ELSEVIER

International Journal of Pharmaceutics 116 (1995) 179–189

international journal of pharmaceutics

Calorimetric analysis of powder compression: I. Design and development of a compression calorimeter

Dale Eric Wurster [a,*], Colin E. Rowlings [a,b], J. Richard Creekmore [c]

[a] *College of Pharmacy, The University of Iowa, Iowa City, IA 52242, USA*
[b] *Rhone-Poulenc Rorer, Collegeville, PA 19426, USA*
[c] *Zeneca Pharmaceuticals, Wilmington, DE 19897, USA*

Received 28 February 1994; modified version received 6 September 1994; accepted 8 September 1994

Abstract

The heat of compression and work of compression of three common pharmaceutical excipients (Avicel PH-101, anhydrous lactose, and Starch 1500) were determined using experimental instrumentation of original design. The heat of compression was independently determined using two different temperature sensors: a tungsten wire temperature sensor positioned within the powder sample and a two-thermistor system positioned behind thin metal plates in the lower surface of the upper punch. The effective heat capacity of the sample when contained within the punch and die apparatus was determined by a simultaneous heating and compression method. An energy correction method was used to account for system heat effects. Upper and lower punch force transducers and a displacement transducer were used to determine the work of compression. In the materials studied, exothermic powder compression subprocesses outweighed the endothermic subprocesses and an overall net exotherm was observed. The rank orders of the heats of compression determined from the in-sample and in-punch temperature sensors were in agreement. This instrumentation and approach, while still being developed, is proposed as a discriminating method to characterize and quantitate fundamental powder compression behavior.

Keywords: Compression calorimeter; Heat of compression; Work of compression

1. Introduction

The term 'compression calorimeter' has been coined to refer to an instrument system 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 new design described in this paper was developed from a system designed to measure the heat evolved on compression of a powder sample (Wurster and Creekmore, 1986). Improvements were made to both the method and the apparatus used in the determination of the heat evolved. Independent temperature measurements were made using a tungsten wire temperature sensor positioned within the powder sample and a two-thermistor system positioned behind thin metal

* Corresponding author.

SSDI 0378-5173(94)00289-4

plates in the upper punch surface. Upper and lower punch force and upper punch displacement transducers were used for the purpose of determining the mechanical energy expended during the one-sided compression process. Three pharmaceutically relevant tableting excipients were studied in the preliminary experiments described in this paper.

2. Background

One of the important goals of powder compression research in the pharmaceutical industry is to predict the compression behavior of powder formulations on high speed rotary tablet presses from basic material properties. No theory of powder compression has gained universal acceptance and an array of data collection and analysis techniques have been promoted in this field; each with specific applications and limitations. Determination of all of the forms of energy associated with a powder compression event and resolution of the measured energies into the component parts or subprocesses has been pursued on the basis that it might yield a truly predictive understanding of powder compression. Ideally a compression calorimeter should be constructed based upon an operating tablet press. However, a tablet press is a difficult system to treat calorimetrically. Only a few studies have attempted to determine a term comparable to the heat of compression using an operating tablet press (Hanus and King, 1968; Juslin and Jarvinen 1971; Fuhrer and Parmentier, 1977; Nurnberg and Hopp, 1981). The temperature maximum is anticipated to occur rapidly after compression and, in a tablet press, the compressed material is inaccessible to temperature measurement until it is ejected, whereupon it cools rapidly. An operating tablet press is also a complicated and efficient heat transfer system and it is very difficult to resolve the heats of compression, decompression, and ejection from the background or system heat. Immediately after a cold tablet press is turned on, the metal press components, including the die and punches, act as a heat sink and heat transfer will occur from the tablets to the press parts. After time, heat will be transferred from the press to the uncompressed powder. In this fashion, the press will continue to warm until a thermal equilibrium is reached. When the machine has reached thermal equilibrium, the percentage of the heat evolved that is lost before measurement, and the percentage that is picked up from the background, will become constant with time. However, these actual proportions are still unknown and it is difficult to accurately correct for the heat lost to or gained from the environment of the operating tablet machine. Therefore, it is not possible to resolve the heat that is attributable to processes occurring within the tableted material from the measured heat content of the ejected tablets. Single compression studies using thermally insulated punch and die sets have been used to address the problems associated with operating tablet presses (Lammens, 1980; Coffin-Beach and Hollenbeck, 1983; Wurster and Creekmore, 1986). A single compression study allows the resolution of the heat of compression from the other thermal processes and presents a simpler system to account for the various heat loss pathways. This is made possible because tablet ejection does not occur and attempts are made to thermally insulate the compressed powder from its environment.

