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A comparison between two powder compaction parameters of plasticity;

The effective medium A parameter and The Heckel $1/K$ parameter

Foad Mahmoodi, Ingvild Klevan, Josefina Nordström, Göran Alderborn*

and Göran Frenning

Department of Pharmacy, Uppsala University, Uppsala Biomedical Center, P.O. Box
580, SE-751 23 Uppsala, Sweden

*Corresponding author (Goran.Alderborn@farmaci.uu.se)

KEYWORDS

Powder compression; Compression parameter; Yield stress; Effective medium equation;
Heckel equation

Abstract

The purpose of the research was to introduce a procedure to derive a powder compression parameter (EM A) representing particle yield stress using an effective medium equation and to compare the EM A parameter with the Heckel compression parameter ($1/K$).

16 pharmaceutical powders, including drugs and excipients, were compressed in a materials testing instrument and powder compression profiles were derived using the EM and Heckel equations. The compression profiles thus obtained could be sub-divided into regions among which one region was approximately linear and from this region, the compression parameters EM A and $1/K$ were calculated.

A linear relationship between the EM A parameter and the $1/K$ parameter was obtained with a strong correlation. The slope of the plot was close to 1 (0.84) and the intercept of the plot was small in comparison to the range of parameter values obtained. The relationship between the theoretical EM A parameter and the $1/K$ parameter supports the interpretation of the empirical Heckel parameter as being a measure of yield stress. It is concluded that the combination of Heckel and EM equations represents a suitable procedure to derive a value of particle plasticity from powder compression data.

1. Introduction

Mathematical equations can be used to describe the powder compression process and through their parameters allow the characterisation of the powder being compressed. To this end, many workers have taken the approach of developing compression equations, and/or attempting to isolate and shed further light on the physical significance of their parameters (Adams and McKeown, 1996; Adams et al., 1994; Denny, 2002; Hassanpour and Ghadiri, 2004; Heckel, 1961a, b; Kawakita and Lüdde, 1971; Klevan et al., 2009; Klevan et al., 2010; Nordstrom et al., 2009; Nordström et al., 2008; Samimi et al., 2005; Sonnergaard, 1999, 2001). The effective medium (EM) equation was derived in our group as an attempt to contribute to this effort (Frenning et al., 2009). The initial article (Frenning et al., 2009) focussed on the derivation of the equation and its application in the description of the compression behaviour of spherical granules. The main assumptions made in the derivation of the EM equation were that the powder only undergoes perfect plastic deformation and that the end point of compression is a solid specimen with zero porosity. The A parameter of the EM equation was rooted in single particle properties which could be experimentally determined, namely; yield stress. A second article was published (Mahmoodi et al., 2012) where the effective medium equation was transformed to be in terms of powder bed height with a variable end point of compression. In this second article we experimentally evaluated the EM equation with two materials of contrasting mechanical properties; plastically deforming sodium chloride (Hardman and Lilley, 1970; Hersey and Rees, 1971), and fragmenting lactose (Hersey and Rees, 1971). In the current article we present a new procedure for using the EM equation which is analogous to the way in which the Heckel equation is typically applied. Furthermore, the current article also compares the EM and Heckel equations when applied to a diverse set of materials previously used in our group (Klevan et al., 2010). In

this article we have returned to the approach used in the derivation of the EM equation (Frenning et al., 2009) where the end point of compression was assumed to be a compact of zero porosity. The aim was to compare the EM A parameter with the Heckel $1/K$ parameter to see if they correlate and if so how well. The Heckel equation was chosen since it is one of most widely used and accepted tools for the analysis of powder compression, and its $1/K$ parameter has been used to characterise powder plasticity and is thought to represent the yield stress of the powder system. The comparison of the Heckel $1/K$ with the EM A parameter is relevant since in its derivation the value of the A parameter is primarily dependent on the yield stress of a single particle, meaning that the A parameter has *a priori* been theoretically established as a measure of plastic deformation (Frenning et al., 2009).

