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Mechanistic investigation on pressure dependency of Heckel parameter

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ABSTRACT

This work proposed to study the influence of varying compaction pressure on the plastic energy, elasticity (Young's modulus), particle yield strength, strain hardening, and applied pressures on derived Heckel parameter using material with different densification and deformation mechanisms: ibuprofen (IBN), paracetamol (PCM) (elastic behavior), methyl cellulose (Me-Cel), microcrystalline cellulose (MCC), sodium chloride (NaCl) (plastic behavior), and dicalcium phosphate (DCP) (brittle fracture). Force–displacement data were captured during in-die compaction for all materials having different deformation behavior. The apparent mean yield pressure (Py), plastic energy, Young's moduli, strain hardening parameter and rate of increase in Py were calculated from force–displacement compaction profiles obtained across a pressure range of 65–260 MPa. Materials under confined compression loading showed pressure dependent biphasic behavior in Py upon increasing pressure from 65 MPa to 260 MPa. IBN and PCM showed pressure dependency due to simultaneous elasticity and strain hardening upon increasing applied pressure. Me-Cel, MCC, and NaCl showed lower pressure dependency while DCP showed higher change in Py upon increasing pressure as a result of higher yield strength of DCP particles. Apparent mean yield pressure from Heckel analysis was significantly affected by the applied pressure, viscoelastic behavior, particle yield strength, and strain hardening. The simultaneously occurring events of elastic deformation and strain hardening give a false increase in Py at higher applied pressures.

1. Introduction

Mechanical properties of single particles or agglomerates influence a number of pharmaceutical unit operations like size reduction, handling, and compaction. It has been emphasized that resistance to deformation of bulk material is related to ultimate yield strength of particle undergoing compaction (Rumpf, 1962). Over the years, a number of mathematical models have been proposed to describe the compaction data and understand the inherent compaction behavior under pressure. The first accurate compaction data were probably obtained by Walker (1923). Shapiro (1944) proposed a model for the reduction of porosity of a bed during compaction in the form of a first-order rate process relating the pressure to the porosity. Later, Heckel (1961a,b) plotted the experimental data on the compaction of metal powders based on Shapiro's model, which describes the data of relative tablet density against compaction pressure, and assumes that the rate of change in density with respect to pressure is directly proportional to the remaining porosity.

Depending on the deformation behavior of the material, tablet densities of different powders approach their corresponding true density at rates, which can differ significantly from material to material. The apparent mean yield pressure (Py), derived from Heckel equation, has been used widely in recent years for the compaction characterization of pharmaceutical materials. The plastic deformation of the particles favors the densification process, while higher yielding materials resist densification. The derived yield pressure is affected by the series of factors like interparticulate rearrangement, friction between particles and die-wall, fracturing of the particles, elastic and plastic deformation, resistance against deformation, strain hardening and pressure course (Hassanpour and Ghadiri, 2004; Paronen, 1986; Patel et al., 2007; Sonnergaard, 1999, 2000; Sun and Grant, 2001b). Normally, it is assumed that there is limited interparticulate repositioning and particle fragmentation in the linear part of the Heckel analysis, and therefore the contribution of above factors on derived Py is neglected. But in confined compression loading on a rotary tablet press, all above factors play a significant role in Heckel analysis, thus making it necessary to understand dominant contribution of each factor.

The systematic study of Heckel parameter vis-a-vis powder densification process can help in predicting compaction behavior. The pressure dependency of Heckel parameter has been reported previously (Patel et al., 2007; Sonnergaard, 1999); use of the distinct element method was reported to simulate the bulk deformation

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based on single particle and results were applied to analyze Heckel parameter; however a systematic experimental investigation on the variability in value of Py at a range of pressures for differently deforming materials is lacking. The present work studies the influence of varying compaction pressures on the plastic energy, elasticity (Young's modulus), particle yield strength, strain hardening, and applied pressures on derived Heckel parameter using material with different densification and deformation mechanisms: ibuprofen, paracetamol (elastic behavior), methyl cellulose, microcrystalline cellulose, sodium chloride (plastic behavior), and dicalcium phosphate (brittle fracture). Compaction studies were carried on a fully instrumented rotary tableting machine that allows study of basic stress–strain relationship, with respect to actual tableting condition (Oates and Mitchell, 1989).

2. Materials and methods

2.1. Materials

Ibuprofen (IBN) (Arbro Pharmaceuticals Ltd., New Delhi, India), paracetamol (PCM) (Arbro Pharmaceuticals Ltd., New Delhi, India), methyl cellulose (Me-Cel) (The Dow Chemical Company, NY, USA), microcrystalline cellulose (MCC—low moisture grade) (Avicel®—PH-112, FMC BioPolymer, PA, USA), sodium chloride (NaCl) (S.D. Fine-Chem Ltd., Mumbai, India), and dicalcium phosphate dehydrate (DCP) (Emcompress®, JRS Pharma LP, NY, USA) were used as obtained.

