AAPS PharmSciTech, Vol. 10, No. 2, June 2009 (© 2009)
DOI: 10.1208/s12249-009-9225-2

Research Article

Comparison of the Halving of Tablets Prepared with Eccentric and Rotary Tablet Presses

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Received 17 December 2008; accepted 1 March 2009; published online 21 April 2009

Abstract. The aim of this study was to compare the densification of powder mixtures on eccentric and rotary tablet presses and to establish relationships with the halving properties of the resulting scored tablets. This is an important problem because the recent guidelines of EU require verification of the equal masses of tablet halves. The models of Walker, Heckel, and Kawakita were used to describe the powder densification on the two machines. The calculated parameters revealed that the shorter compression cycle of rotary machines results in poorer densification and lower tablet hardness at a given compression force. This is manifested in poorer halving properties, which are influenced mainly by the hardness. Better densification improves the halving even at lower tablet hardness. This demonstrates that these parameters can be good predictors of tablet halving properties.

KEY WORDS: direct compression; halving; Heckel analysis; Kawakita analysis; Walker analysis.

INTRODUCTION

Tablets are the most common dosage form in medicine. For the individual therapy of patients, it is important to vary the dose. In the pharmaceutical industry, this problem is often solved through the production of scored tablets. A difficult problem associated with the use of such tablets is to ensure their breaking into equal halves. This is a multi-factorial problem, the solution of which must be verified in accordance with the EU guidelines.

Numerous parameters can influence the structure of tablets, and this in turn exerts effects on the breaking. The properties of the compressed materials, the shape of the punches, and the type of the tablet press, for instance, all influence the halving properties. Powder densification is not achieved in a uniform manner with the different tablet presses: With eccentric machines, only the upper punch is active during the compression, whereas with rotary presses, both punches penetrate in the die, and the compression time is shorter as compared with eccentric presses. For both types of machines, the measurement of axial forces is relatively easy through the application of strain gauges; however, the determination of the displacement is easier with eccentric machines because it is influenced only by the movement of the upper punch. The productivity of eccentric machines is much less than that of rotary machines, so they are not use in industrial production. However, the deformation and densification properties of materials can be studied very well with these presses, and it is therefore very important to establish relationships between the densification performances of the machines and to predict the behavior of materials on rotary presses.

In the past century, many different models have been proposed with which to describe the densification of materials during compression. The first model was developed by Walker (1), whose analysis is based on the reduction in volume of the powder bed as a function of the logarithm of the applied compression force.

The model devised by Heckel (2,3) is based on the theory that there is a linear relationship between the behavior of materials and the compression force during the compaction and thus between the densification and the pressure. Despite some critical observations (4), this model is probably the most widely used in pharmaceutical technology (5–8), often in comparison with other models (9–12), such as the Kawakita equation, developed 10 years later (13,14). In this latter model, the volume reduction at the applied pressure is described as a function of the pressure. In most of the publications, the data measured in the die are used in the calculations. Busignies *et al.* (15) studied the compaction behavior of granular lactoses, comparing the results of the Heckel equation measured with in-the-die method with those calculated from the properties of the ejected tablets, i.e., with the out-of-the-die method. In our study, we have also used this latter model to compare the densification on eccentric and rotary presses, for which Palmieri *et al.* (16) applied the in-the-die-method.

MATERIALS AND METHODS

Binary mixtures of microcrystalline cellulose (Vivapur 102, J. Rettenmeier & Söhne, Germany) and spray-dried mannitol (Pearlitol SD 200, Roquette Pharma, France),

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lubricated by the addition of 1% of magnesium stearate (Ph. Eur.), were compressed (Table I).

The powders were mixed with a Turbula mixer (Willy A. Bachofen Maschienenfabrik, Switzerland; 8 min+2 min after the addition of the magnesium stearate, 50 rpm).

The flow properties of the materials and mixtures were determined with a PharmaTest PTG-1 powder rheological tester (Pharma Test Appartebau, Germany).

The compaction behavior of the materials was tested with an Engelsmann stampfvolumeter (JRS Pharma, Germany).

A Korsch EK0 (E. Korsch Maschienenfabrik, Germany) eccentric and a Ronchi AM8S (Officine Meccanice F.lli Ronchi, Italy) rotary tablet press mounted with strain gauges and an eccentric press with a displacement transducer of the upper punch were applied for tablet compression, with flat single punches 8 mm in diameter and with a bisecting line.