2. Materials and methods

2.1 Materials

The analyses in this article are based on uniaxial compression data derived from work previous conducted by our group (Klevan et al., 2010), as such, for a full description of the experimental methods, the reader is directed to the work of (Klevan et al., 2010). For convenience the materials for which data are presented are listed in Table 1 and their respective bulk and apparent densities are presented in Table 2. Furthermore, the data for talc are not presented since it was not possible to obtain slopes for all runs during Heckel analysis; a problem experienced both by (Klevan et al., 2010) and in the current work.

2.2 Heckel analysis

The Heckel equation (Heckel, 1961b) is an empirical equation based on the relationship between the densification of a powder bed and applied pressure,

$$\ln\left(\frac{1}{1-D}\right) = KP + \text{Intercept}, \quad \text{Eq. (1)}$$

where D is the relative density of the powder, thus equating $1-D$ to porosity, P is pressure and K is a constant and slope of the linear region of the plot. The inverse of the slope ($1/K$) is known as the Heckel parameter and is thought to be related to the yield stress of the powder system and has the unit of pressure. When the Heckel equation is used, one often finds a curvature at low pressures before the linear region, which is generally attributed to rearrangement and/or fracture (Klevan et al., 2009).

The slopes of the Heckel plots were determined via linear regression using an excel (Microsoft corporation) macro developed in our group. The linear regression was conducted by locating the minimum value of the first derivative and extending the linear region until the derivative increased by 25%.

In the calculation of the powder bed height, the measurement point at which the signals from the external extensometer and the motor of the materials testing instrument were synchronized had to be determined manually. The same synchronization point was used for all runs for all powder materials. However, the synchronization point chosen in this study differed slightly from the point used in the earlier paper (Klevan et al., 2010). Thus, new Heckel profiles were derived in this paper, using the same synchronization points as in the derivation of the EM-profiles. The change in this synchronising point affected the Heckel slope and pressure ranges for the linear regressions, and although it was a systematic change, its effect was more pronounced in some runs than others and gave a new set of values of the Heckel parameters that deviated slightly from the earlier published values (Klevan et al., 2010). In addition, some changes were made to correct some experimental parameter values, which only affected a few of the materials in the derivation of the EM and Heckel profiles presented in this paper. Overall what is

apparent is that even in light of these changes the Heckel parameter values in this and the previous article (Klevan et al., 2010) are very similar.

2.3 EM analysis

The transformed EM equation (Eq. 2) describes the complex relationship between compression pressure as a function of yield stress and powder bed height. The EM equation establishes the relationship between compression pressure P and powder bed height H between a starting pressure P_1 , its corresponding height H_1 and a minimum height $H_{\min}$ corresponding to the endpoint of compression,

$$P - P_1 = A \left[\alpha \ln \left(\frac{H}{H_1} \right) - \ln \left(\frac{H - H_{\min}}{H_1 - H_{\min}} \right) \right] \quad \text{Eq. (2)}$$

and when linearised takes the form

$$\frac{-(P - P_1)}{\ln(H/H_1)} = A \frac{\ln[(H - H_{\min})/(H_1 - H_{\min})]}{\ln(H/H_1)} - B \quad \text{Eq. (3)}$$

The A parameter is the slope of the linear plot and is proportional to the yield stress of the particles. The B parameter is the intercept and is the product of A and α . The role of the α parameter remains less certain, however, based on the derivation of the EM equation we conjecture that it indicates some aspect of initial compressibility since it depends on the initial coordination number and initial relative density (relative to the maximum value obtained during compression) and the Watson integral (Frenning et al., 2009; Thorpe et al., 1989). For a derivation of the EM equation and an elaboration of the experimental application of it, the reader is directed to (Frenning et al., 2009; Mahmoodi et al., 2012) respectively.

For the purposes of this article H_1 was calculated based on unsettled bulk density determined using a glass cylinder with a diameter of 11.47 mm to closely mimic the punch/die environment (Klevan et al., 2010), P_1 was set at 0 MPa, and $H_{\min}$ was calculated based on a compact with a porosity of zero (see Table 2).