Lammens (1980) and Coffin-Beach and Hollenbeck (1983) both used temperature sensors external to the powder bed and a die-within-a-die design in their systems. The die-within-a-die design was based on the use of a thin inner metal die that separated and protected the temperature sensing system from the compressed powder. The inner metal die and temperature sensor(s) were contained within a large non-metal die that provided thermal insulation. The punches were also made out of a thermal insulator (fiberglass). Ideally, the inner metal die and temperature sensing device should have a small heat capacity and high thermal conductivity in order to maximize the sensitivity of the system.

Lammens (1980) measured the temperature by surrounding the compressed powder with 11 thermistors positioned in the inner metal die and in metal punch tips. Compressions were performed in a single punch press that was modified to

prevent tablet ejection after decompression. The measured temperature rise was thus influenced by both the compression and decompression phases of the tableting cycle. Determination of the effective system heat capacity was accomplished by dissipating energy in the punch and die assembly with a resistance heater contained in a tablet. The heater energy was controlled by manipulation of the voltage applied to the heater and the heating time. The areas beneath the temperature vs time profiles were linear functions of the energy evolved by the heater, thus allowing determination of the heat of compression from the temperature rise measured during compression.

Coffin-Beach and Hollenbeck (1983) used a quartz probe that was immersed in a mercury bath contained between the inner metal and outer plastic die. Compressions were performed in a motorized hydraulic press and long dwell times were used to allow thermal equilibration throughout the system. The temperature rise was measured prior to decompression. The temperature rise observed on compression of the empty punch and die set was subtracted from the temperature rise measured during powder compression to correct for the heat evolved due to the deformation of the punches. Determination of the effective system heat capacity was accomplished in a manner similar to the method used by Lammens (1980).

Wurster and Creekmore (1986) developed a tungsten wire resistance-type temperature sensor that was centrally located within the powder sample being compressed. A plexiglass punch and die assembly provided thermal insulation and the sample was compressed for a dwell time of 40 s. A hydraulic laboratory press with a hybrid pneumatic-hydraulic closure system was used for these compressions. The temperature rise was measured in the compressed state and it was corrected to account for background heat effects. A resistance heater was used in the determination of the effective heat capacity of the punch and die assembly, which had been sealed and filled with 5 ml of water. The effective heat capacity of a compacted sample contained within the punch and die assembly was determined by correcting for the presence of the water, sealant, and the material of interest. The heat capacities of the sealant and the compressed sample were determined by differential scanning calorimetry (DSC) and a literature value was used for the heat capacity of water.

3. Materials and methods

The compression behaviors of Avicel PH-101 (FMC Corp., Philadelphia, PA), anhydrous lactose (Sheffield Products, Norwich, NY) and Starch 1500 (Colorcon, West Point, PA) were studied in the experiments described in this paper. These materials were selected because they are commonly used tableting excipients that form intact tablets when compressed under typical tableting pressures. Compressions were performed with a hydraulic laboratory press (Carver Model C, Wabash, IN) fitted with a hybrid pneumatic-hydraulic closure system (Carver Model 2735, Wabash, IN). A plexiglass punch and die assembly was employed and a cross-sectional view of this apparatus is shown in Fig. 1 (Rowlings,

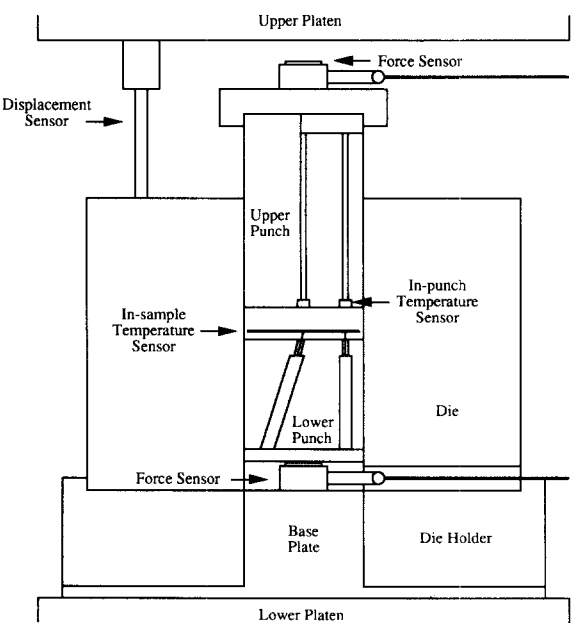

Fig. 1. Cross-sectional view of the plexiglass punch and die assembly.