The hardness of the resulting tablets was measured with a Heberlein tablet hardness tester (Heberlein & Co. AG, Switzerland).

For measurement of the force required to break the tablets into halves, a laboratory-constructed hardness tester was utilized (Fig. 1), using three-bend tablet hardness testing. The tablet must be centered under the breaking item, which moves vertically down. The load is detected with a computer-connected measuring cell, which is placed under the sample holder.

The true densities of powders and tablets were determined with a Quantachrome helium stereopycnometer (Quantachrome GmbH., Germany).

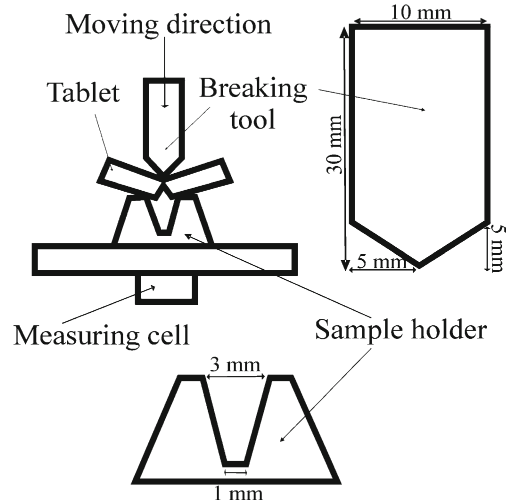

Fig. 1. Schematic figure of laboratory constructed tablet hardness tester

RESULTS

The primary aim of this work was to study the densification behavior of binary powder mixtures of two widely used pharmaceutical excipients on eccentric and rotary tablet presses. We used the models of Walker, Heckel, and Kawakita to describe the powder densification and sought relationships with the halving properties of the tablets. The dry binder microcrystalline cellulose Vivapur 102 and the filler material spray-dried mannitol (Pearlitol SD 200) were mixed in different ratios, as indicated in Table I. The results of the preformulation tests for these materials and their mixtures are presented in Table II. The anisometric particles of Vivapur 102 (Fig. 2) exhibited poor flow properties during powder rheological tests, and this resulted in lower bulk density values. The rearrangement of the particles was irregular but took place quickly in response to tapping, giving rise to an exponential-type rearrangement profile. The results with Pearlitol indicated that this material can greatly improve the poorer properties of Vivapur. It displays excellent flow properties, and the isometric particles (Fig. 3) demonstrate linear rearrangement behavior. The properties of the different powder mixtures varied between the end points of the two component materials. An increasing quantity of Pearlitol improved the compactibility of the powder, but the cohesiveness decreased, which resulted in lower inter-particulate binding forces. This may be due to a lower number of contact points between the isometric particles. These parameters were calculated from Eq. 1, described by Kawakita *et al.* (17):

$$N/C=[N/a+1/ab] \quad (1)$$

where N is the number of taps applied for powder densification, while a and $1/b$ are constants referring to the compressibility and cohesiveness, respectively. C is the volume reduction, which can be calculated via the following equation:

$$C=[(V_0-V)/V_0] \quad (2)$$

where V_0 is the initial volume of the powder bed, and V is the current volume of the powder after a given number of taps.

Equation 1 is a modification of Eq. 3, which was proposed by Kawakita and Lüdde in 1971 to describe powder densification behavior during compression:

$$P/C=[P/a+1/ab] \quad (3)$$

where P is the applied pressure and C is calculated according to Eq. 2, where V is now the volume of the powder bed at the applied pressure.

We determined the Kawakita constants from the data on samples compressed at 5, 10, or 15 kN, plotted according to the out-of-the-die method. The values of constant a decreased on elevation of the Pearlitol quantity, as an indication of the better rearrangement of the particles during compression, which corresponds to the preformulation data (Table III). The values of the constant a are very similar for the two tablet machines, suggesting that it depends only on the properties of the materials. In contrast, the values of $1/b$, which varied characteristically with the composition in the preformulation tests, displayed a minimum at a mass ratio of 50:50. This means that, at this ratio, the lowest energy is needed to reduce the volume of the powder to half of the original. This may be due to the better utilization of the

