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Force-displacement measurements in tableting

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The influence of particle interaction, i.e. friction and bonding, on the net work (NETW) during compaction and on Heckel plots was tested by varying the particle size, the lubrication or the moisture content. The NETW was found to be significantly affected by particle interaction. The yield pressure, calculated from Heckel plots, was far less dependent on particle interaction and appears to be more useful for the evaluation of the deformation properties of materials. The NETW may be useful as a test of inter-lot variations in compaction behaviour of materials, due to its high sensitivity to both inter- and intraparticle properties, good reproducibility and low dependence upon die wall conditions. However, it appears to be a poor measure of the plastic properties of the substance.

In a recent study, we obtained very large differences in net work of compaction when compressing granulates of identical composition but prepared by two different granulation methods (Ragnarsson & Sjögren 1982). The differences may be due to changes in the deformation properties or the interactions between the particles.

When de Blaey et al (1971a, b, c) introduced the net work calculation, it was an attempt to calculate the work used for plastic deformation of the material and for bond formation. The work needed to overcome die wall friction and the elastic work were considered and subtracted from the gross input, while the work needed for particle rearrangement and interparticle friction were assumed to be negligible. It was further assumed that the work for plastic deformation, i.e. the total net work, or a certain fraction of it, was used for bond formation, which would explain the good correlation between net work and tablet crushing strength (de Blaey et al 1971b).

The method of calculating the net work has been discussed (e.g. Ragnarsson & Sjögren 1983a) and the basic assumptions have been widely accepted. The quotient between the net input and the gross input was used by Armstrong & Morton (1977) as a measure of the proportion of the total work input that contributes to tablet strength and by Stamm & Mathis (1976) as a direct measure of the plasticity of materials.

In several papers (e.g. Dürr et al 1972; Stamm & Mathis 1976; Kala et al 1981) a high net work or a high ratio between the net work and the gross work has been considered to correlate with the ability of a material to deform plastically and to form a strong compact.

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When a crystal is subjected to forces that exceed the intermolecular forces, plastic deformation or fracture will occur. The plastic deformation can often be schematically described as taking place along slip planes inside the crystal (see review articles by Moldenhauer et al 1980; York 1983). A compact may be considered to be deformed plastically if it undergoes irreversible deformation, either by plastic flow or by fragmentation of the crystals in the compact, and shows little elastic recovery when the pressure is removed. There might thus be some discrepancy between the plasticity of a single crystal and of the compact as a whole, but very often this distinction has not been clearly made (e.g. Kala et al 1981). To be able to characterize the inherent deformation properties of a material by force-displacement measurements in an instrumented tablet machine, the measure should be unaffected by particle interaction during compaction, i.e. friction and bonding. Very few experimental data on this subject have been published and we therefore studied the influence of particle interaction on the force-displacement results, i.e. net work and Heckel plots (Heckel 1961a, b; Hersey et al 1972).

MATERIALS AND METHODS

Materials

Magnesium stearate USP (Unilever Emery, The Netherlands). Sodium chloride (Kebo-Grave, Sweden, AKZO Zout Chemi, Holland). Saccharose (Svenska Socker AB, Sweden). Lactose (BP/USP Coarse Powder, AB Svenskt Mjölksocker, Sweden). Corn starch (Sta-Rx 1500, A. E. Staley Mfg. Co., USA). Dibasic calcium phosphate dihydrate (Emcompress, Albright & Wilson Ltd, UK).

Microcrystalline cellulose (Avicel PH101, FMC Corporation, USA).

Test procedures

The materials were compressed with flat 1·13 cm circular punches in a reciprocating tablet machine at a rate of 30 tablets min^{-1}. The machine was equipped with piezoelectric load washers on the upper and lower punches, strain gauges at the die wall and inductive displacement transducers to measure punch movement, as described by Hölzer & Sjögren (1979) and Ragnarsson & Sjögren (1983a). The tablet weight for each material was chosen so as to give a tablet height of about 4·0 mm at an upper punch pressure of 150 MPa or to match the limits of the tablet strength tester (0–400 N). The die was prelubricated by repeated compression of a mixture of each material and excessive amounts of magnesium stearate (25% unless otherwise stated). The reason for die lubrication was to obtain a low and reproducible friction level and to avoid tablet disruption or strength reduction during the ejection phase (Ragnarsson & Sjögren 1983b).

