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Compressibility Characteristics of Matrices Prepared with Ethylcellulose Aqueous Dispersion

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ABSTRACT

Granules of acetaminophen (APAP) and Lactose Fast Flo were prepared by wet granulation method using Surelease aqueous dispersion as a granulating liquid. Acetaminophen granules containing different total solids (from Surelease) were compacted into tablets using instrumented tablet press to investigate the effect of the levels of Surelease (total solids) on the compressional properties of various formulations. Measurements were made of their compressibility, force displacement, works and forces analysis during compaction. All formulations containing Surelease utilized the compaction energy better than formulations of the same composition prepared without Surelease. As the level of total solids from Surelease was increased in the formula, the compressibility characteristic was enhanced. Granules with Surelease exhibited better deformation and densification behaviors and gave tablets of better mechanical strength compared to control tablets.

INTRODUCTION

Through years of studies of material behavior during compaction it had been demonstrated that drugs exhibit different compaction and consolidation characteristics. It is also known that the compaction characteristics may be changed by the addition of different components to the original powder (1-3), by precompression (4), and by the method used for preparing compacts (5-6). Some studies revealed that the compaction characteristics of some drugs can be changed by the addition of fillers (7) or other additives such as magnesium stearate (8). Also moisture content (9-10), punch velocity (11), particle shape (12), and type of excipients (13) can affect the compressibility characteristics of some materials.

Klinger et al. (14) found that the use of the ethylcellulose aqueous dispersion appears to enhance the processing characteristics of the material under study.

The poor compressibility of acetaminophen and the problems of capping during compression have led to the

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objectives of this study. In this work, the effect of total solids from Surelease on the compaction behavior and on the mechanical properties of acetaminophen tablets were evaluated.

MATERIALS AND METHODS

Materials

Acetaminophen (supplied by Warner Lambert Inc., P.R.) was chosen as the drug model. Surelease was used as the granulating liquid (supplied by Colorcon Inc., Philadelphia, PA), and Lactose Fast Flo was used as the diluent (supplied by Foremost Inc.). The lubricant used was magnesium stearate (Ruger Chemical Co.).

Preparation of Acetaminophen Granules

The wet granulation method was chosen for preparation of the granules. A blend of powder containing 10% acetaminophen and 90% Lactose Fast Flo was granulated with Surelease dispersion in a planetary mixer (Hobart Manufacturing Co.) until the mixture achieved suitable consistency. The wet granules were milled and dried in a hot-air conventional oven at 40°C over 15 hours.

In order to obtain granules with a high level of Surelease, a second and a third granulation was performed to a known weight portion of granules from the first granulation using the same procedure described above. The dried granules were milled and lubricated with 0.5% magnesium stearate.

Control Preparation

Control tablets were prepared by mixing acetaminophen (10%) and Lactose Fast Flo (90%) in a planetary mixer for 10 minutes. Magnesium stearate (0.5%) was added to the blend.

Compaction into Tablets

The different formulations were compacted into tablets using a single punch instrumented tablet press (Korsch EKO) equipped with 11/32-inch flat-face punches. Target tablet weight was 450 mg ± 5%. The target hardness varied according to experiment specifications. The diameter, thickness, hardness, porosity, and tensile strength for the different tablet formulations were measured.

Dissolution Studies

The dissolution test for tablets was carried in 900 mL distilled water at 37°C ± 0.5 using the rotating basket apparatus (Hanson Research, Model SR2,USA) at a speed of 50 rpm. Filtered samples of 10 mL were withdrawn manually at predetermined time intervals and assayed using a UV spectrophotometer (Beckman Instruments, Model DU 65, USA) at 244 nm. Three replicates were tested and their mean percent release was calculated.

RESULTS AND DISCUSSION

The compressibility characteristics of the different formulations were greatly enhanced as the amount of total solids from Surelease was increased. As shown in Table 1, the upper compressional forces, lower compressional forces, and ejection forces needed to produce tablets with an average hardness of 6.8 Kp were reduced as the percent of total solids (from Surelease) was increased. Surelease enhanced the compression and consolidation process during compaction of acetaminophen. Also it was found that the difference between upper compressional force and force transmitted to the lower punch decreased as the level of total solids from Surelease increased in the formula.

ANOVA one-way analysis for data shown in Table 1 indicated that the difference in the mean values among the treatment groups (tablets with different total solids from Surelease) was greater than would be expected by chance; there was a statistically significant difference ($p < 0.001$) and all pairwise multiple comparisons (Bonferroni t-test method) showed significant difference between pairs of treated groups ($p < 0.05$).

It appears that as the level of total solids was increased, the behavior of the formulation during compression changed from brittle fracture to a more plastic deformation (Figure 1). Slopes of Heckel plots for control and formulation containing 13.41% total solids (from Surelease) were 0.052 and 0.061 and the yield pressure values were 19.23 and 16.39 respectively.

