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RESEARCH PAPER

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Kinetic Evaluation of the Mechanical Strength of Briquette Granules

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ABSTRACT

The mechanical strength of the granules is defined by the friability index (FI). This index describes the condition at the end of a certain time period. However, the mixing process during industrial manufacturing displays a continuity that changes as a function of time. In this study, the mechanical strength of a briquette granule composed of a mixture of lactose, microcrystalline cellulose, and microfine cellulose, and obtained by the dry granulation (slugging) method was examined as a function of its duration of friability. In addition, the effect of the length of friability period on the physicopharmaceutical and compression properties of the briquette granules was observed. It was found that the friability event in the briquette granules occurs as an interparticular milling instead of as a breakdown of the binding bridges as in the wet granulation method, and that compressibility and other properties change to interfere with the validity of the process.

INTRODUCTION

To avoid erosion by the mechanical forces present during the mixing procedure, each granulate must have an adequate mechanical strength (1). If this strength is not sufficient, size and distribution of the particles in the granule then display an alteration in an uncontrolled manner. This alteration in the mechanical strength of the granule causes changes in the compressibility of the material compressed and in the physical properties of the tablet (2).

The friability test has been suggested for determination of mechanical strength of the granules, and by using this test, the value of the friability index (FI) has been numerically calculated (3). FI is obtained by the ratio of the mean particle size of pulverized granules (FR) to the mean particle size of the unpulverized granules (UFR). If no erosion occurs during the test, no

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reduction in the particles is seen and FI equals 1.0, which is the ideal state. In practice, however, abrasion occurs to some extent in the particles and FI becomes smaller than 1.0. According to the FI value, whether it is near to or distant from 1.0, it is concluded whether the mechanical strength of the granule is sufficient or not.

FI is a parameter that defines a single point. However, the friability event in the granules shows a continuity, changing as a function of time during the mixing period at the industrial manufacturing stage. Therefore, indicating the friability of granules as "friability rate constant" (FRC) is a more realistic approach than the one-point identification (4). The higher the value of FRC, the more friable is the granule.

Grinding of particles in solid materials is a kinetic event. Similarly, decomposing of a unit of a granule into its ingredients is also considered as a kinetic event (5,6).

In granule production by the wet granulation method, the binding bridges allowing the particles to stay in together may be broken due to mechanical force during the sieving and mixing processes after drying procedure. Eventually the unitary structure of the wet granule is deformed. In the case of continuance of these mechanical forces, breaking of the bridges begins to slow down and the milling process at the surface of particles is accelerated (7). Since no bindings or binding bridges that hold the units together are present in briquette granules prepared to develop the compressibility in production of a tablet with the slugging method, the reduction of the particles that occurs during mechanical compulsion of the granules is due only to rubbing (superficial milling) (7).

In this investigation we studied the friability phenomenon as a function of time in a briquette granule composed of lactose, microcrystalline cellulose, and microfine cellulose, and containing no active material. We observed the effects of mechanical force on the physicopharmaceutical and compression properties of the granule.

EXPERIMENTAL

Materials

Lactose EP D 30 (Meggle GmbH)
Microcrystalline cellulose (Avicel PH 101, FMC Corp.)
Microfine cellulose (Elcema F 150, Degussa)

Methods

Slugging Process

A briquette granule was prepared by following formulation:

Lactose EP D 30	45%
Avicel PH 101	45%
Elcema F 150	10%

All these ingredients were mixed in a cubic mixer (Erweka, 15/UG) at 40 ± 1 rpm for 20 min. Then slugs were prepared with a flat-faced and bevel-edged punch of 20-mm diameter in a single-punch machine (Korsch EK-O). Finally, slugs were knocked in a cracking mill, and by processing in an oscillating granulator, the particle size was reduced to 2.0 mm.

Determination of Granular Friability

The granular friability was determined using the friability test with a Roche Friabilator, as suggested by Rubinstein et al. and Baykara et al. (2,3). Granules, 100 g, were placed in a Roche Friabilator together with 10 rubber balls of 15-mm diameter. The apparatus was rotated for 5, 10, 15, 20, 30, 60 and 90 min at 25 rpm. All the material was then transferred to the nest of sieves, and the mean particle size was determined after abrasion in the friabilator as before.

