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International Journal of Pharmaceutics 140 (1996) 61–68

international journal of pharmaceutics

Compression behavior of spray dried rice starch

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Received 21 April 1995; revised 6 November 1995; accepted 26 April 1996

Abstract

Compression behaviors of spray dried rice starch (SDRS), as well as pregelatinized starch (PS), and microcrystalline cellulose (MCC) were characterized using Heckel analysis. SDRS was found to undergo plastic deformation with lower elasticity compared with PS. SDRS showed very low fragmentation tendency due to the fact that the difference between extrapolated and actual densification of its Heckel plot was low. Having aggregate sphere in shape, its densification could be initiated by deaggregation and tight packing without requiring high pressure. The above evidence explains why the compactibility of SDRS is excellent. MCC on the other hand, showed some fragmentation before undergoing plastic deformation. The fragmentation might have increased the contacts among particles which resulted in higher crushing strength of the tablets compared with that of SDRS. The slope of the Heckel plot of a mixture of each excipient and hydrochlorothiazide fairly agreed with the summation of the weight fraction of each component. The deformation of the mixture tested could be easily predicted. Since SDRS possesses both good compactibility and flowability, this new direct compression excipient has a high potential for successful tablet formulation.

Keywords: Direct compression fillers; Spray dried rice starch; Compaction; Compression; Heckel analysis; Densification; Pseudo-yield pressure; Deformation

1. Introduction

Spray dried rice starch (SDRS) is produced in Thailand and marketed under the trade name Era-Tab®. SDRS is an agglomerated rice starch which is used as a directly compressible tablet excipient. Scanning electron photomicrograph of SDRS is shown in Fig. 1. It has been shown that SDRS exhibited excellent flowability and binding properties, and can be combined with the other fillers such as α-lactose monohydrate or β-lactose anhydrous for good tablet properties (Mitrevej and Varavinit, 1988; Bos et al., 1992). The physi-

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PII S0378-5173(96)04576-0

cal properties of the tablets made from SDRS and its combination with other fillers such as weight variation, crushing strength, friability, and disintegration time, have been extensively evaluated. The compression characteristics of this excipient, however, are unclear. Although, tablet crushing strength has been employed as an indicator to evaluate the compactibility, Jones (1981) objected that the tablet crushing strength was only a limited index. Measuring only the final force required to produce tablet failure does not truly reflect the conditions occurring during compression. The study of densification with increase in applied pressure is believed to be more meaningful.

Powder packing with increasing compression load is normally attributed to particle rearrangement, elastic and plastic deformation, and particle fragmentation (Duberg and Nyström, 1986). Heckel analysis is a popular method to determine the volume reduction mechanism under the compression force (Heckel, 1961a,b). According to the analysis, the degree of a compact densification, with increasing compression pressure, is directly proportional to its porosity as follows:

$$\frac{dD}{dP} = k\epsilon \tag{1}$$

where D is the relative density at pressure P and ϵ is the porosity. The relative density is defined as the ratio of the density of the compact at pressure P to the density of the compact at zero void or to the true density of the material. The porosity can be defined as

$$\epsilon = \frac{V - V_\alpha}{V} = 1 - D \tag{2}$$

where V and V_α are the volume at any applied load and the volume at the theoretical zero porosity, respectively.

Thus, Eq. (1) can be expressed as

$$\frac{dD}{dP} = k(1 - D) \tag{3}$$

and then transformed to

$$\ln \frac{1}{(1 - D)} = kP + A \tag{4}$$

Plotting between natural logarithm of the reciprocal of the porosity, which may be referred to as tablet densification, and applied load should yield a linear line having slope k and intercept A. This analysis has been extensively applied to pharmaceutical powders for both single (Duberg and Nyström, 1986) and multiple components (Kurup and Pilpel, 1978; Garr and Rubinstein, 1992).

The densification is described as a three-stage process (York, 1978; Chowhan and Chow, 1980), i.e.(i) densification by filling the die (denoted the corresponding relative density as D_0)(ii) densification by particle movement and re-arrangement (D_B), and(iii) densification by particle deformation after inter-particulate bonding has become appreciable (D_A).