Table I. Compositions of Powder Mixtures

Sample[a]	Vivapur 102 (%)	Pearlitol SD 200 (%)
1	90	10
2	70	30
3	50	50
4	30	70
5	10	90

[a] The mixtures were lubricated by the addition of 1% Mg-stearate

Table II. Preformulation Results on Materials and Mixtures

Parameter	Vivapur 102	1	2	3	4	5	Pearlitol SD 200
Flow time (s)	4.9	4.5	4.2	4.3	3.6	3.1	3.1
Angle of repose (deg)	31.7	30.1	28.8	26.7	24.8	23.5	22.8
Bulk density (g/cm^3)	0.39	0.46	0.53	0.65	0.76	0.83	0.73
Hausner factor	1.37	1.24	1.25	1.19	1.15	1.07	1.12
Carr index (%)	26.76	19.34	20.27	15.67	12.67	6.27	10.40
Compactibility	0.03	0.02	0.02	0.02	0.01	0.01	0.01
Cohesiveness	2.93	1.99	1.89	1.68	0.59	0.31	0.92

transmitted energy, which can be a result of the lower adhesion and friction of the particles on the die wall. This reduces the loss of the energy during the process, so a bigger proportion of the demanded energy is assigned to the volume reduction. Overall, the less energy investment is needed at this ratio to given volume reduction. This effect is corresponding with the results of other calculations discussed below. Figure 4 reveals that the intercepts of the plots obtained with the two machines are different: the calculated *1/b* values are two- to threefold higher for the rotary press. This suggests that the shorter compression time and the simultaneous action of the two punches result in a lower volume reduction for rotary presses at a given compression pressure. With the rotary press, a local minimum can be observed in factor *1/b* also at ratio 10:90. A possible explanation of this phenomenon can be that the different compression mechanism of the rotary press results to a better rearrangement of particles at this ratio as on eccentric press.

Optimum points are also observed in the results calculated from the Walker equations:

$$\log P = -LV + C_1 \quad (4)$$

$$100V = -W \log P + C \quad (5)$$

where P is the applied pressure, V is the relative volume, calculated as V'/V_0, *i.e.*, the ratio of the volume at the applied pressure and the initial volume of the powder bed, and C and C_1 are constants. The coefficient L is the pressing modulus, which can be calculated from Eq. 4. It likewise exhibits a maximum at a ratio of 50:50 (Table III), reflecting the smallest volume reduction at a given pressure at this ratio. This also may be due to the better utilization of the transmitted energy. As a result of the already low-energy investment, strong bonds are formed between the particles. This is supported by the small value of the coefficient W at this ratio (Table III), which shows the percentage volume reduction when the pressure changes on a logarithmic scale. Thus, the increase of the compression force causes only a minor further volume reduction because almost the biggest possible bonding forces have developed already at lower ones. A difference can be seen in the slopes of the Walker plots relating to the eccentric and rotary presses (Figs. 5 and 6).

We also used the equation developed by Heckel to acquire more information concerning the powder densification (Fig. 7):

$$\ln(1/1 - D) = KP + A \quad (6)$$

where D is the relative density of the tablet (calculated as the ratio of the apparent density of the tablet and the true density of the powder) at pressure P, while K and A are constants. The reciprocal of constant K is the mean yield pressure (P_y). Constant A gives the densification of the powder due to the