2.2. Methods

2.2.1. Characterization of materials

Median particle size was determined by optical microscopy by measuring diameter along the longest axis for at least 300 particles (DMLP microscope, Leica Microsystems, Wetzlar, Germany). The moisture content of the excipients was determined by Karl Fisher (KF) titration (Metrohm 794 Basic Titrino, Herisau, Switzerland). The instrument was calibrated with disodium tartrate dihydrate for the accuracy of moisture determination. Sample size of 100–120 mg was utilized for the determination of moisture content.

Particle density was determined for powder samples in triplicate by helium pycnometry (Pycno 30, Smart Instruments, Mumbai, India) at 25 ± 2 °C temperature and 40 ± 5% relative humidity conditions.

2.2.2. Tableting and data acquisition

Rotary tablet press (Mini II, Rimek, Ahmedabad, India) was equipped at one of the 8 stations with 8 mm D-tooling with flat punch tip. Feed frame was used for uniform die filling and blind dies were used at all other positions. Precompression rollers were set out of function. Tablets of each material were compressed at constant volume and applied force was leveled by moving the pressure roller with a hand wheel. Temperature (25 ± 2 °C) and relative humidity (40 ± 5%) conditions were controlled throughout the study.

Data was acquired by Portable Press Analyzer™ (PPA) version 1.2, revision D (Data Acquisition and Analyzing System, PuuMan Oy, Kuopio, Finland), through an infrared (IR) telemetric device with 16-bit analog-to-digital converter (6 kHZ). Force was measured by strain gauges at upper and lower punches (350 Ω, full Wheatstone bridge; I. Holland Tableting Science, Nottingham, UK), which were coupled with displacement transducers (linear potentiometer, 1000 Ω). Upper and lower punch data were recorded and transmitted on separate channels by individual amplifiers ("Boomerangs"). The amplifiers truncated the raw data from 16 bit to 12 bit after measuring to check IR transmission (data transmission rate-50 kbaud; Internal data buffer—1024 measurement points). Analysis of compaction data was carried out by PPA software (version 1.2, revision D). Accuracy of force and displacement transducers was 1% and 0.02%, respectively. The suitability of the data acquisition system has previously been reported (Matz et al., 1999).

Each material was compacted at different compaction pressures on an instrumented rotary tablet press ranging from around 65 MPa to 260 MPa, with additional five measurements between minimum and the maximum compaction pressures. The tableting speed was kept constant at 14.1 rpm.

3. Results

3.1. Characterization of materials

Particle size, moisture content, and particle density determined for each material are given in Table 1. Moisture content of all the materials was below 2% (w/w) and shall not affect the compaction properties.

3.2. Heckel analysis

The Heckel model provides a method for transforming a parametric view of the force and displacement signals to a linear relationship for materials undergoing compaction. The equation is based on the assumption that the dependence of densification on pressure is of first-order (Heckel, 1961a,b):

$$\ln\left[\frac{1}{1-D}\right] = KP + A \qquad (1)$$

where D is the relative density of the tablet (the ratio of tablet density to particle density of powder) at applied pressure P, and K is the material-dependent constant i.e. the slope of the straight line portion of the Heckel plot and the reciprocal of K is the mean yield pressure (Py). In the present study, in-die measurements of the tablet thickness were obtained to derive Py.

Force–displacement compaction profile obtained from the instrumented tableting press was mathematically transformed to fit Heckel equation and values of Py at all pressures were calculated considering linear part ($R^2 > 0.99$) of Heckel plot with minimum 10–12 points (Fig. 1). Energy involved during the compaction process (plastic energy), Young's modulus, and strain hardening exponent were also calculated at each studied pressure.

Table 1
Particle size, moisture content and particle density for each material.

Material	Particle size (μm)	Moisture content (%, w/w) ($n = 3$)	Particle density (g/cm^3)
IBN	210–540; $d_{50} = 250$	0.11 ± 0.032	1.117
PCM	200–550; $d_{50} = 320$	0.20 ± 0.035	1.294
Me-Cel	180–560; $d_{50} = 380$	1.55 ± 0.049	1.341
MCC	160–380; $d_{50} = 210$	1.34 ± 0.198	1.570
NaCl	270–400; $d_{50} = 380$	0.09 ± 0.021	2.134
DCP	220–480; $d_{50} = 280$	0.26 ± 0.075	2.389