These relative density values reflect some powder behaviors. D_A represents the total compact density.

$$D_A = D_0 + D_B \tag{5}$$

D_A is obtained from the extrapolated intercept of Heckel plot (Chowhan and Chow, 1981; Humbert-Droz et al., 1983; Duberg and Nyström, 1986),

$$A = \ln \frac{1}{(1 - D_A)} \tag{6}$$

Thus,

$$D_A = 1 - e^{-A} \tag{7}$$

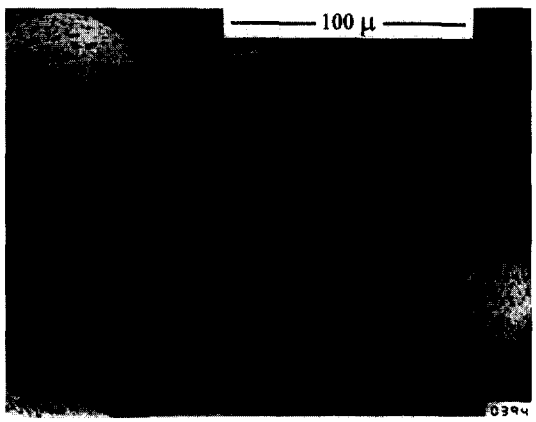


Fig. 1. Photomicrograph of spray dried rice starch.

D_0 is experimentally determined, it is equal to the ratio of the bulk density to the true density of powder before compression (Chowhan and Chow, 1980). It can also be obtained from the Heckel plot,

$$A_0 = \ln \frac{1}{(1 - D_0)} \quad (8)$$

Thus

$$D_0 = 1 - e^{-A_0} \quad (9)$$

where A_0 is actual intercept. D_0 which represents relative bulk density is dependent on size and surface irregularities (Humbert-Droz et al., 1983). Importantly, D_B exhibits further arrangement which implies particle fragmentation (Chowhan and Chow, 1980; Humbert-Droz et al., 1983).

The purpose of this study was to investigate the compression behavior of SDRS and compare to other direct compression fillers. Deformation of SDRS under compaction would be characterized. This study also tried to predict the total deformation of the binary mixture from the knowledge of individual components.

2. Materials and methods

2.1. Materials

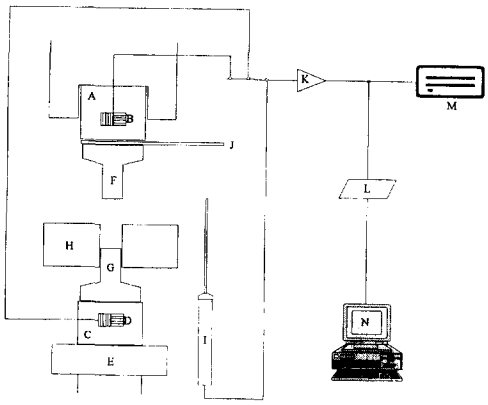
Three directly compressible fillers were employed throughout the study. These fillers were spray dried rice starch, SDRS (Era-Tab®, Erawan Pharmaceutical Research and Laboratory, Thailand), microcrystalline cellulose, MCC (Avicel® PH102, Asahi Chemical industrial, Japan) and pregelatinized starch, PS (Starch® 1500, Colorcon, UK). Hydrochlorothiazide (HCTZ) B.P. 1980 (Pharmaceutical Science, Thailand) and magnesium stearate (Volvskoya, Yugoslavia) were used as active drug, and lubricant, respectively. True densities of SDRS, MCC, PS and HCTZ determined by pycnometer method were 1.399, 1.411, 1.423 and 1.594 g cm^{-3}, respectively