1989). The punch diameter is 1.25 inch. This system is a modified form of the previously developed system (Creekmore, 1986; Wurster and Creekmore, 1986). The closure system provided a reproducible loading rate and also maintained the load constant at a preset maximum value. A compression pressure of approx. 4000 lb/inch^2, a 40 s dwell time, and a sample weight of 5.0 g were used for all compressions.

Two different temperature sensors were used to independently determine the heat of compression. A tungsten wire temperature sensor was used to measure the temperature within the powder sample during the compression event. This sensor was a planar coil of 0.25 mm diameter tungsten wire confined to the coil shape by a small cross-shaped plastic support. The resistance of the tungsten wire was temperature dependent and the temperature within the powder sample was determined via measurement of the resistance of the wire. Temperature measurements were also made using two thermistors (Yellow Springs Instrument, no. UUa35J3, 5000 Ω at 25°C) positioned behind thin metal plates that were recessed into the lower surface of the upper punch (Fig. 1). The thermistors were connected in a series circuit and the measurement of the total resistance across the two thermistors was used to determine the temperature in the punch surface. Since the temperature during the compression process is not likely to be the same at all points within the powder bed and since the concentric coils of the tungsten wire measure an average temperature across the diameter of the tablet, one of the thermistors was placed at the center of the punch while the other was placed at the edge of the punch. The series connection between the two thermistors resulted in an average temperature being obtained. Two digital multimeters, Keithley Models 195A and 196 (Keithley Instruments, Inc., Cleveland, OH), were used to measure the resistances of the tungsten wire and the two thermistors, respectively. The signals from the two temperature sensors were sampled at approx. 3 Hz.

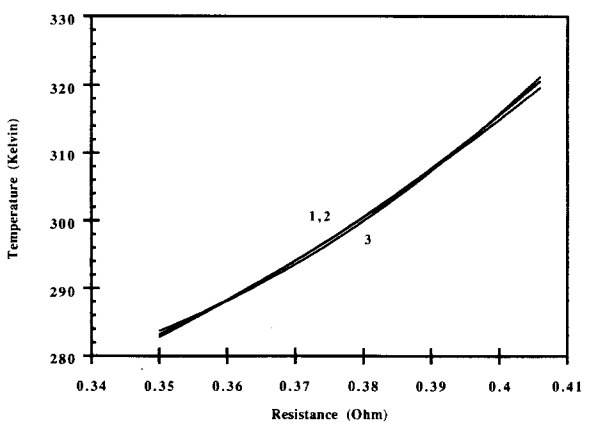

Fig. 2. Effect of compression pressure on the calibration curve obtained from the tungsten temperature sensor calibration. (1) Before compression, (2) during compression, and (3) after compression. (The data sets are indistinguishable.)

Two piezoelectric force transducers (Piezotronics Model 200A05, Depew, NY) and a displacement transducer (Lucas Schaevitz Model GCA-121-1000, Pennsauken, NJ) were used to determine the mechanical energy expended during the compression event. The signals from the force and displacement transducers were sampled at 100 Hz.

A data acquisition and control system was developed that allowed simultaneous measurement of the upper punch force, the lower punch force, the upper punch displacement, the in-sample temperature, and the in-punch temperature. The system was based on an IBM PC compatible computer (Leading Edge Model D, Canton, MA) and the ASYST software package (Asyst Software Technologies, Inc., Rochester, NY). An IEEE interface board (Metrabyte Model IE488, Taunton, MA) was used to connect the digital multimeters and plotter to the computer. Another interface board (Data Translation Model DT2801A, Marborough, MA) was used to receive signals from the force and displacement transducers and digitize them. This board was also capable of sending a control signal to a DC power supply (Hewlett Packard Model 6263B, Palo Alto, CA). The nichrome heater was made from a planar coil of 26-gauge nichrome wire (Fisher Scientific, Pittsburgh, PA) and was used in conjunction with the DC power supply.

3.1. Calibration of the tungsten temperature sensor

Calibration of the two-thermistor temperature sensor was not considered necessary because the thermistors employed had a well characterized change in resistance with temperature and all calculations involved changes in temperature, not absolute temperature. In the case of the tungsten temperature sensor, calibration of the sensor was required. The calibration procedure involved simultaneously subjecting the tungsten sensor and a calibration thermistor to varying temperatures using a water-jacketed plexiglass die. Heated water was continuously pumped from an external heated bath to the jacketed die. The calibration procedure covered a temperature range of approx. 15–35°C. A non-isothermal technique was used so that the temperature range could be covered in several hours. Because the system was not at thermal equilibrium when resistance measurements were made, the effect of the position of the thermistor relative to the tungsten coil was studied. This ensured that the small thermistor sensor was located such that it sensed the same average temperature as the larger coil-shaped tungsten sensor. The effect of pressure on the tungsten sensor was also studied. A tungsten sensor was calibrated before, during, and after compression. Identical calibration curves were obtained which showed that the tungsten sensor was not affected by the compression pressure employed (see Fig. 2). Initial calibrations were performed with a single thermistor. However, during the course of the study the two thermistor in-punch temperature sensor was developed and it was used in some of the later tungsten sensor calibrations.

