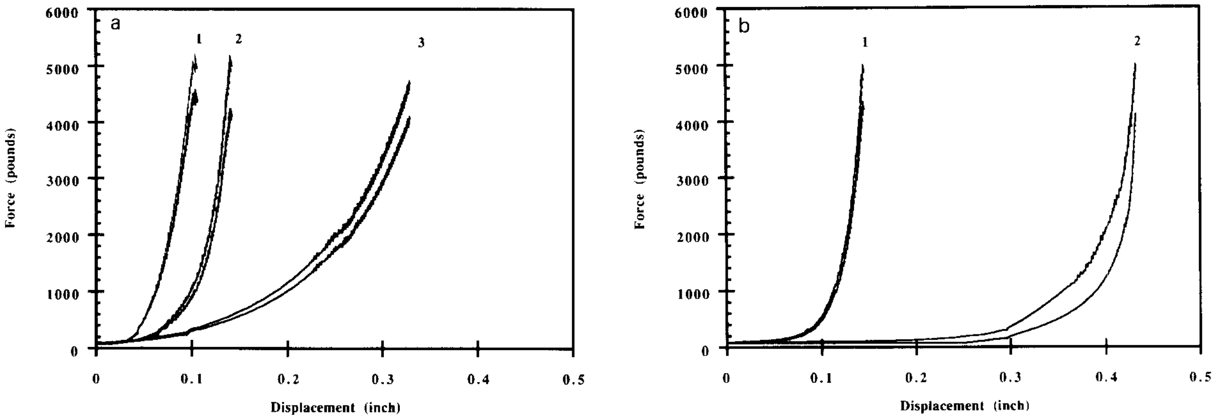

Fig. 3. (a) Typical punch force vs displacement profiles for (1) Starch 1500, (2) anhydrous lactose, and (3) Avicel PH-101. The upper curve is the upper punch force and the lower curve is the lower punch force. (b) Typical punch force vs displacement profiles for (1) phenacetin and (2) polyethylene. (Upper curve) Upper punch force; (lower curve) lower punch force.

(SA) of each material, both before and after compression, and the changes in surface area caused by compression are also presented in Table 3.

The internal energy change for the compression process was calculated from the heat of compression and the work of compression according to the first law of thermodynamics. The first law of thermodynamics may be written as follows:

$$\Delta E = \mathrm{UPW} + Q_c \qquad (1)$$

where ΔE is the internal energy change of the system, UPW denotes the upper punch work, and Q_c is the heat of compression. The sign convention that was adopted for heat and work was: heat flow out of the system was negative, and work done on the system was positive. Based on the in-sample temperature sensor data, the internal energy changes for Avicel PH-101, anhydrous lactose, Starch 1500, phenacetin and polyethylene, were −2.14, −1.50, −0.82, −2.51, and −3.04 cal/g, respectively. Based on the in-punch temperature sensor data, the internal energy changes for Avicel PH-101, anhydrous lactose, Starch 1500 and polyethylene, were −0.36, −0.20, −0.06, and −1.19 cal/g, respectively. The in-sample and in-punch sensors yielded different heats of compression and therefore differ-

Table 3
Tablet properties

Material	F[a] (lb)	W_f (mcal)	Initial SA (m^2/g)	Final SA (m^2/g)	ΔSA (m^2/g)
Avicel PH-101	> 57	> 9.5	1.06 (0.06)	1.99 (0.05)	0.93
Anhydrous lactose	18 (2)	2.3 (0.4)	0.42 (0.01)	1.04 (0.03)	0.62
Starch 1500	13 (1)	2.0 (0.3)	0.21 (σ)	0.75 (σ)	0.54
Phenacetin	[b]	[b]	0.31 (0.01)	0.59 (0.01)	0.28
Polyethylene	[b]	[b]	[c]	[c]	[c]

Standard deviations are in parentheses. (σ) Standard deviation was less than 0.005.

[a] Symbols are defined in the text.

[b] No intact tablet was formed.