2.2. Tablet machine instrumentation and force-displacement measurement

A single punch tablet machine (Fette type E1, Germany) was instrumented to detect upper and lower punch forces as well as upper punch displacement. A pair of metal foil resistance 'self-temperature compensated' strain gauges (Micro Measurements, USA) were bonded to either side of the upper punch holder. The strain gauge configuration chosen consisted of two grid elements, perpendicular to each other, mounted along the length of the gauge backing. The gauges were oriented so that one of each pair was parallel to the major strain. Another pair of strain gauges were bonded to the lower punch holder in the same manner. The bonding and wiring procedures were similar to that described by Salpekar and Ausburger (1974). A displacement transducer (Model DT-100E, Kyowa Electronic instruments Co. Ltd., Japan) was installed on the lower part of the tablet machine body. A specially designed beam which was attached to the upper punch holder moved along with the upper punch, during compression, thereby contacting the displacement transducer core to track the displacement. The mechanical events were then transformed to electrical signals ready for data processing by a dynamic strain amplifier (Model DMP-621A, Kyowa Electronic instruments Co. Ltd., Japan) and an analog to digital converter (A/D converter) using an IBM compatible personal computer (PC) (Sherry Computer Technology, USA). A complete set up of the system is diagrammatically shown in Fig. 2.

2.3. Compression behavior of single material-Heckel analysis

Using a 10-mm flat faced tooling, a single material was compressed on the instrumented tablet machine. With a speed of 50 tablets/min, and at approximately 150 MPa maximum load, the single material compacts were produced. For a compression cycle, the A/D converter sampled the electrical signals from the strain gauges and displacement transducer at 0.5 ms interval. The signals were then stored in the memory of the PC.



Configuration:

A	Upper punch holder	H	Die
B	Upper punch strain gauges	I	Displacement transducer
C	Lower punch holder	J	Beam
D	Lower punch strain gauges	K	Dynamic strain amplifier
E	Upper collar	L	Analog-to digital converter
F	Upper punch	M	Recorder
G	Lower punch	N	Personal computer

Fig. 2. Diagrammatical view of an instrumented tablet machine linked with A/D converter and computer system.

The sampling was done for 6 cycles (i.e. six tablet compressions). The compression force and displacement-time profiles are shown in Fig. 3. During one compression process, the thickness of the in-die-tablet at any compression pressure was equal to the difference between the maximum depth of the die fill and the upper punch displacement. The density of the in-die-tablet could be calculated from the tablet weight and thickness. The relative density, D, at any compression pressure was calculated from the knowledge of the density of the in-die-tablet and the true density of the material. Individual material compression characteristic was determined from the effect of the increase in compact density with increasing compression pressure (Heckel, 1961a,b).

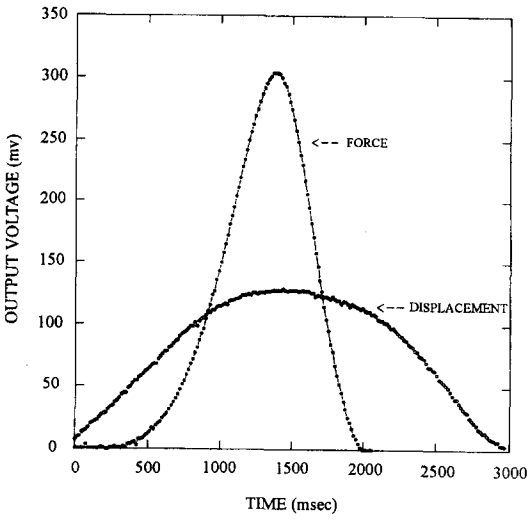


Fig. 3. Force and displacement–time profiles obtained from the instrumented tablet machine.

2.4. Compression behavior of binary mixtures of a direct compression filler and HCTZ

The tablets containing 50 mg of HCTZ were prepared as follows. Each filler was mixed with HCTZ in a V-shaped blender for 10 min. Then, magnesium stearate was added to the mixture and the mixing was continued for another 5 min. Due to the infinitesimal amount of magnesium stearate added, the mixture was classified as a binary mixture. Each mixture was compressed to 300 mg tablets using the conditions described previously. Force-displacement data were treated by Heckel analysis.