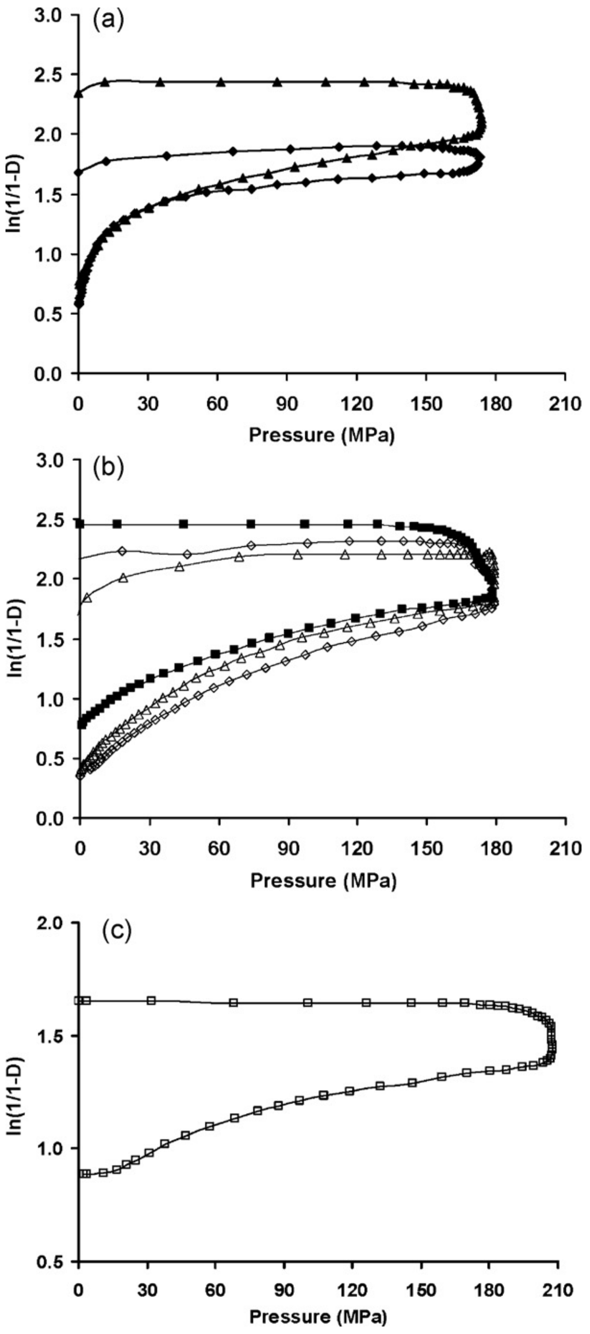

Fig. 1. In-die Heckel plots for (a) IBN (◆) and PCM (▲), (b) Me-Cel (△), MCC (◇), and NaCl (■), and (c) DCP (□) at given pressures.

3.3. *Effect of applied pressure on derived Heckel parameter, Py*

Table 2 shows the values of Py at different pressures calculated for various materials included in the study. All the samples showed increase in values of Py, however the degree of change between lower and higher pressure differed from material to material. The power law relation between applied pressure and the Py was applied and following equation was modeled:

$$\mathrm{Py} = kP^n \tag{2}$$

where k is the constant and n is the exponent describing rate of change in Py as the pressure is increased. The first derivative of Py (dPy/dP) with respect to applied pressure gives the rate of change in Py as a function of applied pressure. The biphasic rate of change

Table 2
Apparent mean yield pressure (Py), apparent Young's modulus (YM) at different pressures (P) for each of the materials. The values in parenthesis for Py value indicate the pressure range used for linear regression of Heckel analysis. The values of minimum correlation coefficient, R^2 for YM and Py are given in parenthesis.