The die wall friction was characterized by the friction coefficient at maximum pressure (Hölzer & Sjögren 1981). The tablets were compressed to a constant mean punch pressure (MPP), since the MPP appears to be a better measure of the compaction load than the upper punch pressure (Ragnarsson & Sjögren 1983b, 1984). Upper and lower punch force, upper punch displacement and die wall force were measured and recorded each ms during the compression cycle. The net work of compaction (NETW) was calculated according to Ragnarsson & Sjögren (1983a) by subtracting the frictional work and the expansion work (EXPW) from the upper punch work. The calculated EXPW will underestimate the true expansion work since the tablet expansion within a die is incomplete, even with low die wall friction (Ragnarsson & Sjögren 1983a) or long decompression times (Carless & Leigh 1974). The total tablet expansion (elastic recovery) was therefore also calculated to increase the possibilities of detecting differences in elastic properties of the materials. The Heckel plots were based on MPP (Ragnarsson & Sjögren 1984) and the slope of the Heckel plot in the pressure range of 40 to 100 MPa was calculated (Duberg & Nyström 1982). The reciprocal of the slope is referred to as yield pressure in the text. The plots were obtained during the compression and not after the tablet ejection and will therefore include both plastic and elastic deformation of the material. A steep slope, giving a low yield pressure, means that the compact is easy to deform and will approach zero porosity at low pressure. The density of the materials was measured with a Beckman Air Comparison Pycnometer 930.

The crushing strength of the tablets was tested immediately after compression in a hardness tester operating at a constant speed of 0·6 mm min^{-1}.

Preparation of test materials

The interparticulate friction and bonding was varied by (a) varying the particle size of the materials, (b) lubrication with magnesium stearate and (c) varying the moisture content of microcrystalline cellulose.

(a) Samples of sodium chloride (Kebo-Grave), saccharose and lactose were divided into two size fractions using ordinary laboratory test sieves. The size intervals were 0·500–0·710 and 0·125–0·180 mm for sodium chloride, 0·212–0·250 and 0·063–0·090 mm for lactose and 0·710–1·00 and 0·212–0·250 mm for saccharose.

(b) Emcompress and Sta-Rx, which represent a brittle and a plastic material respectively, were mixed with 0·5% magnesium stearate for 1 and 30 min in a Turbula mixer (W.A. Bachofen AG, Switzerland) at 90 rev min^{-1}. The amount of lubricant and the longer mixing time were chosen so as to eliminate the interparticle bonding for Sta-Rx (Bolhuis & Lerk 1977).

The bonding properties of sodium chloride are not eliminated by lubricants (Bolhuis & Lerk 1977; Ragnarsson et al 1979) and we used a smaller amount of magnesium stearate (0·05%) and a low mixing intensity (0·5 and 50 min at 42 rev min^{-1}) to achieve a reduction in interparticle friction and bonding.

The pure materials were compressed in a prelubricated die while the mixtures with magnesium stearate were compressed in an unlubricated die.

(c) To obtain acceptable tablet dimensions, Avicel was dry-granulated by repeated compaction and milling. The sieve fraction 0·4–0·7 mm was used. Avicel stored under ambient conditions had a moisture content of 4·9%. The moisture content was reduced to 1·1% by drying at 100 °C and storage over silica gel until compaction. Another portion was stored over a saturated sodium chloride solution (rh 75%) for three days to obtain a water content of 8·2%.

RESULTS AND DISCUSSION

A reduction in the particle size resulted in stronger tablets when the materials were compressed to a constant pressure (Table 1). The smaller particle sizes gave thicker tablets at maximum pressure, i.e.