FI was calculated as the ratio of the mean particle size of friabilator-treated granules (FR) to the mean particle size of the non-friabilator-treated granules (UFR). The logarithm of FI of granules was plotted against time. The slope of the FI line was called the friability rate constant (FRC).

Determination of Consolidation Properties of FR and UFR Granules

Ten milliliters from each of granules FR and UFR were poured into a 10-ml graduated cylinder with a funnel without percolating the pile, and the weight of the recorded volume was determined. With these results the bulk density and the Hausner factor (HF) were calculated.

The graduated cylinder containing the sample was tapped from a height of 25 mm and the volume reduction of the powder mass was measured at the end of each tapping (5, 10, 20, 30, 40, 50, 60, 75, 100, 120, 200, 250, 300, and 400) and the double (Ln) of the relative changes (A) [Eq. (1)] obtained after each tap-

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ping were plotted against the (Ln) of the tapping values, and the profiles of curves obtained were examined (8,9).

$$A = \frac{TD - BD}{TD} \quad (1)$$

where A = relative density change; TD = tap density; BD = bulk density.

Determination of Compressibility of FR and UFR Granules

The compression properties of FR and UFR granules and their yield values were determined. For this purpose, a flat punch of 12-mm diameter and a hydraulic press were used, and at each time granule masses with equal volume (1915.2 mm^3) were pressed at relative pressure values (383.5, 767.0, 1150.5, 1534.0, 1917.5, 2301.0, and 2684.5 kgf/cm^2). When the desired pressure was reached, it was kept at this value for 30 sec. For this pressure, the tablet volume, V_p, formed at each pressure level was calculated. $Ln(V_p/V_p - V_\infty)$ values were plotted against increasing pressure values according to the Heckel equation. Results were calculated with a computer program written using the equation of Heckel and Kawakita (10). The Heckel equation is:

$$\mathrm{Ln}\frac{V_p}{V_p - V_\infty} = kP + \frac{V_0}{V_0 - V_\infty} \quad (2)$$

where V_0 = initial powder volume; V_p = the volume at each pressure value; V_∞ = the true volume of the solid (without pores); k is a constant, Heckel correlated the slope of the compaction curves, k, with the yield strength of the material being compressed ($k = 1/P_y$); and P_y = yield pressure.

The Kawakita equation is:

$$\frac{P}{C} = \frac{1}{ab} + \frac{1}{a}P \quad (3)$$

where C = degree of volume reduction $[(V_o - V_p/V_0) = C]$; V_0 = initial apparent volume of powder; V_p = powder volume under applied pressure (P); and a, b are constants, characteristics of the powder.

After calculating regression lines, the point at which linearity was disturbed the yield value was determined (11).

RESULTS AND DISCUSSION

Friability values corresponded with increasing time; FI values diminished as time increased (Table 1).

When this event was examined kinetically, in the first-order kinetics, there was an exponential relationship between FI and time, and FRC was calculated as 32.1 $\times 10^{-3}$ min^{-1}. If the 60th and 90th minute values were counted in regression, FRC would become 2.90 $\times$ 10^{-3} min^{-1}; that is, it is decreased 11 times (Table 2).

Friability shows a closer correlation with the first-order kinetics in shorter mixing periods. This is documented by the differences between the values of r^2 (Fig. 1). This fact may be explained by the fact that the abrasion in prolonged rubbing deforms the granular state of particles. As time passes (between 60th and 90th min), the elements that form the units rub as interparticular milling.

As the duration friabilator treatment continued, the particle size in granules decreased and bulk density increased. This is confirmed by the increase in HF values. Also, TD and BD values showed an alteration (Table 3).

Since the mean particle size in the powder mass was reduced at the end of the friabilator process, there was an elevation in HF values while mass and consolidated densities decreased. Changes in the consolidation parameters were also observed in granules; their particle size was changed as a result of exposure to abrasion (Table 4).

Table 1

FI Values of the Briquette Granules at Different Times

	Time (min)						
	5	10	15	20	30	60	90
FI	0.788	0.606	0.527	0.442	0.346	0.321	0.218

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Table 2

FRC and r^2 Values Calculated by the First-Order Kinetics of Friabilator-Treated Granules[a]

a(*)		b(*)	
r^2	Slope (FRC, min^{-1})	r^2	Slope (FRC, min^{-1})
0.862	-2.90×10^{-3}	0.977	-3.21×10^{-3}

[a]At the 60th and 90th min, values *a* were evaluated; *b* were not evaluated.