IBN			PCM			Me-Cel			MCC			NaCl			DCP		
P (MPa)	YM (GPa) ($R^2>0.97$)	Py (MPa) ($R^2>0.98$)	P (MPa)	YM (GPa) ($R^2>0.97$)	Py (MPa) ($R^2>0.98$)	P (MPa)	YM (GPa) ($R^2>0.98$)	Py (MPa) ($R^2>0.99$)	P (MPa)	YM (GPa) ($R^2>0.99$)	Py (MPa) ($R^2>0.99$)	P (MPa)	YM (GPa) ($R^2>0.97$)	Py (MPa) ($R^2>0.99$)	P (MPa)	YM (GPa) ($R^2>0.98$)	Py (MPa) ($R^2>0.99$)
64.5	1.24	98.94 (16–56)	73.11	0.86	115.36 (18–69)	72.45	0.23	76.79 (13–65)	67.18	0.15	89.64 (16–62)	64.53	0.32	74.00 (12–62)	65.19	0.46	154.45 (26–63)
82.0	1.65	158.21 (22–75)	88.91	1.09	152.38 (25–84)	85.29	0.52	83.78 (24–84)	91.22	0.36	109.60 (27–90)	113.28	0.60	143.07 (31–108)	87.92	0.77	221.91 (38–84)
108.3	2.98	192.78 (25–95)	131.00	1.78	214.14 (40–127)	109.99	0.74	84.43 (37–108)	124.80	0.52	134.35 (42–123)	154.44	1.14	191.08 (46–151)	90.23	0.85	242.99 (42–86)
160.0	4.24	426.32 (50–155)	173.00	2.17	247.22 (30–168)	154.44	1.23	164.54 (53–132)	159.38	0.77	162.01 (54–157)	178.46	1.77	285.12 (74–175)	115.90	0.97	273.04 (41–110)
173.2	4.48	659.22 (55–167)	206.50	2.77	271.95 (39–185)	179.14	2.05	274.20 (85–175)	178.82	0.81	201.02 (80–165)	209.75	2.62	351.85 (92–207)	138.30	1.15	335.68 (48–136)
192.3	5.68	847.28 (67 –186)	240.40	4.07	438.21 (101–233)	226.55	5.34	459.8 (114–212)	202.19	1.22	249.24 (86–182)	250.26	4.54	539.35 (140–244)	210.09	2.36	621.46 (100–206)
259.8	7.37	1139.52 (76–224)	273.96	5.72	614.87 (124–260)	273.33	5.95	725.80 (130–257)	261.80	2.20	368.54 (104–252)	268.69	5.29	648.77 (147–264)	239.71	2.97	806.41 (109–237)

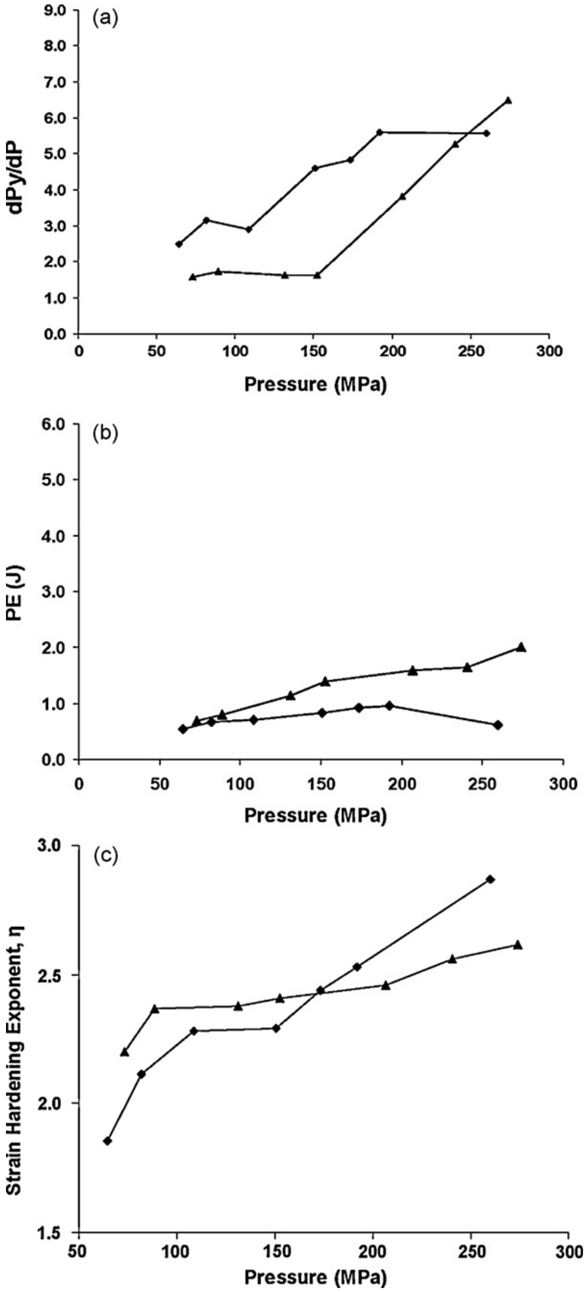

Fig. 2. Applied pressure vs. (a) rate of change in Py per applied pressure—dPy/dP, (b) plastic energy—PE, and (c) strain hardening exponent, η from compaction of IBN (♦) and PCM (▲) at various applied pressures.

in Py as a function of applied pressure for all materials is described in Figs. 2a, 3a and 4a.