Table 1. The effect of particle size on compaction variables and tablet crushing strength. Mean of 10 measurements.

Materials and sieve fractions	MPP[a] MPa	Tab.[b] ht mm	NETW[c] Nm	EXPW[d] Nm	Elast.[e] recov. %	Yield press. MPa	μ^f	Crush. strth N
Saccharose								
0·71–1·0	144	4·02	5·80	0·28	2·7	133	0·37	61
0·21–0·25	144	4·06	6·64	0·27	2·6	133	0·34	80
Sodium chloride								
0·50–0·71	140	4·03	8·78	<0·05	0·7	87	0·32	85
0·13–0·18	140	4·08	9·99	<0·05	0·5	91	0·34	91
Lactose								
0·21–0·25	141	4·02	7·02	0·43	3·9	114	0·37	61
0·06–0·09	141	4·07	6·85	0·49	4·3	125	0·35	91

[a] Mean punch pressure.
[b] Tablet height at maximum pressure.
[c] Net work.
[d] Expansion work.
[e] Difference between tablet height at maximum pressure and after ejection.
[f] Friction coefficient at maximum pressure (Max. upper punch force–max. lower punch force)/max. die wall force.

less punch displacement, but higher NETW for sodium chloride and saccharose.

The force-displacement curves for lactose indicated that some work was needed to fragment the coarser lactose particles during the initial part of the compression, which resulted in a slightly higher NETW. The NETW-values were very reproducible and the relative standard errors of the means were within 0·2–0·6%.

The elastic properties (EXPW and elastic recovery) of the two size fractions were not affected by the particle size (Table 1). According to the theories discussed in the introduction, an increase in NETW should indicate a higher ability to deform plastically. It has been reported, however, that different particle fractions obtained by simple sieving do not differ in their consolidation properties (Alderborn & Nyström 1982; McKenna & McCafferty 1982). This conclusion is supported by the fact that the calculated mean yield pressures were unaffected by the particle size for saccharose and sodium chloride (Table 1), indicating that the deformation properties were unchanged.

The particle size had some effect on the yield pressure for lactose. A similar effect has been reported by Hersey et al (1973), who suggested that a decrease in the particle size of lactose will increase the stress necessary to cause extension of crystal cracks and thus increase the mean yield pressure.

In general, it appears to be reasonable to assume that the effect of the particle size on the NETW is not due to differences in the plasticity but is caused by differences in particle interaction. This interaction may be due to interparticle friction or a different degree of bonding.

In order to change the interparticle friction and bonding to a larger extent, magnesium stearate was admixed with sodium chloride, Sta-Rx and Emcompress. The results at one of the compaction pressures are given in Table 2, and the effect on NETW, EXPW and crushing strength at different pressures for Emcompress and Sta-Rx are shown in Figs 1 and 2.

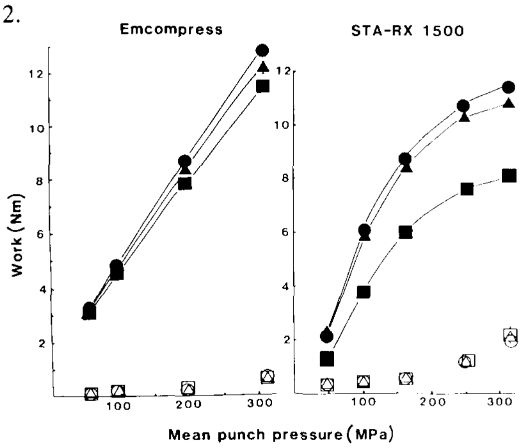

FIG. 1. The effect of magnesium stearate admixture on net work (filled symbols) and expansion work (open symbols) in the tableting of Emcompress and Sta-Rx 1500. ●, pure substance; ▲, 0·5% magnesium stearate admixed for 1 min; ■, 0·5% magnesium stearate admixed for 30 min. The 95% confidence limits (n = 5) are given when not covered by the symbols.