3.2. Method used to determine the heat of compression

Determination of the heat of compression involved the following steps for both the in-sample and in-punch temperature sensors: (a) measurement of the compression-induced temperature rise; (b) determination of the effective heat capacity of the material when contained in the punch and die assembly; and (c) correction for the background heat effects.

Each compression experiment was 60 s long and the press closure system was manually activated and deactivated at the 10 and 50 s time points, respectively. The baseline temperature, obtained by averaging the temperature data from the first 10 s, was subtracted from the maximum temperature achieved, thereby yielding the compression-induced temperature rise. Typically, 5–10 compressions were performed to determine the mean temperature rise.

Simultaneous heating and compression experiments were used to determine the effective heat capacity of the material of interest when contained in the punch and die assembly. 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 heater was positioned within the powder sample prior to compression. A 4.9 s heating time was initiated at the same time as the start of the compression process and the amount of energy evolved by the heater was manipulated by varying the applied voltage. Three equally spaced heater power settings were used to cover a heater energy input range comparable to the anticipated heat of compression that was to be measured. The heater energy input was corrected to account for the presence of the nichrome heater. The energy required to elevate the temperature of the nichrome heater was calculated from the heat capacities and masses of the nichrome and plastic components of the heater and the in-sample temperature rise. This energy value was subtracted from the heater energy to yield the corrected heater energy. Identical compression conditions, numbers of compression repetitions, and analyses of the temperature data were used as for the compression only runs. The averaged data (temperature rise vs corrected heater energy) obtained from this procedure were combined with the mean temperature rise measured without heating. The temperature rise was found to be a linear function of the heater energy over the range of inputs studied. Importantly, the average temperature rise for the compression only runs lay on exactly the same line as the data from

the simultaneous heating and compression experiments. This indicated that the heat produced by the resistance wire was superimposable on the heat produced by the compression process. The data analysis, therefore, involved the linear regression of the mean temperature rise and the corrected heater energy data. The reciprocal of the slope of the regression line yielded the effective heat capacity.

A correction was applied to take into account the portion of the measured heat that was attributable to system effects such as deformation of the punches and frictional interactions between the punches and die. This was necessary in order to determine a heat value that was due solely to processes occurring within the compressed sample. This correction method involved the following four steps:

(a) Calculation of the uncorrected heat of compression using the following relationship:

$$Q_{\text{uncorr}} = -\Delta T \cdot C_{\text{p,effective}} \quad (1)$$

where Q_{uncorr} is the uncorrected heat of compression (cal/tablet), ΔT denotes the uncorrected temperature rise (°C), and $C_{\text{p,effective}}$ is the effective heat capacity (cal/°C per tablet) of the material when contained in the system. The sign convention that was adopted for the heat of compression was that heat flow out of the system was negative.

(b) Calculation of the heat capacity contribution of the empty punch and die using the following relationship:

$$C_{\text{p,system}} = C_{\text{p,effective}} - C_{\text{p,compound}} \quad (2)$$

where $C_{\text{p,system}}$ is the heat capacity (cal/°C per tablet) contribution of the punch and die assembly to the contents of the die cavity which, for a blank compression, is air, and $C_{\text{p,compound}}$ denotes the heat capacity of the compressed material as measured by DSC (cal/°C per tablet).

(c) Calculation of the background (empty die cavity) heat of compression using the following relationship:

$$Q_{\text{system}} = -\Delta T_{\text{blank}} \cdot C_{\text{p,system}} \quad (3)$$

where Q_{system} is the background heat of compression (cal/g) and ΔT_{blank} represents the blank temperature rise (°C).

(d) Calculation of the corrected heat of compression using the following relationship:

$$Q_{\text{c}} = (Q_{\text{uncorr}} - Q_{\text{system}})/m \quad (4)$$

where Q_{c} is the corrected heat of compression (cal/g) and m denotes the sample mass (g). This background heat correction method was used with both the in-sample and in-punch temperature sensor data.