The results of Py indicated that for IBN, the rate of increase in Py was higher throughout the whole pressure range, while for PCM, the rate of rise in Py was found to be lower up to ∼150 MPa, and sudden rise in rate was observed above ∼150 MPa, which was comparable to IBN above ∼150 MPa. Me-Cel, MCC and NaCl showed different values of Py as pressure was raised from ∼65 MPa to ∼150 MPa. Me-Cel and MCC showed slightly lower values of Py and rate of rise in Py as compared to NaCl in this pressure range. The results indicated that up to pressure range of ∼150 MPa, Me-Cel and MCC exhibited higher values of relative density as compared to NaCl. Above ∼150 MPa Me-Cel exhibited lower values of relative density as compared to MCC and NaCl. The rate of increase in Py was found to be in an order of Me-Cel > NaCl » MCC from ∼65 MPa to ∼270 MPa. DCP showed linear increase in Py as pressure was raised from ∼65 MPa to ∼240 MPa. The rate of rise in Py of DCP was similar to IBN.

3.4. Calculation of plastic energy and Young's modulus

It has been reported that Heckel parameter, Py relates the viscoelastic behavior of material (Denny, 2002; Ilkka and Paronen, 1993; Muller and Augsburger, 1994; Nokhodchi et al., 1996; Ramberger and Burger, 1985). The plastic energies of each material at different compaction force were therefore calculated from the force–displacement compaction profiles (Antikainen and Yliruusi, 2003; Hoblitzell and Rhodes, 1990; Ragnarsson and Sjogren, 1985) to validate the description obtained from Heckel parameter.

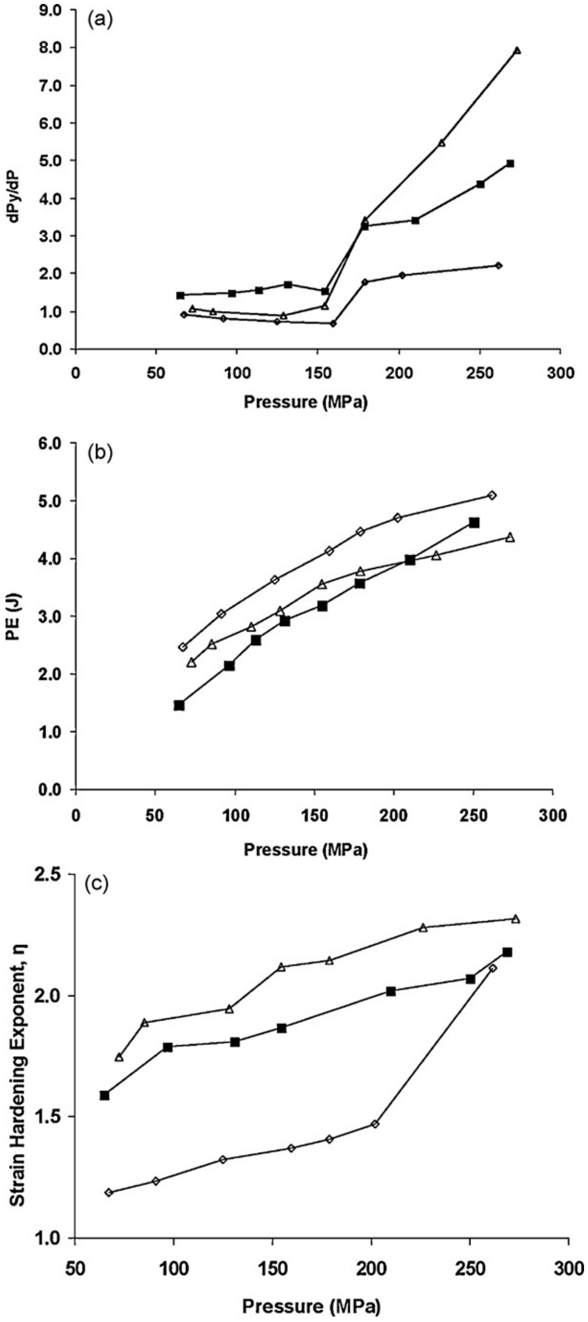

Fig. 3. Applied pressure vs. (a) rate of change in Py per applied pressure—dPy/dP, (b) plastic energy—PE, and (c) strain hardening exponent, η from compaction of Me-Cel (△), MCC (◊), and NaCl (■) at various applied pressures.