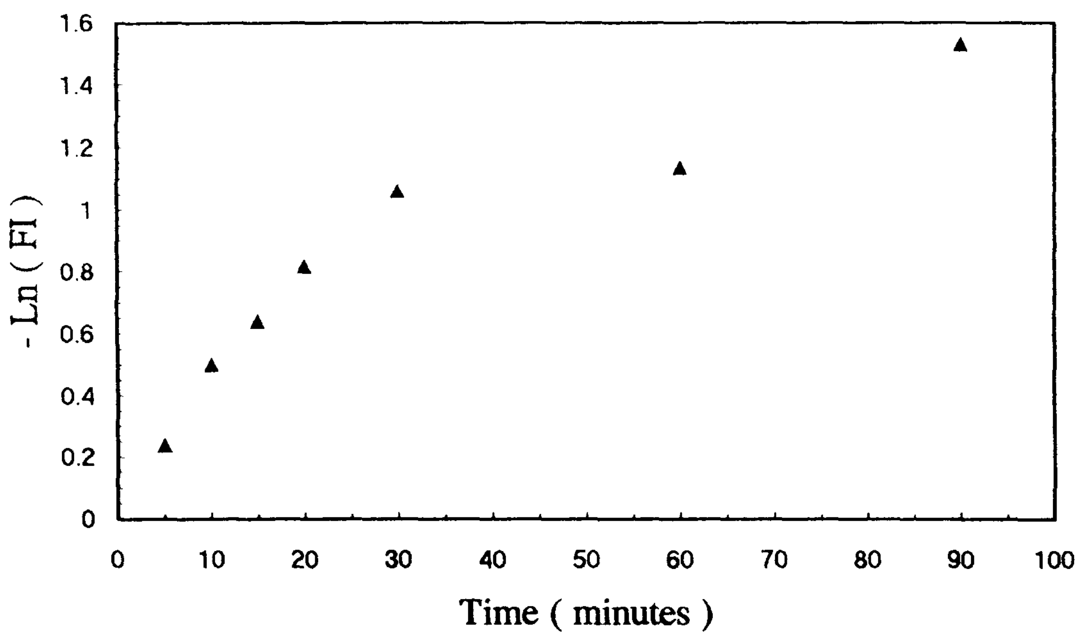

Figure 1. A variation of Ln (FI) values depending on time (at the 60th and 90th min values *a* were evaluated; *b* were not evaluated).

Table 3

Bulk and Consolidated Densities of FR and UFR Granules, and HF Values

Briquette Granule	Bulk Density (g/cm^3)	Consolidated Density (g/cm^3)	HF
UFR	0.46	0.66	1.43
FR-5	0.48	0.62	1.30
FR-10	0.45	0.63	1.41
FR-15	0.45	0.67	1.52
FR-20	0.48	0.71	1.47
FR-30	0.44	0.63	1.43
FR-60	0.43	0.65	1.52
FR-90	0.42	0.70	1.67

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Table 4

Consolidation Parameters of UFR and FR Granules

Granule Type Tested	Slope	r^2	HF
UFR	$0.117 \pm 3.14 \times 10^{-3}$	0.979	1.43
FR-5	$0.114 \pm 6.02 \times 10^{-3}$	0.910	1.32
FR-10	$0.117 \pm 7.82 \times 10^{-3}$	0.860	1.43
FR-15	$0.126 \pm 6.79 \times 10^{-3}$	0.881	1.59
FR-20	$0.143 \pm 9.48 \times 10^{-3}$	0.866	1.49
FR-30	$0.157 \pm 11.1 \times 10^{-3}$	0.853	1.45
FR-60	$0.183 \pm 10.5 \times 10^{-3}$	0.896	1.52
FR-90	$0.193 \pm 13.5 \times 10^{-3}$	0.851	1.67

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Reduction in particle size resulted in proportional increments in slopes. This is evidence that the consolidation of powder mass was influenced negatively by an uncontrolled alteration in the size and distribution of the particles. The declined slope in consolidation results in an increase of the punch distance and in uncontrolled changes in compressing properties of the tablets (2,12). The consolidation relationship between UFR and FR is shown in Fig. 2.