3.3. Method used to determine the work of compression

The upper punch work and lower punch work for the one-sided compression process were determined by the well documented method of numerical integration of the upper and lower punch forces with respect to the upper punch displacement (Nelson et al., 1955; DeBlaey and Polderman, 1970). The punch displacement was corrected using the Maxwell model and the frictional work was obtained from the difference between the upper and the lower punch work (DeBlaey and Polderman, 1970; Krycer et al., 1982). Correction of the punch displacement data was necessary in order to account for the deformation of the plexiglass punches that occurred during compression. The Maxwell model, which was used to model punch deformation (Polakowski and Ripling, 1966), is given by the relationship:

$$\epsilon = (\sigma/E) + (\sigma t/B) \quad (5)$$

where ϵ is the strain, σ represents the applied stress, t is the time after loading and E and B are constants.

The Maxwell model has two terms that allow for both the time-dependent deformation ($\sigma t/B$) and the elastic deformation (σ/E). Nonlinear least-squares regression analysis (SAS NLIN procedure, SAS User's Guide, 1982) was used to estimate the two constants, B and E. The value of E obtained from the elastic model was used as an initial estimate in the curve fitting procedure. An initial estimate for the constant B was calculated from the observation that approx. 0.002

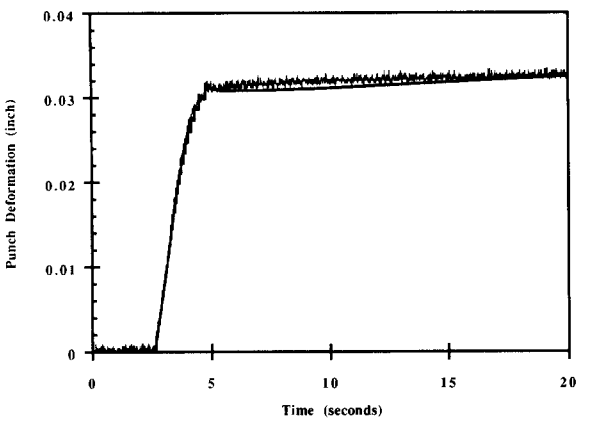

Fig. 3. Displacement vs time profile and the Maxwell model fit of the punch deformation data.

inch deformation occurred over approx. 15 s when the system was under load. Fig. 3 shows the displacement vs time profile and the fitted Maxwell model. The line representing the Maxwell model is partially hidden behind the data and this model obviously fits the data well.

4. Results and discussion

4.1. Work of compression

Several validation experiments were performed prior to the routine use of the system. The accuracy of the trapezoidal formula used in the numerical integration was checked by comparison of the computed area to the area determined by cutting and weighing the region under the plotted force vs displacement curve. The two methods of area determination agreed with an error of less than 0.5%. The effect of the data collection rate (force and displacement sensors) on the calculated work was also studied. The calculated punch work values were shown to be insensitive to increases in the data collection rate above 100 Hz. Fig. 4 shows typical upper and lower punch force vs punch displacement profiles for Starch 1500, anhydrous lactose and Avicel PH-101.

For a single-sided compression, the upper punch work represents the total mechanical energy expended during compression and it can be considered as being the sum of the net compression energy, the elastic energy, and the die wall frictional energy. The net compression energy is the non-recoverable mechanical energy imparted to the material being compressed and can also be considered as the sum of several components. The major constituents of the net compression energy are the energies expended in the fracture and/or plastic deformation of the particles and in interparticulate bonding. The elastic energy is the mechanical energy that is stored in the elastically deformed particle structure. This energy is subsequently recovered from the material on decompression and ejection. Accurate measurement of the elastic energy has not been accomplished and will require a three-dimensional force and displacement analysis of the tablet after ejection (Krycer et al., 1982). The lower punch work is the sum of the net compression energy and the elastic energy. The use of the term 'lower punch work' is considered to be inadequate on the basis that the lower punch is stationary and does not perform work (Ragnarsson and Sjogren, 1983). However, this term has gained common usage in the literature and will be used here to facilitate comparison with previous studies. The difference in the upper punch work and lower punch work is the die wall frictional energy (DeBlaey and Polderman, 1970; Krycer et al., 1982). In tableting,

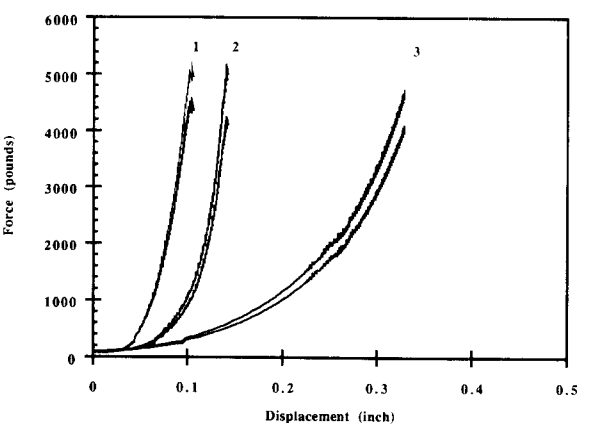

Fig. 4. Typical punch force vs punch displacement profiles for (1) Starch 1500, (2) anhydrous lactose, and (3) Avicel PH-101. (Upper curve) Upper punch force; (lower curve) lower punch force.