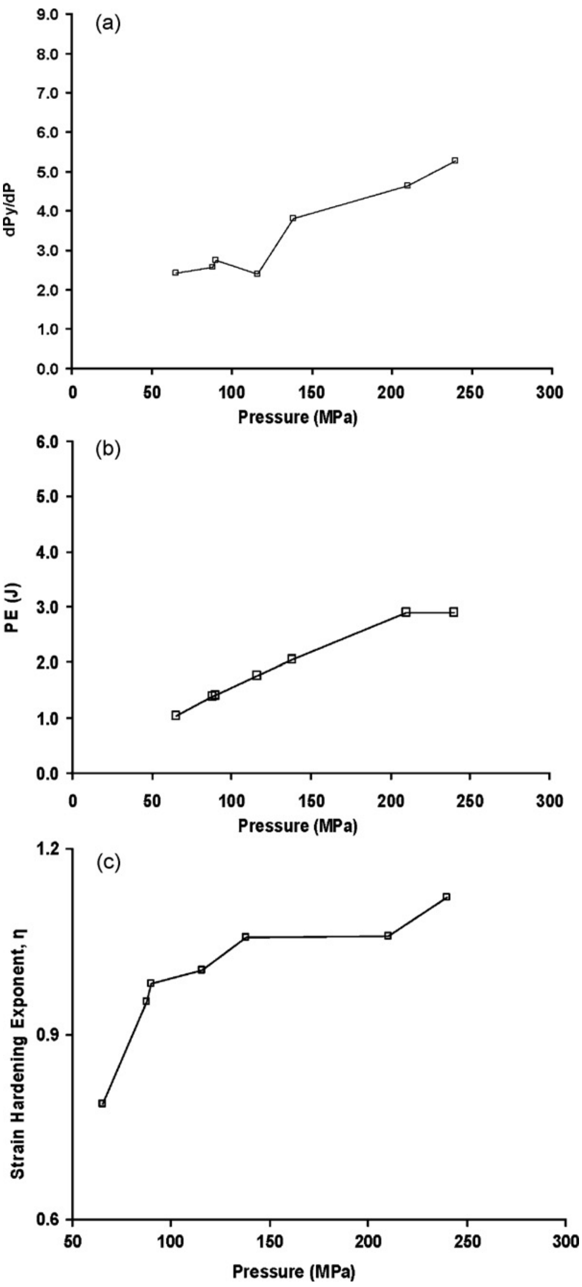

Fig. 4. Applied pressure vs. (a) rate of change in Py per applied pressure—dPy/d*P*, (b) plastic energy—PE, and (c) strain hardening exponent, η from compaction of DCP (□) at various applied pressures.

The "plastic energy" has also been termed as work of compaction as it reflects the contribution from viscoelastic deformation and interparticulate/particle–wall friction (David and Augsburger, 1977; Hiestand, 1985; Malamataris et al., 1984; Rees and Rue, 1978). The results showed (Figs. 2b, 3b and 4b) an increase in plastic energy for each material with increase in the applied pressure. However, there was a distinct difference in the extent of plasticity of the different materials based on their ductility. IBN and PCM showed lower values of plastic energy in the pressure range studied, whereas Me-Cel, MCC and NaCl showed higher values of plastic energy while DCP had an intermediate behavior.

Young's modulus (YM) which describes the elasticity of a material is one of the mechanical properties controlling powder processing and performance (Roberts and Rowe, 1987). Elasticity has been assessed either as fundamental material property (Young's modulus), referring to zero porosity or "apparent" Young's modulus, referring to a certain compaction state or porosity. Apparent Young's moduli were calculated from the gradient of stress–strain relationship at different compaction pressures for each material (Malamataris et al., 1996):

$$\mathrm{YM} = \frac{\mathrm{Stress}}{\mathrm{Strain}} = \frac{F/A}{\Delta H/H_0} = \frac{FH_0}{A\Delta H} \tag{3}$$

where F is the force applied during tableting, A is the cross-sectional area of punch tip, H_0 is the height of the compact at zero force, and ΔH is the change in height due to applied force.

The values of YM were observed to be higher for IBN (1.24–7.37 GPa) and PCM (0.86–5.72 GPa) for all applied pressures. MCC (0.15–2.20 GPa) and DCP (0.46–2.97 GPa) showed lower values of YM as the pressure was increased. The lower values of YM for NaCl (0.32–1.77 GPa) and Me-Cel (0.23–1.23 GPa) were observed up to ∼150 MPa applied pressure however, upon increasing the pressure above ∼150 MPa to ∼270 MPa, YM was found to increase considerably. Results of Young's moduli and Py at various applied pressures for different materials are summarized in Table 2. Both Py and YM values increased with the increasing compaction pressure.

3.5. *Strain hardening*

The increase in Py as pressure is raised has been attributed to strain hardening (Patel et al., 2007; Sonnergaard, 1999, 2000; Sun and Grant, 2001b). Strain hardening in materials requires additional pressure to deform the material. Strain hardening for the materials was calculated from the true stress–strain curves. It has been reported that the non-linear part of stress–strain curve follows the Zener–Hollomon relationship (Hirsch, 1975; Jain et al., 1996; Sing and Rao, 1997).

$$\sigma = \kappa\varepsilon^{\eta} \tag{4}$$

where σ is the true stress, ε is the true strain, η is the strain hardening exponent and κ is a constant. From the slope of the log(true stress) vs. log(true strain) plots, the strain hardening exponents were calculated. The values of η at different pressures were calculated from true stress–strain relationship.