The slopes of the EM plots were also determined via linear regression using an excel (Microsoft corporation) macro. Contrary to the Heckel analysis, where the first derivative always exhibited a distinct minimum, the first derivative typically exhibited a maximum for the EM analysis. For this reason, the basic EM macro located the maximum value of the first derivative and extended the linear region until the derivative decreased by 25%. However, two maxima were obtained for two of the materials. Since the first maximum was within a very narrow range, the second maximum was used in these two cases. In all cases, the maximum value of the first derivative was determined from a manually selected subset of the data. Furthermore, the maximum corresponding to the smallest tablet height was used. The linear region was then extended until the magnitude of the derivative changed by 25%.

3. Results and Discussion

The EM and Heckel plots of all materials taken from run 3 are presented in Figure 1 (the presented curves do not contain the decompression section of the compression cycle), and are grouped according to the classification system used by (Klevan et al., 2010; Nordström et al., 2012). In this classification; class I corresponds to powders that undergo extensive rearrangement, IIA corresponds to ductile powders that undergo limited rearrangement, and IIB corresponds to brittle powders that undergo limited rearrangement (Nordström et al., 2012).

From looking at Figure 1 it is apparent that there are two general types of EM curves. The first has an initial curvature followed by a linear mid region preceding a plateau, as represented by the plots of the class I and IIB materials in Figures 1a and c. The second has a convex arching shape as represented by the plots of class IIA materials in Figure 1b. The slope of the linear region of the EM plots is a measure of the yield stress of the system. Although not perfect, the EM and Heckel curves shown in Figure 1 seem to be mirror images of one another. This is of interest as it suggests that they are essentially the same and as such their slopes should have similar values if the axes of either plot are swapped around. Table 3 lists the values of the EM A and α parameters as well as the Heckel $1/K$ parameter along with the R^2 values obtained for the linear regression lines for both EM and Heckel analyses. It can be observed that the α values range from 1.18 to 3.24.

A comparison of the average pressure ranges ($n=5$) within which the respective slopes of the EM and Heckel equations were determined are presented in Figure 2, on top of which the value for each run is overlayed to show the variation. It is apparent, that although not exactly matching, the average pressure ranges shown for the EM and Heckel analyses in Figure 2 do overlap to a great extent. The exceptions to this rule are maize starch and PVP, which are the only two materials that do not have overlapping pressure ranges between their respective EM and Heckel analyses. This is due to the fact that the EM plots of the maize starch and PVP possessed two maxima (see above and Figure 1b) and of these, the region corresponding to the smallest tablet height was manually chosen. It is possible that the Heckel plots for these two materials also possessed two linear regions, and of these, the region corresponding to the larger tablet height was selected by the Heckel macro, resulting in the observed differences in the pressure range values. It is also apparent from Figure 2 that there is generally little

variation within the lower and upper pressure limits of the EM A and Heckel $1/K$ slopes. The exception to this can be seen for the upper pressure limits of paracetamol and sodium chloride for both the EM A and Heckel $1/K$ slopes.

Figure 3 is a plot of the EM A parameter against the Heckel $1/K$ parameter. It is apparent that a correlation exists between the EM A parameter and the Heckel $1/K$ parameter with an R^2 of 0.992. The slope of the plot is close to 1 with a value of 0.84, and the intercept is relatively small in comparison to each single observation. The point with the largest standard deviation belongs to Avicel HFE-102. The mean R^2 values for the EM and Heckel slopes ($n=5$) are presented in Table 3 and range from 0.996 to 1.000.

The correlation observed in Figure 3 suggests that the Heckel $1/K$ parameter is a measure of yield stress, the same as the EM A parameter. We come to this conclusion based on the fact that the physical significance of the A parameter was established during its derivation. The role of the Heckel parameter has been open to conjecture (Sonnergaard, 1999). Since interpretation of the A parameter had been established, a strong correlation with the Heckel $1/K$ parameter would suggest that it too is a measure of yield stress, and our correlation seems to firmly support this idea. This is consistent with an earlier paper (Roberts and Rowe, 1987) where it was reported that the $1/K$ parameter was related to the particle hardness. Furthermore, as mentioned above the EM and Heckel curves shown in Figure 1 are near mirror images of one another, as such it may be that the EM equation is a theoretically derived version of the empirical Heckel equation. This is further bolstered by the overlapping pressure ranges of the linear regression for both analyses (see Figure 2) i.e. their linear regions generally coincided in the same vicinity of the compression cycle.