The lubricant reduced the crushing strength and the NETW of all materials and this effect was very pronounced for sodium chloride and Sta-Rx. A mixing time of 30 min eliminated the bonding properties of Sta-Rx and reduced the NETW by about 30% (Table 2, Figs 1, 2). The reduction in NETW is not due to increased elastic properties of

Table 2. The effect of magnesium stearate and its mixing time on compaction variables and tablet crushing strength at one of the compaction pressures. Mean of 5 measurements.

Materials and mix times	MPP[a] MPa	Tab.[b] ht mm	NETW[c] Nm	EXPW[d] Nm	Elast.[e] recov. %	Yield press. MPa	μ[f]	Crush. strth N
Sodium chloride	144	4·06	8·98	<0·05	0·9	84	0·34	75
Sodium chloride + Mg-stearate								
0·5 min	144	4·04	7·83	<0·05	1·0	82	0·28	41
50 min	144	4·02	7·47	<0·05	1·2	79	0·27	26
Sta-Rx	163	3·28	8·72	0·52	15·9	69	0·31	57
Sta-Rx + Mg-Stearate								
1 min	165	3·26	8·41	0·53	16·0	67	0·32	44
30 min	164	3·24	5·99	0·53	—	70	0·28	0
Emcompress	197	3·94	8·67	0·21	2·4	312	0·25	117
Emcompress + Mg-stearate								
1 min	199	3·93	8·33	0·21	2·3	320	0·24	117
30 min	198	3·89	7·86	0·27	2·4	320	0·28	107

[a–f] See Table 1.

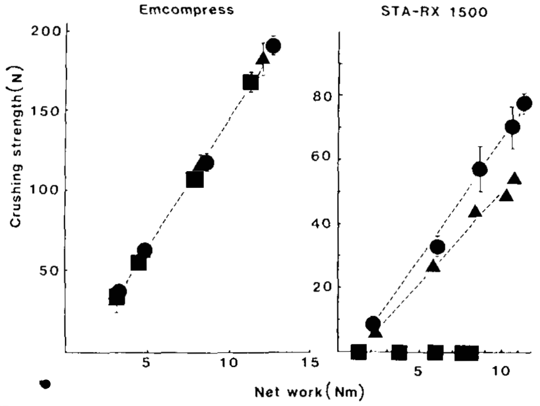

FIG. 2. Crushing strength versus net work for tablets of Emcompress and Sta-RX 1500. ●, pure substance; ▲, 0·5% magnesium stearate admixed for 1 min; ■, 0·5% magnesium stearate admixed for 30 min. The 95% confidence limits (n = 5) are given when not covered by the symbols.

the lubricated materials, as suggested by Paris et al (1977), as both the EXPW and the elastic recovery are practically unaffected (Table 2, Fig. 1). Nor is it likely that it is caused by an altered ability of the material to deform plastically, as the yield pressures were approximately constant (Table 2).

The decrease in NETW therefore appears to be due solely to reduced particle interaction, i.e. friction and bonding. The very drastic effect of a long mixing time on plastic materials indicates that the bonding properties of the materials have a significant effect on the work of compaction.

Moisture has been suggested to affect the compaction properties of Avicel, due to internal lubrication, which facilitates slippage and flow within the individual microcrystals (Khan et al 1981). This is in agreement with our results. Increased moisture levels gave a lower yield pressure and tablet height but also a lower NETW (Table 3, Fig. 3). The differences between the materials were only slightly affected by die wall lubrication. The EXPW was reduced at high friction levels, due to a retarded tablet expansion. The effect on the calculated NETW was small.

The sample with a low moisture content (1·1%) gave considerably lower tablet strength than the one with a normal moisture content (4·9%) throughout the pressure range. The bonding properties of the moist sample (8·2% water) were good at low pressure but were less affected by an increase in the pressure and did not differ much from those of the dried material at the highest pressure level (Table 3). To achieve a constant strength, a higher NETW was needed for the dried material (Fig. 3).