The values of strain hardening exponent with increasing pressures, differ across materials. Materials like IBN and PCM showed greater strain hardening (Fig. 2c), while MCC and DCP showed lesser strain hardening (Figs. 3c and 4c). NaCl and Me-Cel had an intermediate behavior (Fig. 3c). From the plot of strain hardening exponent with increasing compaction pressure, it is apparent that DCP, MCC, and Me-Cel showed lower rate of strain hardening, while IBN and PCM showed higher rate of strain hardening.

4. Discussion

The proceeding section discusses the behavior of elastic (PCM and IBN), plastic (Me-Cel, MCC and NaCl), and brittle (DCP) materials under various applied pressure. The study of Py at various compaction pressures gives an idea about the pressure required for a given material to undergo viscoelastic deformation and densification.

4.1. *Py behavior in elastic materials (IBN and PCM)*

An analysis of results for Py indicated that IBN exhibited lower values of relative density (higher Py, Table 2) and higher rate of increase in Py as compared to PCM. However the plastic energy for both IBN and PCM did not increase significantly as the pressure was raised (Fig. 2b). IBN showed lowest value of plastic energy among all the materials, but it had the highest rate of increase in Py throughout entire pressure range (Fig. 2a). This indicated that the applied energy in form of pressure was not utilized for plastic deformation. The values and trend of change in Py does not always reflect the plasticity of the material due to contribution by simultaneously occurring other events like elastic deformation, plastic deformation, and strain hardening (Paronen, 1986; Patel et al., 2007; Sonnergaard, 1999, 2000; Sun and Grant, 2001b). The sudden rise in Py as the pressure is increased may be attributed to the elastic deformation and strain hardening. The resistance against deformation due to elastic deformation is reflected by the YM. IBN showed a higher YM value as compared to PCM at all the pressures. As the force is increased, the elastic resistance increases, which indicates reduced plasticity of the material.

Plastic deformation occurs as a consequence of work being done on a material. The applied energy should be significant enough to move existing dislocations and produce new dislocations. Accumulation of dislocations hinders the movement of a dislocation and plastic deformation cannot occur at normal stresses (Johnston and Gilman, 1959; Rice and Thomson, 1974; Taylor, 1934). Upon application of stress, the non-plastically deforming material will continue to deform by elastic deformation. At still higher stress (beyond the yield point), the applied energy overcomes the strain-field interactions and plastic deformation resumes, however, ductility which is the extent to which a material can undergo plastic deformation, decreases (Nadgornyi, 1988).

In a multi-particulate scenario, the strain hardening is closely related to the shear modulus (modulus of rigidity) of the material (Hirsch, 1975; Sing and Rao, 1997). Apparent particle size during compression and viscoelastic behavior influences the strain hardening of the material. Higher the values of strain hardening exponent, the more rigid is the material since for the same change in strain, a higher force (stress) is required. The lower plasticity of IBN as compared to PCM at the same pressure can also be attributed to the higher rate of rise in η as the pressure is increased (Fig. 2c). The resistance against dislocation motion in the crystallite (and hence to the plastic deformation) is slow at lower dislocation velocities (at lower applied pressure) but increases at higher velocities as the pressure is raised. In fact elastic deformation at higher force increases the strain hardening.

YM and strain hardening together contribute towards the values of Py. The yield pressure is an apparent value which has been reported to be affected by particle size and applied force (Patel et al., 2007), particle deformation (Armstrong and Palfrey, 1989; Eriksson and Alderborn, 1995; Gabaude et al., 1999; Garekani et al., 2001; Sun and Grant, 2001b), and polymorphism (Joiris et al., 1998; Suihno et al., 2001). However plastic deforming materials yield at lower pressure and hence give lower value of Py. Similar observations for plastic materials have been reported for MCC (Busignies et al., 2006), starch (Zhang et al., 2003), hydroxypropyl methylcellulose (Hardy et al., 2006), ethyl cellulose (Katikaneni et al., 1995), L-lysine monohydrate (Sun and Grant, 2001a), tolbutamide (Suihko et al., 2001), hydroxypropyl-β-cyclodextrin (Suihko et al., 2001), and theophylline monohydrate (Suihno et al., 2001).

4.2. Py behavior in plastic materials (Me-Cel, MCC and NaCl)

The plastic energy for Me-Cel, MCC and NaCl was found to be higher than IBN, PCM, and DCP at all the pressures (Fig. 3b). Amongst all the materials, MCC was found to be the highest plastic deforming material and the applied energy on the powder bed, is utilized for plastic deformation, which was reflected as lower pressure required for particle yielding and deformation (Fig. 3a). YM for Me-Cel, MCC and NaCl indicated that the applied energy in the form of compaction pressure is probably enough to move existing dislocations, and produce a large number of new dislocations which further assist the plastic deformation (Table 2) (Bandyopadhyay and Grant, 2002; Johnston and Gilman, 1959; Nadgornyi, 1988; Rice and Thomson, 1974; Taylor, 1934).