4. Conclusions

The strong correlation observed between the theoretical EM A parameter and the empirical Heckel $1/K$ parameter supports the interpretation of the Heckel $1/K$ parameter as being a measure of particle yield stress. The use of both the Heckel and the EM equations may provide a more reliable and theoretically underpinned value of the yield stress of particles derived from powder compression analysis.

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Figures and Tables

Fig.1. EM and Heckel plots of all materials taken from run 3. a) EM Group I materials, b) EM Group IIA materials, c) EM Group IIB materials, d) Heckel Group I materials, e) Heckel Group IIA materials, f) Heckel Group IIB materials.

Fig.2. Average pressure ranges corresponding to the EM A and Heckel 1/K determinations (n=5). The filled circles indicate individual runs.

Fig.3. EM A parameter Vs Heckel 1/K parameter (n=5). Error bars are standard deviations.

Table 1. Evaluated materials.

Material	Source
Aspirin	Sigma–Aldrich, Stockholm, Sweden
Dicalcium phosphate	Sigma–Aldrich, Stockholm, Sweden
Maize starch	Sigma–Aldrich, Stockholm, Sweden
Mannitol	Sigma–Aldrich, Stockholm, Sweden
Paracetamol	Sigma–Aldrich, Stockholm, Sweden
Sodium bicarbonate	Sigma–Aldrich, Stockholm, Sweden
Sodium chloride	Sigma–Aldrich, Stockholm, Sweden
Lactose (α -monohydrate)	Pharmatose 90 M, donated by DMV Fonterra Excipients, Goch, Germany
Polyethylene glycol 6000	PEG 6000, Sigma Aldrich, Steinheim, Germany
PVP 17PF	BASF, Limburgerhof, Germany
FlowLac 100	Spray-dried α -monohydrate lactose, donated by Meggle, Wasserburg, Germany
MicroceLac	Spray-dried mixture of 75% Lactose monohydrate and 25% MCC, donated by Meggle, Wasserburg, Germany
StarLac	Spray-dried mixture of 85% Lactose monohydrate and 15% Maize starch, donated by Meggle, Wasserburg, Germany
Avicel HFE-102	Microcrystalline cellulose and Mannitol, donated by FMC BioPolymer, Leeds, England
Avicel PH-102	Microcrystalline cellulose, MCC, donated by FMC BioPolymer, Leeds, England
Starch 1500	Partially pregelatinized Maize starch, Colorcon, Dartford, England

Table 2. Values of apparent and bulk densities adopted from Klevan et.al. (Klevan et al., 2010), as well as EM H_1 and H_{min} . Relative standard derivations given in parentheses.

Powder	ρ_{app}^a (g/cm ³)	ρ_{poured}^b (g/cm ³)	H_1 (mm)	H_{min} corresponding to zero porosity (mm)
Aspirin	1.398 (0.001)	0.78 (0.01)	6.408 (0.008)	3.572 (0.008)
Avicel HFE-102	1.647 (0.0002)	0.38 (0.02)	13.209 (0.009)	3.007 (0.009)
Dicalcium phosphate	2.358 (0.001)	0.50 (0.03)	10.061 (0.004)	2.112 (0.004)
FlowLac100	1.565 (0.001)	0.60 (0.03)	8.330 (0.000)	3.183 (0.000)
Lactose (α -monohydrate)	1.551 (0.001)	0.72 (0.01)	6.976 (0.003)	3.217 (0.003)
Maize starch	1.506 (0.001)	0.45 (0.04)	11.112 (0.005)	3.287 (0.005)
Mannitol	1.494 (0.0003)	0.50 (0.02)	9.986 (0.006)	3.314 (0.006)
Avicel PH-102	1.584 (0.001)	0.34 (0.03)	14.550 (0.006)	3.135 (0.006)
MicroceLac	1.572 (0.0002)	0.48 (0.02)	10.440 (0.001)	3.168 (0.001)
Paracetamol	1.293 (0.0004)	0.23 (0.08)	21.611 (0.012)	3.819 (0.012)
PEG 6000	1.245 (0.006)	0.47 (0.03)	10.724 (0.003)	4.019 (0.003)
PVP	1.195 (0.0003)	0.36 (0.01)	13.553 (0.011)	4.079 (0.011)
Sodium bicarbonate	2.227 (0.001)	0.81 (0.03)	5.986 (0.016)	2.184 (0.016)
Sodium chloride	2.146 (0.001)	1.16 (0.03)	4.297 (0.006)	2.323 (0.006)
Starch 1500	1.503 (0.0002)	0.58 (0.001)	8.546 (0.003)	3.311 (0.003)
StarLac	1.553 (0.0002)	0.57 (0.02)	8.783 (0.001)	3.202 (0.001)