3. Results and discussion

3.1. Compression behavior of single material

The Heckel plots of the individual materials are shown in Figs. 4–7. It can be seen that there is a non-linearity in the early stage of compression which, Heckel (1961a) suggested, is due to the effect of rearrangement and the general behavior of the powders as individual particles rather than as a coherent mass. Thus, both the actual intercept and the intercept (A) extrapolated from the linear portion of the plot truly reflect the densification of powders in this early stage of compaction. The linear portion of the plot was obtained from a straight line which fitted most data points, mostly in the range of compression pressure of 50–150 MPa, with a criterion that the correlation coefficient was not less than 0.95. The

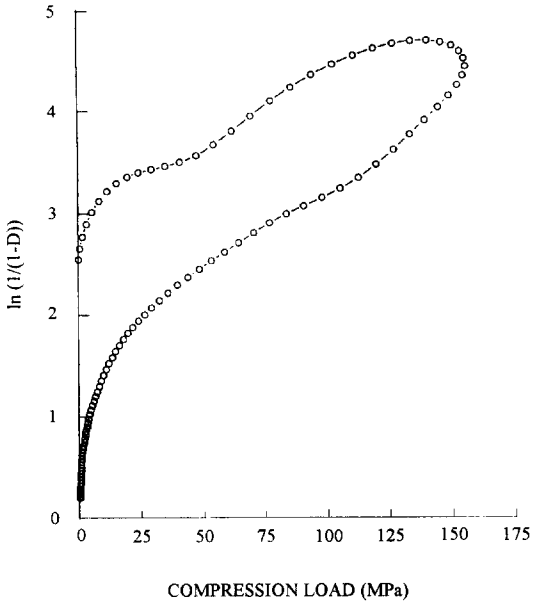


Fig. 4. Heckel plot of microcrystalline cellulose.

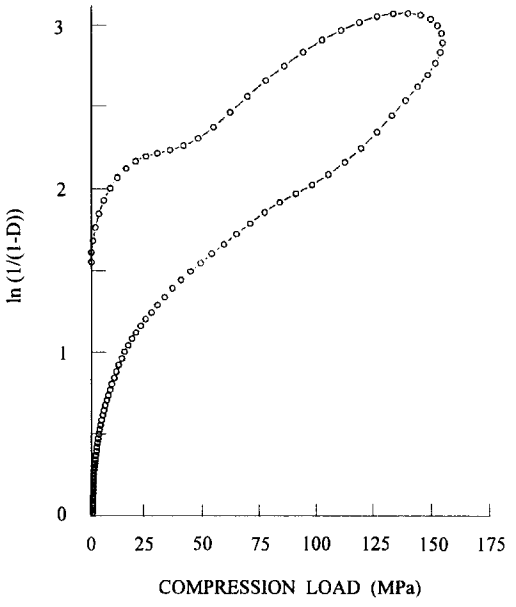


Fig. 6. Heckel plot of pregelatinized starch.

slope and intercepts of Heckel plots of each material are tabulated in Table 1. The values reported were the averages of six compression events.

With increasing compression pressure, the powders undergo elastic or plastic deformation or fragmentation. The pseudo-yield pressure (P_Y) which is the reciprocal of the slope of the linear portion of the Heckel plot, and the corresponding relative densities determined from the slopes and intercepts are tabulated in Table 2. Obviously,

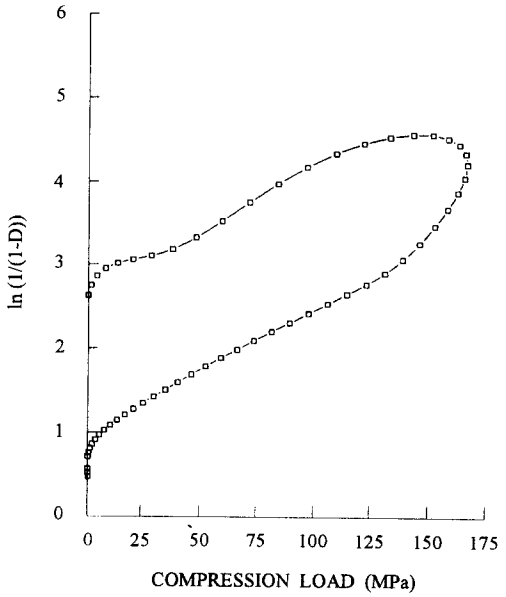


Fig. 5. Heckel plot of spray dried rice starch.