Compressibility properties of briquette granules P_y values obtained from the Heckel equation did not change much because particular grinding has not caused any significant increase of P_y values. According to P_y values obtained from the Heckel equation, compressibility properties of briquette granules after the friabilator process did not change. Stability of r^2 values from the Heckel equation also confirmed the data of P_y values. Also, this can be seen in the Kawakita equation of a values because a change in a value shows a change in the initial porosity of bulk powder. However, there is not a great change in a values (Table 5).

Finally, mechanical strength of briquette granules when investigated kinetically, are reasoned positively. Kinetic order of the reaction, like in the milling process,

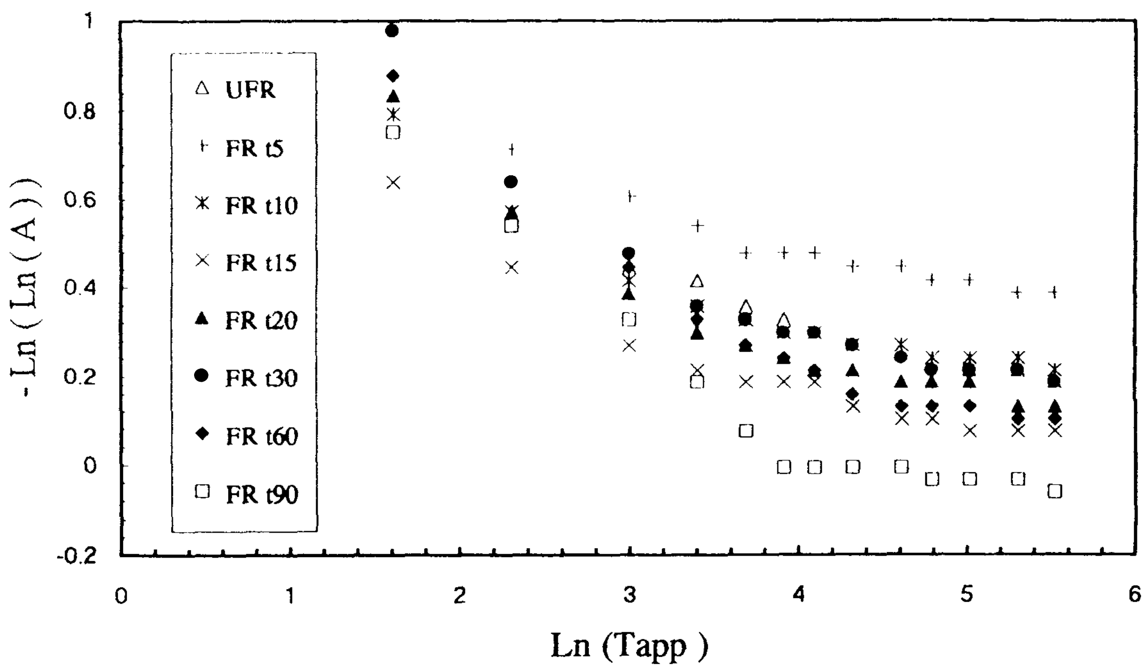

Figure 2. The consolidation relationship between UFR and FR.

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Table 5

Compressibility Parameters of the Granules According to the Heckel and Kawakita Equations

	Heckel		Kawakita	
Granule Type Tested	r^2	$P_y(\text{kgf} \cdot \text{cm}^{-2})$	r^2	$a \times 10^{-1}$
UFR	0.909	419	0.999	7.31
FR-5	0.884	955	0.999	7.24
FR-10	0.944	645	1.000	7.42
FR-15	0.985	603	1.000	7.64
FR-20	0.920	219	1.000	7.44
FR-30	0.919	434	1.000	7.55
FR-60	0.942	539	1.000	7.68
FR-90	0.848	422	1.000	7.50

is a first-order reaction. Briquette granules unlike the granules obtained by wet granulation, do not have binding bridges, so the grinding is substantiated by only superficial milling, not by breaking the bridges. Friability phenomena in briquette granules is only effected to the consolidation stage, but any negative effect in the compressibility is concluded.

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