[c] Surface area was too small to measure accurately.

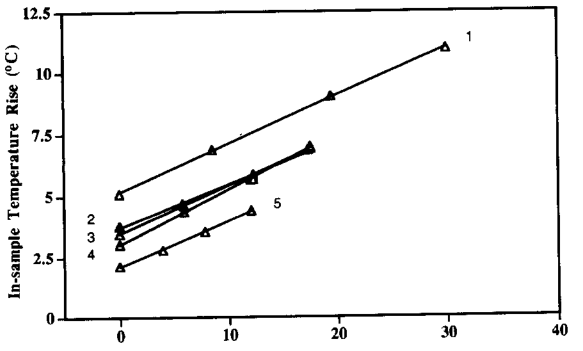

Fig. 4. In-sample temperature rise vs corrected heater energy input plots for (1) Avicel PH-101, (2) polyethylene, (3) phenacetin, (4) anhydrous lactose, and (5) Starch 1500.

ent internal energy changes. However, both methods yielded negative compression-induced internal energy changes and the rank orders were the same.

The negative internal energy change indicated that, in each case, the material was at a lower energy state in the compressed form than in the original powder. The magnitude and sign of the internal energy change is dependent on the interconversion of the mechanical energy into other forms of energy and the potential release of latent internal energy from the compressed material. Mechanical energy that is converted into heat will be lost from the tablet. In the absence of the release of latent internal energy, complete conversion of the mechanical energy into heat will not result in any net change in the internal energy. The mechanical energy may also be retained in the tablet in the form of residual stress energy and/or surface energy, if the surface area increased, and thereby contribute to an increase in the internal energy. Considering the conservation of energy principle, release of latent internal energy from the powder must occur in those cases where a negative internal energy change is observed. Solid state transitions involving the transition of a metastable or amorphous form to a more stable crystalline form and bonding phenomena between particles are exothermic processes that offer possible mechanisms by which latent internal energy may be evolved from a compressed material.

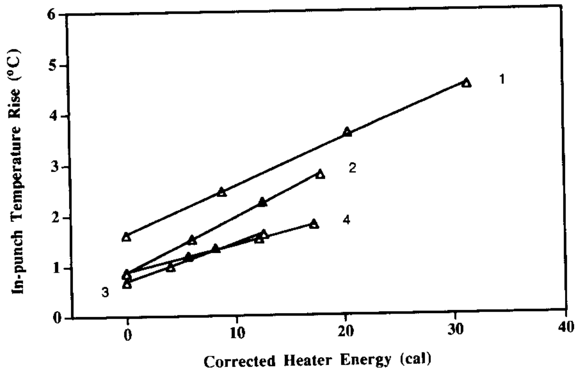

Fig. 5. In-punch temperature rise vs corrected heater energy input plots for (1) Avicel PH-101, (2) polyethylene, (3) anhydrous lactose, and (4) Starch 1500.

Negative internal energy changes have been reported for the compression of the following pharmaceutical excipients: Avicel, DiTab, Fast Flo Lactose and Starch 1500 (Coffin-Beach and Hollenbeck, 1983). It was noted that the negative internal energy change was positively correlated with tablet strength and it was proposed that interparticulate bonding was a major contributor to the heat of compression, thus explaining the negative internal energy change. The final state for the energy terms measured by Coffin-Beach and Hollenbeck (1983) is the compressed material still under loading and prior to decompression. This allows comparison with the data reported in this paper. Coffin-Beach (1982) reported data for the compression of Avicel PH-101 at a pressure of 3830 lb/inch^2. Terms analogous to the work of compression, heat of compression, and internal energy change were calculated to be 2.39, 2.48, and -0.09 cal/g, respectively. This compares with the value of -0.36 cal/g for the compression-induced internal energy change obtained in this work with the in-punch temperature sensor. Differences were evident in the die geometry (especially the means of insulation), the temperature sensor and the weight of the sample while the press system and the compression pressure were similar. Given the differences in the two compression calorimeters and the vagaries of applying the first law of thermodynamics to the powder compaction process, it is thought that these values represent reasonable agreement.