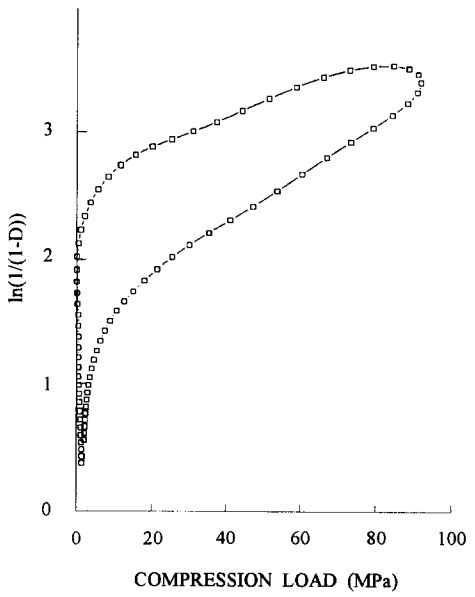


Fig. 7. Heckel plot of hydrochlorothiazide.

Table 1
Linear regression analysis of Heckel plot of each material

Material	Slope × 10^3	Intercept		Correlation coefficient
		Actual	Extrapolated	
HCTZ	7.960	0.512	1.822	0.973
MCC	12.940	0.750	1.791	0.969
PS	11.480	0.335	0.889	0.977
SDRS	17.220	0.521	0.905	0.984

HCTZ has highest values of D_B and P_Y, showing brittle fracture as a major deformation which is agreeable with the results already published (Humbert-Droz, 1983).

The other materials have relatively low pseudo-yield pressures ranking from low to high as follows: SDRS, MCC, and PS, respectively. Nonetheless, for some elastic materials, there might be falsely low P_Y, which Paronen (1986) mentioned that the value could be the combination between plastic and elastic deformations. Elastic properties, however, can be seen by characterizing the decompression curve. During decompression, compact elasticity results in an increase in porosity which can be determined from the decompression intercept. Therefore, the reliability of P_Y to show the plastic deformation tendency can be confirmed with the decompression intercept.

Table 2
Heckel parameters used to determine material deformation

Parameter	Material			
	HCTZ	MCC	PS	SDRS
[a]D_0	0.401	0.528	0.285	0.406
[b]D_A	0.838	0.833	0.589	0.596
[c]D_B	0.438	0.305	0.304	0.189
[d]P_Y	125.624	77.271	87.078	58.405

[a]Relative bulk density, $D_0 = 1 - \exp(-A_0)$, where A_0 is actual intercept of Heckel plot.
[b]Relative density of plastic deformation, $D_A = 1 - \exp(-A)$, where A is extrapolated intercept.
[c]Relative density of fragmentation, $D_B = D_A - D_0$
[d]Pseudo-yield pressure, $P_Y = 1/\text{slope}$, where slope is the slope of linear portion of Heckel plot, i.e. between 50 and 150 MPa applied loads.

During decompression, elastic properties of the compact could result in an increase in porosity. Duberg and Nyström (1986) proposed that the downward or decompression part of the Heckel plot would be possible to use for describing the elastic property of the materials during the compression process.

Since

$$\epsilon = 1 - D \tag{2}$$

and

$$A_c = \ln \frac{1}{(1 - D_c)} \tag{10}$$

where A_c is the decompression intercept of Heckel plot.