This sets up favorable condition for increased local particle deformation and interparticulate contact area. The latter helps in formation of more interparticulate bonds and hence a reduction in elastic deformation is seen. Greater dislocation of the molecules, as the pressure is raised, reduces the accumulation of dislocations and assists the plastic deformation. Me-Cel and NaCl showed higher values of η as compared to MCC, throughout the pressure range (Fig. 3c). Branching of the polymer has been reported to affect strain hardening and material stiffness (Arruda et al., 1995). The polymer's resistance to deformation may arise mainly due to intermolecular interactions and a network resistance due to stretching and orientation of the underlying molecular network (Boyce et al., 2000). Largely due to lack of molecular orientation, the additional branching in Me-Cel as compared to MCC may be responsible for its increased elasticity and strain hardening. This indicated that the increase in resistance to deformation (higher Py) can also be attributed to co-existence of strain hardening and elasticity in plastic deforming polymers. Slip planes are present in the NaCl which assist the plastic deformation and exhibit very fast deformation as the force is raised. However at higher compaction pressures, limited dislocation and resistance to slip deformation cause greater strain hardening.

4.3. Py behavior in brittle material (DCP)

The value of plastic energy for DCP was intermediate between plastic and elastic materials (Fig. 4b). The higher values of Py and relatively higher rate of increase in Py, along with low plastic deformation at higher pressure indicated that the applied energy is utilized for the fragmentation of the particles (Fig. 4a). The comparatively lower values of YM as the pressure was raised also indicated that DCP did not show resistance against deformation due to elastic deformation (Table 2). The pressure dependent rise in Py can also be explained on the basis of the fact that as the pressure is increased, more and more primary particle fragment to smaller particles, which have higher yield strength. Existence of shearing between the particles can also have influence on the outcome of Py.

The values of strain hardening exponent, η was also found to be lower (Fig. 4c). These results indicated a minimum rigidity in the DCP for the same change in strain as the pressure is increased, in contrast apparent reduction in particle size and simultaneous elastic recovery are mainly responsible for the rigidity during compaction for IBN and PCM. The fast moving cracks in DCP nucleate the dislocations which do not move fast enough to escape from the stress field of the moving crack, and this contributes to the major stress relaxation at fractured edge. Therefore, the absence of elastic deformation and internal stress relaxation by extensive fragmentation reduces the strain hardening. Extensive fragmenting materials are known to exhibit higher porosity as compared to plastic materials (Bolhuis et al., 2001; Wu and Sun, 2007; Zuurman et al., 1994). The available porosity upon further densification reduces the rigidity and is reflected as a lower value of strain hardening. Therefore the requirement of higher pressure for yielding of the material in case of DCP can only be attributed to the higher yield strength of DCP particle in confined compression loading.

5. Conclusion

The rise in Py at increased pressure in case of PCM and IBN can be attributed to the elastic deformation and strain hardening at all applied pressure. In case of plastic deforming materials, the additional branching in Me-Cel as compared to MCC, may be responsible for increased elasticity and strain hardening largely due to lack of molecular orientation at higher applied pressure. Slip planes present in NaCl assist the plastic deformation and allow a very fast deformation as the force is raised. However at higher compaction pressures, limited dislocation and slip resistance to further deformation cause strain hardening. The requirement of higher pressure for yielding of the material in case of DCP can only be attributed to the higher yield strength of DCP particle in confined compression loading.

The entire phenomenon collectively describes how materials achieve critical density during the course of densification as the pressure is increased. Therefore, the rate at which materials approach the critical density can be reflected as the outcome of Py from Heckel analysis. This rate of increase in critical density as the pressure is increased reflects as rate of rise in dPy/dP. Depending on the pressure range used, Py behavior changes across the materials, depending on their dominant deformation and densification behavior.

Py is used as a marker to quantify mechanical behavior of material, hence decision regarding compaction behavior, should carefully assesses as the same material, under different pressures, can give different values of Py. This could have ramifications on formulations and process optimization of solid dosage forms. A formulation development protocol, incorporating the above parameters can help in selection of excipients, optimization of manufacturing process, and identification of critical process parameters, thereby facilitating successful transfer of technology to the production stage. A due consideration to the variables of compaction process, can aid a pharmaceutical scientist to design optimum formulation devoid of problems like capping, lamination, picking, and sticking. The implications are going to be more serious while dealing with high dose poorly compressible drugs. More investigations in terms of molecular behavior under dynamic pressure need to be carried out.

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