Positive internal energy changes have been reported for the compression of directly compressible forms of lactose, calcium phosphate and a calcium hydroxide powder (Lammens, 1980). It was found found that 85–92% of the mechanical energy was converted into heat, except for one series where 100% conversion was observed. The increase in internal energy was attributed to the development of residual stresses in the tablet. Alternative mechanisms such as entrapment of air, air and heat loss from the system, phase transitions including evaporation of moisture, and particle bonding were not considered to be significant with respect to their contribution to the internal energy change. The final state was the compressed material after decompression but prior to ejection from the die. Therefore, direct comparisons with the values of Coffin-Beach and Hollenbeck (1983) or those reported in this paper are not possible. Other investigators have generated data using operating tablet presses that allow the calculation of positive compression-induced internal energy changes (Fuhrer and Parmentier, 1977; Nurnberg and Hopp, 1981; Ketolainen et al., 1993). However, it is difficult to apply a rigorous calorimetric treatment to an operating tablet press since it is very difficult to resolve the measured heat into the heats of compression, decompression, ejection and the system or background heat.

The change in surface area caused by tableting has been shown to be dependent on the compression pressure (Higuchi et al., 1953, 1954; Elowe et al., 1954). A number of published articles have found that tableting causes an increase in the surface area of the tableted material (Higuchi et al., 1953, 1954; Elowe et al., 1954; Armstrong and Griffiths, 1970; Armstrong and Haines-Nutt, 1972; Hardman and Lilley, 1973; Stanley-Wood and Shubair, 1980; Alderborn and Nystrom, 1985; Alderborn et al., 1985; Nystrom and Glazer, 1985). Therefore, the increases in surface area noted in this study with the tableting of Avicel PH-101, anhydrous lactose, Starch 1500, and phenacetin are consistent with the literature. The magnitudes of the changes in area, when expressed as percentages of the original powder surface areas, are also consistent with the magnitudes that have been previously reported.

It can be seen that the current literature is divided with respect to the sign of the observed internal energy change. For the three materials that formed intact tablets (Avicel PH-101, anhydrous lactose, and Starch 1500), the rank orders of the heats of compression and the negative internal energy changes were the same as the rank orders of the tablet strengths and the work of failure values. These data supported the proposal that interparticulate bonding is a major contributor to the heat of compression since interparticulate bonding is an exothermic process and can result in the heat of compression being larger than the mechanical energy expended. However, for each of the three materials, tableting caused an increase in the surface area. Since a surface is at a higher energy state than the corresponding bulk material, work performed on the powder to increase its surface area remains associated with the powder. The internal energy change would, therefore, be expected to be positive. If bonding can be thought of as the elimination of powder surface, as it frequently is (Lammens, 1980; Coffin-Beach and Hollenbeck, 1983), then a negative ΔE should not be possible if there is a net increase in surface area. Net surface areas are discussed because, in the absence of interparticulate bonding, the surface area changes under the influence of compression would be even greater than the increases observed. A negative ΔE could only be observed simultaneously with a net surface area increase if the strength of the interparticulate bonds was greater than the strength of the intraparticulate bonds. This is not likely to be the case when a single material is compressed. This situation would presumably be clarified if both the internal energy change and the surface area measurements represented the same final state for the compressed material. However, the calculated ΔE represents the internal energy change for the compression process (pressure still applied) while the surface area increases were measured after tablet ejection and elastic recovery.

When considering all five materials, no general relationship was found between the heat of compression or the internal energy change and the compactibility of the material. The tablet strengths of phenacetin and polyethylene were less than predicted by either the heats of compression or the internal energy changes. The extreme case was that of polyethylene, which could be poured out of the die in what appeared to be its original form and yet yielded the largest change in the internal energy. One interpretation for the relatively large heats of compression is that significant interparticulate bonding occurred during compression but that the majority of the bonds formed during compression did not survive the elastic recovery process that occurred during decompression and ejection. This would explain the poor compactibility of these materials.