Thus,

$$\frac{1}{(1 - D_c)} = e^{A_c} \tag{11}$$

Then

$$\epsilon_c = e^{-A_c} \tag{12}$$

where D_c and ϵ_c denote relative density and porosity at decompression intercept (A_c), respectively.

The decompression porosity ϵ_c of each material was calculated. Table 3 shows material decompression intercepts and their corresponding porosities. The data suggest that PS has high decompression porosity compared with the others. The contribution of elasticity on pseudo-yield pressure for PS is, therefore, significant. It suggests that one cannot determine plastic deformation tendency by looking at only P_Y.

Unlike PS, SDRS exhibits plastic deformation with very low elasticity. This finding helps confirm

Table 3
Heckel decompression intercepts and their porosities

Material	Decompression intercept[a]	Porosity[b]
MCC	2.692	0.068
PS	1.773	0.170
SDRS	2.750	0.064

[a]Decompression intercept of Heckel plot (A_c).
[b]Porosity calculated from decompression intercept, $\epsilon_c = \exp(-A_c)$.

the good tabletting characteristics observed previously (Mitrevej and Varavinit, 1988; Bos et al., 1992). Furthermore, it is unlikely that SDRS exhibits fragmentation owing to low D_B. Having aggregated spherical shape, it does not require much pressure to be tightly packed. The further arrangement may not be due to fragmentation but deaggregation. With increasing pressure, SDRS undergoes plastic deformation. MCC, on the other hand, undergoes fragmentation before being plastically deformed. MCC, generally, has been reported to undergo plastic deformation upon compaction (David and Augsburger, 1977; Shangraw et al., 1981; Rubinstein, 1991). Khan and Rhodes (1975), however, showed that an increase in compression pressure caused some fragmentation of MCC. They further stated that the MCC crystals were compacted close enough so that hydrogen bonding between them could occur. The result in this present study supports Khan and Rhodes' finding. Fragmentation may increase the surface area of contacts between particles resulting in great particulate bonding. In terms of compactibility, MCC is better than SDRS even its PY is slightly greater than that of SDRS.

3.2. Compression behavior of binary mixtures

Total deformation of a mixture under compaction (the linear portion of Heckel plot) may be dependent upon the deformation of the individual materials. If a straightforward assumption could be made, the slope of Heckel plot for the physical mixture should be the summation of weight of those of the individual plots. This assumption is analogous to the mathematical treatment on the prediction of the compression susceptibility of the binary mixture proposed by Leuenberger (1982). To illustrate the assumption, this slope was predicted by weighing the slopes of the individuals with the fractions presenting in the mixture. In this study, the mixture comprised approximately 16.67% HCTZ and 83.33% filler. Taking the slope values from the previous section, the predicted slopes can be calculated using the following relationship.

$$\text{Predicted slope} = 0.1667(\text{HCTZ slope}) + 0.8333(\text{Filler slope}) \quad (13)$$

It can be concluded as shown in Table 4, that the predicted slopes are comparable to the actual values. It is simple to predict the consolidation and deformation for the mixtures of brittle fracture drug such as, in these cases, HCTZ, and a plastically and/or elastically deformed direct compression filler. Thus, one can foresee the compaction properties of the resulting tablets without the complications.

4. Conclusion

SDRS was believed to undergo deaggregation upon compaction and showed plastic deformation with increasing pressure. PS also exhibited plastic deformation, however, it tended to possess high elasticity during the compression process. Initial fragmentation followed by rebonding and plastic deformation could defined the compression behavior of MCC. The slope of Heckel plot of the binary mixture of HCTZ and each one of the

Table 4
Comparison between actual and predicted Heckel slopes of binary mixtures of HCTZ and each filler

Filler	Actual slope $\times 10^3$	Predicted slope $\times 10^3$	% deviation
MCC	12.318	12.109	−2.20
PS	10.939	10.899	−0.37
SDRS	14.679	15.592	+6.22

fillers employed in this study at the specified ratio could be calculated by weighing the slopes of the individuals. The pseudo-yield pressure and deformation characteristic of a mixture of a brittle fracture drug and a plastically and/or elastically deformed direct compression filler could possibly be predicted; however, this prediction should be experimentally confirmed.