As shown in Figure 2, the porosity of the tablets was decreased as the level of total solids (from Surelease) was increased in the formula. This was true for all compressional forces used. It appears that Surelease promotes further plastic deformation to tablet formulation, thus increasing the densification as the amount of total solids increases in the formula.

Table 1

Force and Work Analysis During Compaction of Acetaminophen Tablets

Force and Work Analysis	Control	4.2% Total Solids	9.36% Total Solids	13.41% Total Solids
UCF[a] (KN)	15.87 (±0.17)	11.61 (±0.60)	9.0 (±0.69)	6.28 (±0.22)
LCF[b] (KN)	13.92 (±0.16)	10.72 (±0.58)	8.22 (±0.67)	5.62 (±0.22)
Ejection (KN)	0.6554 (±0.0148)	0.1856 (±0.0129)	0.1116 (±0.0134)	0.0367 (±0.005)
Total Work N^*m	21.71 (±0.23)	15.56 (±0.68)	12.29 (±0.78)	9.00 (±0.26)
Friction Work N^*m	4.50 (±0.04)	2.93 (±0.08)	2.57 (±0.10)	2.17 (±0.04)
Elastic Work N^*m	7.43 (±0.13)	5.86 (±0.34)	1.29 (±0.38)	3.08 (±0.10)
Net Work N^*m	14.28 (±0.12)	9.70 (±0.35)	8.0 (±0.40)	5.92 (±0.16)

[a]Upper compressional force
[b]Lower compressional force

The compressibility characteristics of the formulations and consequently the hardness values were enhanced with the addition of Surelease. As depicted in Figure 3, control tablets exhibited less than 1 Kp hardness value at a compressional force of 5 KN, while tablets containing 13.41% total solids exhibited 3 Kp hardness value at a compressional force of 2 KN.

The ratio of lower compressional force to upper compressional force (F_L/F_U) for formulation containing 13.41% total solids (from Surelease) approached unity (0.94) as the compressional force was increased. For control tablets the F_L/F_U ratio is approximately constant and the increase of compressional force did not increase the F_L/F_U ratio above 0.89 (Figure 4). These data indicated that Surelease appears to reduce the discrepancy between the upper compressional force and that transmitted to the lower punch, and consequently reduces the difference in the degree of compression and consolidation between one region of the tablet and another.

As the upper punch descends into a filled die, there are two general possibilities depending on the behavior of the material being compacted. Either it can exhibit

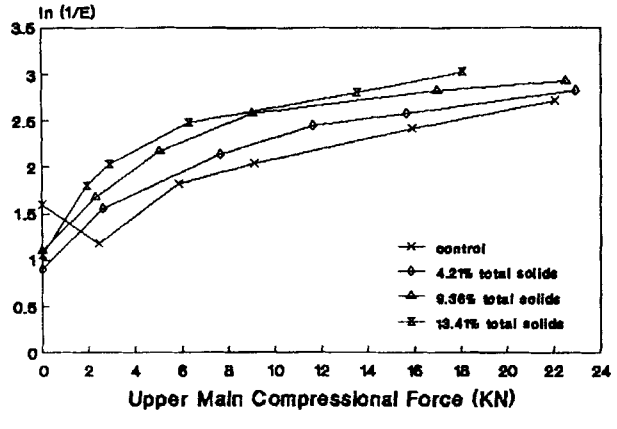

Figure 1. Heckel plots for tablets with total solids (Surelease).

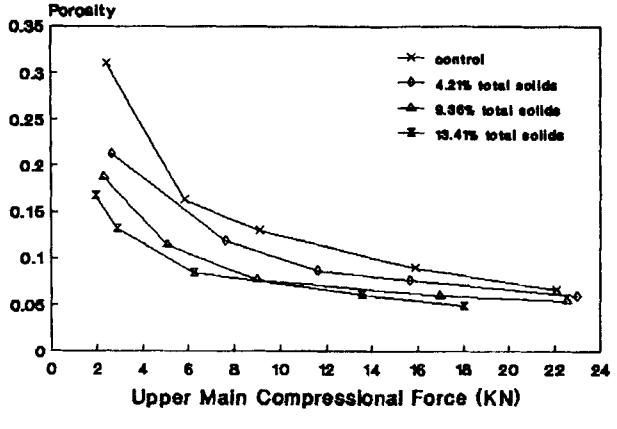

Figure 2. Porosity versus upper compressional forces.