An increase in the moisture content probably affects the NETW by a combined effect of reduced resistance to deformation of the particles, reduced

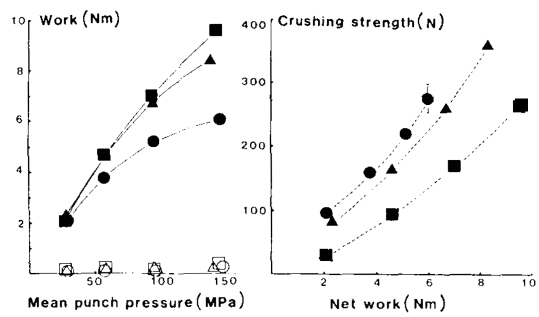

FIG. 3. Net work (filled symbols) and expansion work (open symbols) versus compaction pressure and crushing strength versus net work for Avicel compressed in an unlubricated die. ●, 8·2%; ▲, 4·9%; ■, 1·1% moisture content. The 95% confidence limits (n = 5) are given when not covered by the symbols.

Table 3. The effect of the water content of Avicel and die wall lubrication on compaction variables and tablet crushing strength at one of the compaction pressures. Mean of 5 measurements.

Water cont. and die wall lub.[g]	MPP[a] MPa	Tab.[b] ht mm	NETW[c] Nm	EXPW[d] Nm	Elast.[e] recov. %	Yield press. MPa	μ^f	Crush strth N
8·2%								
UL	148	2·31	5·99	0·23	7·5	59	0·94	276
L	148	2·30	5·88	0·38	7·8	58	0·13	269
4·9%								
UL	141	2·34	8·35	0·18	6·0	74	1·79	360
L	140	2·32	8·20	0·30	6·5	72	0·22	370
1·1%								
UL	146	2·41	9·52	0·29	8·0	104	1·23	264
L	142	2·38	9·16	0·47	10·0	100	0·22	263

[a–f] See Table 1.
[g] UL = unlubricated die, L = lubricated die.

interparticle friction owing to the lubricating effect of the water and perhaps also increased bonding.

When the information provided by the compaction work and the Heckel plot measurements used in this study are compared, the yield pressure appears to be most suitable for expressing differences in the deformation properties of the starting materials. Only small differences in yield pressure were obtained in the series where insignificant effects on the deformation properties of the materials were expected (Tables 1, 2). Reduction of the interparticle friction and bonding by addition of magnesium stearate to Sta-Rx appears mainly to affect the intercept of the Heckel plot and only to a small extent the slope of the linear part used for the yield pressure calculation. On the other hand, the total force-displacement curves, and thus the NETW, are significantly affected, as illustrated in Fig. 4.

We conclude that there is no simple correlation between the NETW and the deformation properties

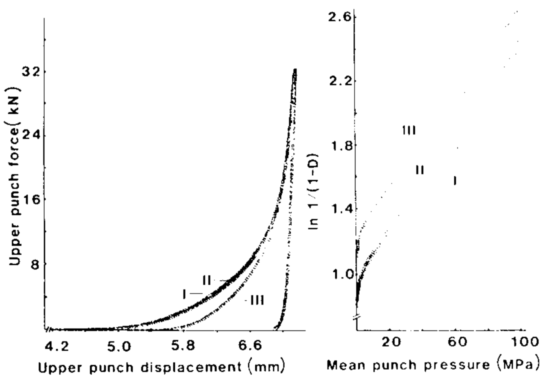

FIG. 4. Force-displacement curves and Heckel plots of Sta-Rx and its magnesium stearate mixtures. I, pure Sta-Rx; II, 0·5% magnesium stearate admixed for 1 min; III, 0·5% magnesium stearate admixed for 30 min. Each curve represents a single but typical result out of 5 measurements.

of a material since the NETW is also substantially affected by the particle interactions.