Table 1
Punch work results obtained from all compressions

Parameter	Avicel PH-101	Anhydrous lactose	Starch 1500
UPW (cal/g) [a]	2.52 (0.03)	0.81 (0.03)	0.91 (0.03)
LPW (cal/g)	2.25 (0.04)	0.71 (0.04)	0.81 (0.03)
FW (cal/g)	0.26 (0.04)	0.10 (0.02)	0.09 (0.01)

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

formulations are designed to minimize the frictional energy component. The values of the upper punch work, lower punch work, and die-wall frictional work obtained from the compression of Avicel PH-101, anhydrous lactose, and Starch 1500 are listed in Table 1. The die wall frictional work was approx. 10% of the upper punch work in these materials and based on this result lubrication of the die was not considered necessary.

4.2. Heat of compression

Fig. 5 and 6 show typical temperature vs time profiles obtained from the in-sample and in-punch temperature sensors, respectively. Fig. 7 and 8 show plots of the uncorrected temperature rise vs the corrected heater energy for the effective heat capacity determinations. The correlation coefficients of the linear fits were greater than 0.99 in all cases. The linearities of these plots demonstrate that the evolution of energy from the heater and the evolution of energy from the compression process occurred at comparable rates. This supports the use of the reciprocals of the slopes of the regression lines from the plots in Fig. 7 and 8 to obtain the effective heat capacities. Table 2 lists the temperature rise and heat capacity data and the results from the heat of compression calculations (Eq. 1–4) for Avicel PH-101. Similar measurements and calculations were performed for all three materials. Table 3 lists the results of the compression-induced temperature rise measurements and the heat of compression calculations for the in-sample and in-punch temperature sensors for the three materials studied. A larger temperature rise and a more rapid response were observed with the in-sample temperature sensor than with the in-punch temperature sensor. This is because the major portion of the heat of com-

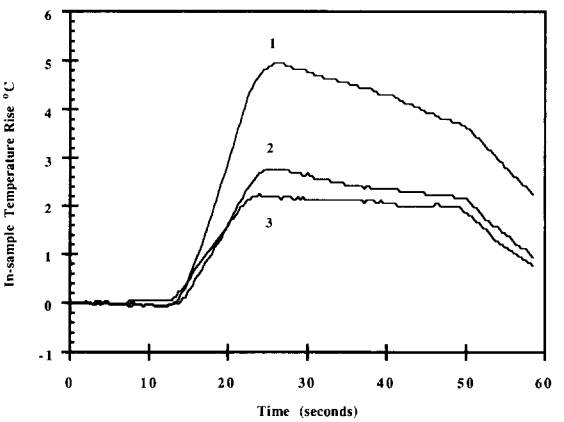

Fig. 5. Typical in-sample temperature vs time profiles for (1) Avicel PH-101, (2) anhydrous lactose, and (3) Starch 1500.

Table 2
Calculation of the heat of compression for Avicel PH-101

Parameter	In-sample data	In-punch data
ΔT (°C) [a]	5.10 (0.18)	1.62 (0.06)
ΔT_{blank} (°C)	0.75 (0.12)	0.37 (0.02)
$C_{p,effective}$ (cal/°C per tablet)	5.11	11.06
$C_{p,compound}$ [b] (cal/°C per tablet)	1.38	1.38
$C_{p,system}$ (cal/°C per tablet)	3.73	9.68
Q_{uncorr} (cal/tablet)	−26.09	−17.87
Q_{system} (cal/tablet)	−2.80	−3.54
Q_c (cal/g)	−4.66	−2.87

Standard deviations are in parentheses.
[a] Symbols are defined in the text.
[b] Heat capacity at 30°C.