Acknowledgements

The authors would like to express gratitude to Erawan Pharmaceutical Research and Laboratory, Bangkok, Thailand, for providing materials and equipment, and Assistance Professor Wibul Wongphuwarak of Department of Pharmaceutical Technology, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Songkla, Thailand, for the computer program calculations.

References

Bos, C.E., Bolhuis, G.K., Lerk, C.F. and Duineveld, C.A.A., Evaluation of modified starch, a new excipient for direct compression. *Drug Dev. Ind. Pharm.*, 18 (1992) 93–106.

Chowhan, C.T. and Chow, Y.P., Compression behavior of pharmaceutical powder. *Int. J. Pharm.*, 5 (1980) 139–148.

Chowhan, C.T. and Chow, Y.P., Compression behavior of granulations made with different binders. *Int. J. Pharm. Tech. Prod. Mfr.*, 2(1) (1981) 29–34.

David, S.T. and Augsburger, L.L., Plastic flow during compression of directly compressible fillers and its effect on tablet strength. *J. Pharm. Sci.*, 66 (1977) 155–159.

Duberg, M. and Nyström, C., Studies on direct compression of tablets XVII. porosity pressure curves for the characterization of volume reduction mechanisms in powder compression. *Powder Technol.*, 46 (1986) 67–75.

Garr, J.S.M. and Rubinstein, M.H., Consolidation and compaction characteristics of three-component particulate system. *Int. J. Pharm.*, 82 (1992) 71–77.

Heckel, R.W., Density-pressure relationships in powder compaction. *Trans. Metal. Soc. AIME.*, 221 (1961a) 671–675.

Heckel, R.W., An analysis of powder compaction phenomena. *Trans. Metal. Soc. AIME.*, 221 (1961b) 1001–1008.

Humbert-Droz, P., Densification behavior of powder mixtures. *Acta Pharm. Technol.*, 29 (1983) 69–73.

Humbert-Droz, P., Gurny, R., Mordier, D. and Doelker, E., Densification behavior of drugs presenting availability problems. *Int. J Pharm. Tech. Prod. Mfr.*, 4(2) (1983) 29–35.

Jones, T.M., The physico technical properties of starting materials used in tablet formulation. *Int. J. Pharm. Tech Mfr.*, 2(2) (1981) 17–24.

Khan, K.A. and Rhodes, C.T., Effect of compaction on particle size. *J. Pharm. Sci.*, 64 (1975) 444–446.

Kurup, T.R. and Pilpel, N., Compression characteristics of pharmaceutical powder mixtures. *Powder Technol.*, 19 (1978) 147–155.

Leuenberger, H., The compressibility and compactibility of powder systems. *Int. J. Pharm.*, 12 (1982) 41–45.

Mitrevej, A. and Varavinit, S., Modifiled rice starch for direct compression. Presented before the industrial Pharmacy Section of the 12th Asian Congress of Pharmaceutical Sciences, Federation of Asian Pharmaceutical Associations, Bali, Indonesia, 1988.

Paronen, P., Heckel plots as indicators of elastic properties of pharmaceuticals. *Drug Dev. Ind. Pharm.*, 12 (1986) 1903–1912.

Rubinstein, M.H., Compaction properties of a cellulose-lactose direct compression excipient. *Pharm. Technol.*, 15 (1991) 76–80.

Salpekar, A.M. and Ausburger, L.L., Magnesium lauryl sulfate in tabletting: effect on ejection and compressibility. *J. Pharm. Sci.*, 63 (1974) 289–293.

Shangraw, R.F., Wallace J.W. and Bowers, F.M., Morphology and functionality in tablet excipients for direct compression: part I. *Pharm. Technol.*, 5 (1981) 68–78.

York, P., Particle slippage and rearrangment during compression of pharmaceutical powders. *J. Pharm. Pharmacol.*, 30 (1978) 6–10.