The attempt to eliminate the interparticle friction and bonding by adding a lubricant to the plastic material Sta-Rx indicated that about 30% of the NETW may be due to such interactions. It may be assumed that bonds are formed during the compaction and that these bonds have to be broken for further densification. The strength of these bonds will therefore have a direct influence on the NETW, which may give rise to a good correlation between NETW and tablet crushing strength. A change in the surface properties, for example, owing to contamination or adsorbed moisture may consequently affect the NETW as well as the crushing strength, although the deformation properties of the material are unchanged. The NETW thus appears not to be suitable for general evaluation of the deformation properties of the starting materials. For this purpose yield pressure calculation is a better approach. The NETW may, however, be useful for detecting batch-to-batch variations in the compaction properties of materials, due to its high sensitivity to both inter- and intraparticle properties, good reproducibility and low dependence upon die wall conditions. By means of yield pressure measurements, it may be possible to judge whether such inter-lot variations are due to intraparticle changes, e.g. polymorphism and lattice defects, or to altered surface properties.

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REFERENCES

Alderborn, G., Nyström, C. (1982) Acta Pharm. Suec. 19: 381–390

Armstrong, N. A., Morton, F. S. S. (1977) J. Powder Bulk Solids Technol. 1: 32–35

Bolhuis, G. K., Lerk, C. F. (1977) Acta Pharm. Technol. 23: 13–20

Carless, J. E., Leigh, S. (1974) J. Pharm. Pharmacol. 26: 289–297

de Blaey, C. J., Polderman, J. (1971a) Pharm. Weekblad 106: 57–65

de Blaey, C. J., van Oudtshoorn, M. C. B., Polderman, J. (1971b) Ibid. 106: 589–299

de Blaey, C. J., Polderman, J. (1971c) Farm. Notisblad 80: 111–118

Duberg, M., Nyström, C. (1982) Acta Pharm. Suec. 19: 421–436

Dürr, M., Hanssen, D., Harwalik, H. (1972) Pharm. Ind. 34: 905–911

Heckel, R. W. (1961a) Trans. Metall. Soc. AIME. 221: 671–675

Heckel, R. W. (1961b) Ibid. 221: 1001–1008

Hersey, J. A., Cole, E. T., Rees, J. E. (1972) in: Goldberg, A. S. (ed.) Proceedings of the First International Conference on the Compaction and Consolidation of Particulate Matter. Brighton, October 1972. Powder Advisory Centre, London, 1973

Hersey, J. A., Rees, J. E., Cole, E. T. (1973) J. Pharm. Sci. 62: 2060

Hölzer, A. W., Sjögren, J. (1979) Int. J. Pharm. 3: 221–230

Hölzer, A. W., Sjögren, J. (1981) Ibid. 7: 269–277

Kala, H., Moldenhauer, H., Giese, R., Kedvessy, G., Selmeczi, B., Pintye-Hódi, K. (1981) Pharmazie 36: 833–838

Khan, K. A., Musikabhumma, P., Warr, J. P. (1981) Drug Dev. Ind. Pharm. 7: 525–538

McKenna, A., McCafferty, D. F. (1982) J. Pharm. Pharmacol. 34: 347–351

Moldenhauer, H., Kala, H., Zessin, G., Dittgen, M. (1980) Pharmazie 35: 714–726

Paris, J., Duchêne, D., Puisieux, F. (1977) J. Powder Bulk Solids Technol. 1: 47–56

Ragnarsson, G., Hölzer, A. W., Sjögren, J. (1979) Int. J. Pharm. 3: 127–131

Ragnarsson, G., Sjögren, J. (1982) Ibid. 12: 163–171

Ragnarsson, G., Sjögren, J. (1983a) J. Pharm. Pharmacol. 35: 201–204

Ragnarsson, G., Sjögren, J. (1983b) Int. J. Pharm. 16: 349–351

Ragnarsson, G., Sjögren, J. (1984) Acta Pharm. Suec. 21: 141–144

Stamm, A., Mathis, C. (1976) Acta Pharm. Technol. Suppl. 1: 7–16

York, P. (1983) Int. J. Pharm. 14: 1–28