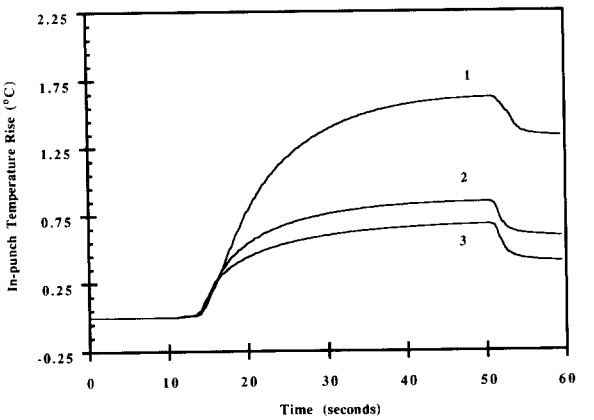

Fig. 6. Typical in-punch temperature vs time profiles for (1) Avicel PH-101, (2) anhydrous lactose, and (3) Starch 1500.

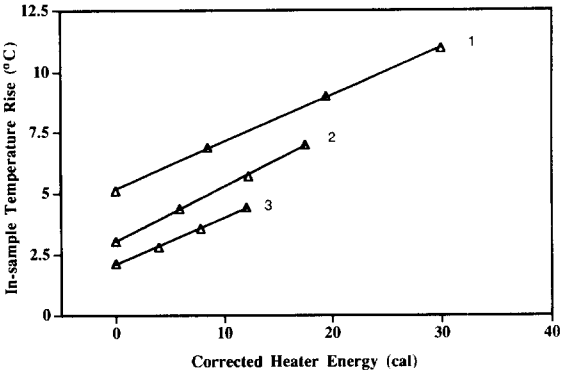

Fig. 7. In-sample temperature rise vs corrected heater energy input plots for (1) Avicel PH-101, (2) anhydrous lactose, and (3) Starch 1500.

pression is due to processes occurring in the bulk of the powder sample being compressed and the in-punch temperature sensor is removed from these processes.

The maximum in-sample temperature occurred 10–15 s after compression while the maximum in-punch temperature occurred close to the point of decompression. In the latter case, the heat had to be conducted across the thin aluminum plates before the thermistors could respond whereas the tungsten wire had no such barrier. This is a significant advantage in sensitivity and this was the rationale behind the development of the in-sample temperature sensor. The coefficients of variation for the in-sample and in-punch temperature rises were in the range of 4–12%. In general, lower variability was found with the in-punch temperature sensor. Presumably, this was a result of the damping effect of the larger effective heat capacity. The connections to the tungsten wire sensor were positioned within the lower punch and the leads to the sensor were of very low resistance copper wire. This arrangement resulted in excellent sensor accuracy and response for this type of sensor. Table 4 shows the results of a pairwise statistical analysis between materials (SAS PROC ANOVA, 95% confidence level, SAS User's Guide, 1982) of the in-sample temperature rise, the in-punch temperature rise, the upper punch work, and the lower punch work. All of the pairwise comparisons were significant at the 95% confidence level.

The tableting cycle is made up of the three stages of compression, decompression, and ejection. Therefore, the heat of compression is only one component of the net heat change associated with the complete tableting cycle. Compression of a powder is made up of the following subprocesses: particle rearrangement, interparticulate friction, particle-die wall friction, particle fracture, elastic and plastic particle deformation, and interparticulate bonding (Parrott, 1980). The

Table 3
Heat of compression results

Parameter	Avicel PH-101	Anhydrous lactose	Starch 1500
In-sample ΔT (°C) [a]	5.10 (0.18)	3.04 (0.35)	2.13 (0.15)
In-sample Q_c (cal/g)	−4.66	−2.30	−1.72
In-punch ΔT (°C)	1.62 (0.06)	0.86 (0.06)	0.68 (0.03)
In-punch Q_c (cal/g)	−2.87	−1.04	−0.97

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

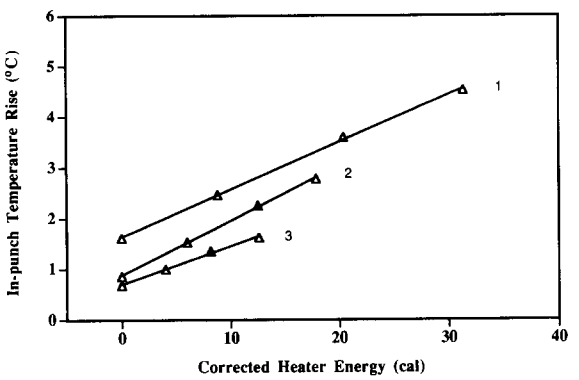

Fig. 8. In-punch temperature rise vs corrected heater energy input plots for (1) Avicel PH-101, (2) anhydrous lactose, and (3) Starch 1500.

thermal importance of particle rearrangement is considered to be negligible, but all of the remaining subprocesses may potentially make important contributions to the heat of compression. The heat of compression is the sum of the heats associated with the exothermic subprocesses less the heats of the endothermic subprocesses. The exothermic subprocesses outweighed the endothermic subprocesses and an overall net exotherm was observed with Avicel PH-101, anhydrous lactose, and Starch 1500. It is inevitable that heat evolution will occur due to the stressing of the punch and die system used to compress the powder and the background energy correction takes this into account. The heat of compression is therefore defined to be the net heat attributable to all subprocesses occurring in a given material under a given set of conditions and is specific to the material.