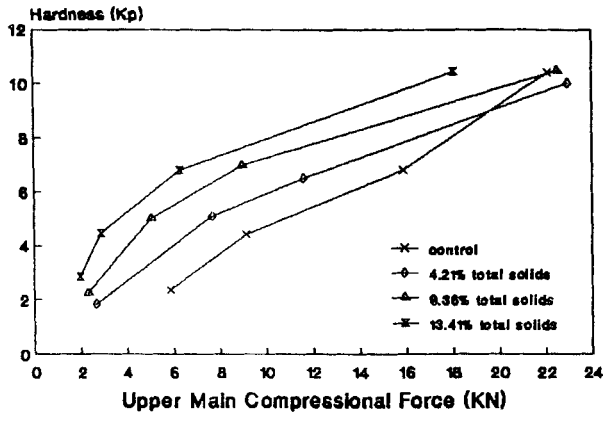

Figure 3. Hardness versus upper compressional forces.

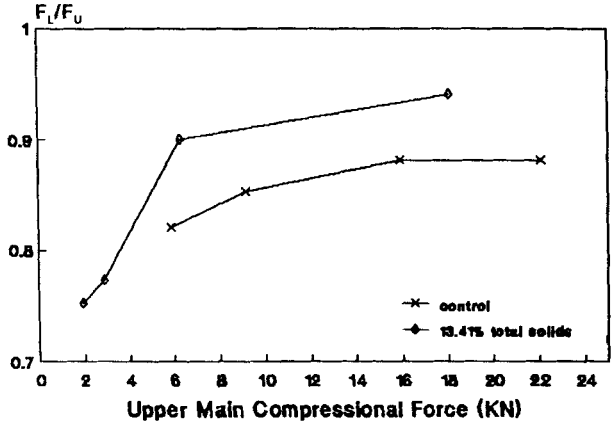

Figure 4. F_L/F_U ratio versus upper compressional forces.

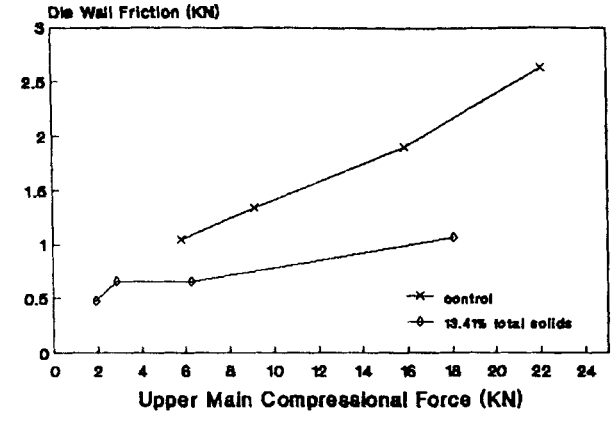

Figure 5. Die wall friction versus upper compressional forces.

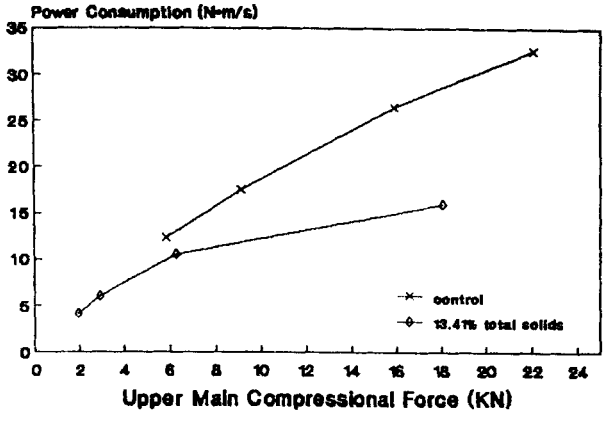

Figure 6. Power consumption versus upper compressional forces.

constant yield in stress, or it can behave as a Mohr body, in which the yield stress is related to the normal stress across the shear plane. As shown in Figure 5, the die wall friction value was decreased as the level of total solids from Surelease was increased, indicating less residual stress. It appears from the data obtained that formulations with high total solids (from Surelease) showed less tendency to behave like Mohr body (brittle fracture) and more tendency to deform plastically.

Figure 6 showed that granules containing 13.4% total solids consumed less power during compaction than control formulations. It appears that better utilization of the energy provided by the machine was achieved when Surelease was added to the formulation. Also tablets of high hardness and crushing strength were obtained.

CONCLUSIONS

In conclusion, it was possible in this work to modify the compaction behavior of acetaminophen through the use of Surelease aqueous dispersion as a granulating liquid. The compaction behavior, densification, hardness, and degree of lubrication were enhanced significantly for granules with total solids from Surelease compared to control formulation. Additionally, as the amount of total solids from Surelease was increased, the die wall friction values decreased, and it appears that the behavior of the formulation during compaction changed from brittle fracture to a more plastic deformation. Also granules containing Surelease used the energy provided by the machine more effectively than control formulation.

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