^aApparent particles densities, n = 2.

^bPoured powder bulk densities (*in-die* start value), n = 3.

H_1 and H_{min} all values are the mean of 5 runs.

Table 3. Values of EM A parameter with its corresponding R^2 , the EM α parameter and the Heckel $1/K$ parameter with its corresponding R^2 . All values are the mean of 5 runs. Standard deviations given in parentheses.

Material	EM A Parameter (MPa)	R^2 from EM linear regression slope	EM α parameter (-)	Heckel $1/K$ parameter (MPa)	R^2 from Heckel linear regression slope
Aspirin	33.3 (0.3)	0.9993 (0.0001)	3.24 (0.01)	30.9 (0.3)	0.9995 (0.0000)
Avicel HFE-102	240.0 (46.4)	0.9985 (0.0001)	2.08 (0.04)	230.9 (40.1)	0.9991 (0.0001)
Dicalcium phosphate	513.3 (9.7)	0.9987 (0.0000)	1.72 (0.01)	438.5 (7.1)	0.9992 (0.0000)
FlowLac100	188.4 (1.4)	0.9997 (0.0000)	1.89 (0.02)	164.5 (1.0)	0.9995 (0.0000)
Lactose (α -monohydrate)	188.9 (11.6)	0.9996 (0.0000)	2.32 (0.01)	164.6 (9.9)	0.9996 (0.0001)
MaizeStarch	56.9 (0.5)	0.9978 (0.0001)	1.21 (0.01)	81.1 (1.1)	0.9996 (0.0001)
Mannitol	159.4 (12.9)	0.9994 (0.0001)	2.11 (0.02)	144.3 (11.5)	0.9997 (0.0001)
Avicel PH-102	93.2 (1.5)	0.9995 (0.0000)	1.44 (0.01)	90.0 (1.5)	0.9996 (0.0000)
MicroceLac	161.1 (0.6)	0.9996 (0.0001)	1.69 (0.01)	146.7 (0.8)	0.9994 (0.0000)
Paracetamol	123.8 (9.4)	0.9990 (0.0001)	1.82 (0.01)	116.2 (9.0)	0.9996 (0.0000)
PEG 6000	34.8 (0.5)	0.9991 (0.0002)	2.03 (0.03)	34.8 (0.8)	0.9993 (0.0001)
PVP	47.7 (1.7)	0.9983 (0.0001)	1.18 (0.02)	53.7 (0.7)	1.0000 (0.0000)
Sodium bicarbonate	296.0 (7.8)	0.9987 (0.0001)	2.15 (0.01)	264.0 (6.2)	0.9992 (0.0001)
Sodium chloride	95.6 (4.1)	0.9990 (0.0002)	1.77 (0.06)	78.6 (1.3)	0.9997 (0.0000)
Starch1500	88.3 (1.0)	0.9958 (0.0003)	1.63 (0.01)	74.5 (0.2)	0.9995 (0.0000)
StarLac	159.7 (1.7)	0.9997 (0.0000)	1.88 (0.00)	140.0 (0.9)	0.9997 (0.0000)