Tablet recompression prior to ejection has been proposed as a means to determine the elastic component of the work of compression (DeBlaey and Polderman, 1971). The recompression method assumes that no more fracture or plastic deformation occurs after the first compression and that the second compression involves only elastic deformation. This technique has been questioned based on stress relaxation data (Krycer et al., 1982), and has not gained general acceptance (Armstrong et al., 1982; Patel et al., 1985). However, recompression studies were performed in an attempt to partition the compression energy terms into the reversible (elastic deformation) and irreversible (brittle fracture, plastic deformation, interparticulate bonding) components. Table 4 lists the in-punch temperature rise (ΔT_{ext}) and the upper punch work (UPW) for the initial compression (subscript 0) and a recompression (subscript 1) for each of the materials studied. The elastic nature of polyethylene manifested itself by smaller relative decreases in the in-punch temperature rise and the upper punch work for the recompression runs. If the assumption that only reversible processes occurred on recompression was valid, calculation of the irreversible internal energy change could be accomplished. The irreversible work of compression can be obtained from the difference in the upper punch work between the initial compression and the recompression. The irreversible heat of compression can be calculated from the temperature data in a similar manner. The assumption was made that the effective heat capacity and the background heat correction both remained constant between the initial compression and the recompression. Based on the in-punch temperature sensor data, the irreversible internal energy changes for Avicel PH-101, anhydrous lactose, Starch 1500 and polyethylene, were −0.12, −0.10, +0.15, and +0.22 cal/g, respectively. It can be seen that the estimates of the irreversible internal energy changes obtained using the recompression data exhibit a proper rank order correlation with the material compactibilities and that for two of the materials a proper sign is obtained. The fact that two of the irreversible internal energy changes remained slightly negative is not surprising in light of the assumption that only reversible pro-

Table 4
Recompression data

Material	$\Delta T_{ext,0}$ [a] (°C)	$\Delta T_{ext,1}$ (°C)	UPW_0 (cal/g)	UPW_1 (cal/g)
Avicel PH-101	1.34 [b]	0.42	2.49	0.06
	(0.04)	(0.01)	(0.06)	(0.09)
Anhydrous lactose	0.74	0.37	0.86	0.03
	(σ)	(0.01)	(0.03)	(0.02)
Starch 1500	0.68	0.43	0.96	0.13
	(0.04)	(0.02)	(0.05)	(0.05)
Polyethylene	0.88	0.86	1.05	0.73
	(0.06)	(0.01)	(0.02)	(0.02)

Standard deviations are in parentheses. (σ) Standard deviation was less than 0.005.

[a] Symbols are defined in the text.

[b] Each entry represents the mean of triplicate determinations.

cesses occurred upon recompression. It should also be noted that if the aforementioned assumption was truly accurate, the internal energy changes and the surface area measurements would now represent the same final state. Based upon these preliminary attempts to subtract the thermal and mechanical consequences of the reversible, predominantly elastic, processes from those processes that are not reversed upon decompression, it is thought that this approach holds promise for the characterization of material compactibilities.

4. Conclusions

Negative compression-induced internal energy changes were observed for all of the materials studied. However, three materials (Avicel PH-101, anhydrous lactose and Starch 1500) formed intact tablets while two materials (phenacetin and polyethylene) did not. In the latter case, it was assumed that the elastic nature of these materials resulted in significant destruction of the bonds formed during compression when decompression occurred. An attempt was made to make the calculated internal energy change reflective of successful bonding by subtracting out the effects of the elastic deformation, thus making the irreversible internal energy change reflective of the compression-decompression cycle. While this approach is an improvement over the original internal energy change calculation and appears to be promising, two of the irreversible internal energy changes remain slightly negative. Thus, it is clear that additional work remains to be done to adequately characterize the energetics of the decompression process before this technique is completely acceptable.

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