Table 4
Statistical comparisons of the compression results

Parameter	Avicel PH-101 and anhydrous lactose	Anhydrous lactose and Starch 1500	Starch 1500 and Avicel PH-101
In-sample ΔT (°C) [a]	+	+	+
In-punch ΔT (°C)	+	+	+
UPW (cal/g)	+	+	+
LPW (cal/g)	+	+	+

[a] Symbols are defined in the text.
(+) Significant difference at the 95% confidence level.

5. Conclusions

This report describes a powder compression instrumentation system designed to allow the determination of the mechanical energy input and two independent determinations of the heat of compression. Based on the results obtained with Avicel PH-101, anhydrous lactose, and Starch 1500, it can be seen that this system provides a useful means to characterize and quantify compression behavior. Although the two temperature sensors did not yield exactly equal heats of compression, the rank orders of the heats determined from the in-sample and in-punch temperature sensors were in agreement. A statistical analysis demonstrated that both of the heat of compression approaches were discriminating methods and could distinguish between the three materials studied.

Acknowledgements

The authors wish to thank Merck and Co., Inc., for the financial support of this research. The authors also wish to thank Mr Lou Zagst of PCB Piezotronics, Inc. for donation of two piezoelectric force sensor power units.

References

Coffin-Beach, D.P. and Hollenbeck, R.G., Determination of the energy of tablet formation during compression of selected pharmaceutical powders. *Int. J. Pharm.*, 17 (1983) 313–324.

Creekmore, J.R., Measurement of the thermal energy evolved upon tablet compression. Ph.D Thesis, The University of Iowa, Iowa City, IA (1986).

DeBlaey, C.J. and Polderman, J., Compression of pharmaceuticals: I. The quantitative interpretation of force-displacement curves. *Pharm. Weekbl.*, 105 (1970) 241–250.

Fuhrer, C. and Parmentier, W., Zur Thermodynamik der tablettierung. *Acta Pharm. Technol.*, 23 (1977) 205–214.

Hanus, E.J. and King, L.D., Thermodynamic effects in the compression of solids. *J. Pharm. Sci.*, 57 (1968) 677–684.

Juslin, M.J. and Jarvinen, M.J., Studies on energy expenditure by compressing tablets with an eccentric tablet machine: II. Relationship between mechanical and thermal energy. *Farm. Aikak.*, 80 (1971) 297–304.

Krycer, I., Pope, D.G. and Hersey, J.A., The interpretation of

powder compaction data – a critical review. *Drug Dev. Ind. Pharm.*, 8 (1982) 307–342.

Lammens, R.F., The evaluation of force-displacement measurements during one-sided powder compaction in a cylindrical die. Ph.D Thesis, University of Leiden, Leiden, pp. 158–259, 1980.

Nelson, E., Busse, L.W. and Higuchi, T., The physics of tablet compression VII. Determination of energy expenditure in the tablet compression process. *J. Am. Pharm. Assoc. Sci. Ed.*, 44 (1955) 223–225.

Nurnberg, E. and Hopp, A., Temperature measurement during tableting. *Pharm. Technol.*, 5 (1981) 81–101.

Parrott E.L., Compression. In Lieberman, H.A. and Lachman, L. (Eds), *Pharmaceutical Dosage Forms: Tablets*, Vol. 2, Dekker, New York, 1980, pp. 153–184.

Polakowski, N.H. and Ripling, E.J., *Strength and Structure of Engineering Materials*, Prentice-Hall, Englewood Cliffs, NJ, 1966, p. 209.

Ragnarsson, G. and Sjogren, J., Work of friction and net work during compaction. *J. Pharm. Pharmacol.*, 35 (1983) 201–204.

Rowlings, C.E., Compression calorimetry. Ph.D Thesis, The University of Iowa, Iowa City, IA, 1989.

SAS User's Guide 1982, Statistics, 1982 Edn, SAS Institute, Cary, NC.

Wurster, D.E. and Creekmore, J.R., Measurement of the thermal energy evolved upon tablet compression. *Drug Dev. Ind. Pharm.*, 12 (1986) 1511–1528.