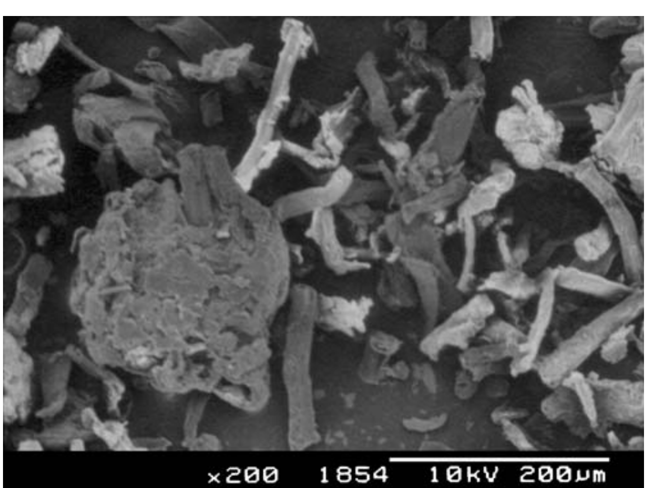

Fig. 2. SEM picture of Vivapur 102

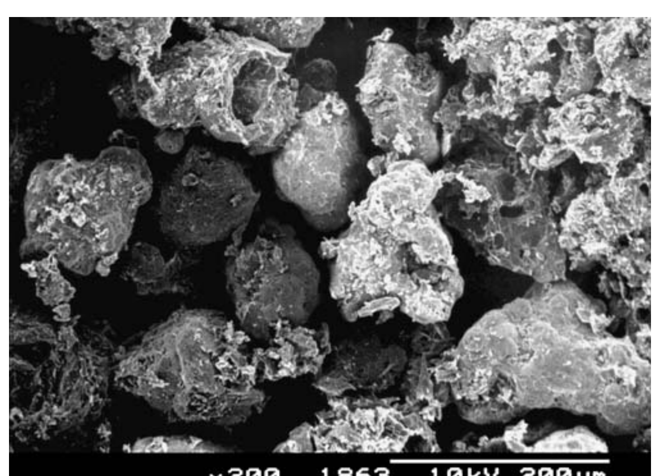

Fig. 3. SEM picture of Pearlitol SD 200

Table III. Parameters of the Different Equations Calculated from Linear Regression Analysis

	Heckel			Kawakita		Walker	
Sample	P_y	D_a	D_b	*a*	*1/b*	*W*	*L*
Eccentric press							
1	217.391	0.775	0.506	0.732	6.907	6.409	15.549
2	196.078	0.782	0.489	0.709	6.088	5.468	17.517
3	217.391	0.775	0.465	0.697	6.267	5.363	18.447
4	256.410	0.785	0.450	0.689	6.863	5.877	17.016
5	312.500	0.779	0.417	0.665	7.649	6.218	15.176
Rotary press							
1	232.558	0.618	0.348	0.727	15.834	14.098	6.534
2	212.766	0.615	0.322	0.701	15.685	13.776	7.116
3	263.158	0.633	0.323	0.687	10.546	9.596	10.364
4	270.270	0.657	0.322	0.691	19.531	14.164	7.035
5	277.778	0.665	0.303	0.671	17.872	14.394	6.278

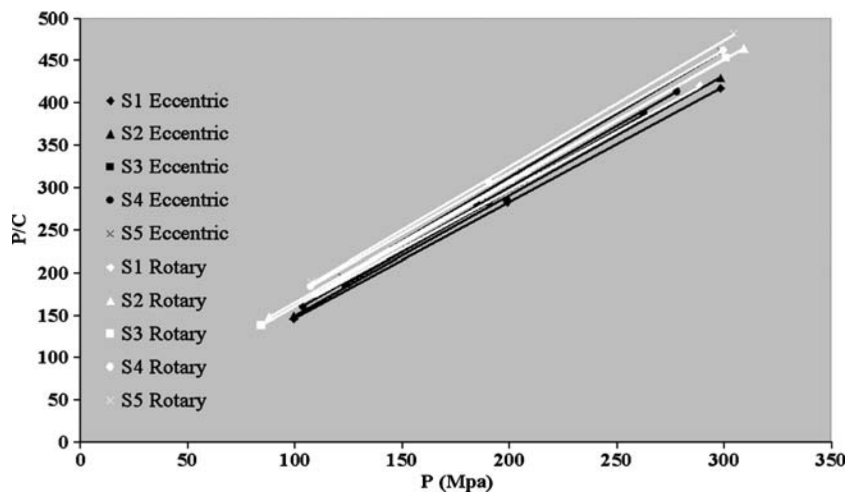

Fig. 4. Kawakita plot calculated with the out-of-the-die method

Table IV. Tensile Strengths of the Tablets (MPa)

	Compression pressure (MPa)		
Sample	100	200	300
Eccentric press			
1	3.626	5.702	6.038
2	2.384	3.759	4.642
3	1.952	2.670	3.385
4	1.168	2.020	2.861
5	1.231	2.056	2.919
Rotary press			
1	1.280	3.576	3.807
2	0.941	2.508	3.269
3	0.591	1.748	2.456
4	0.605	1.511	2.275
5	0.537	1.803	2.595

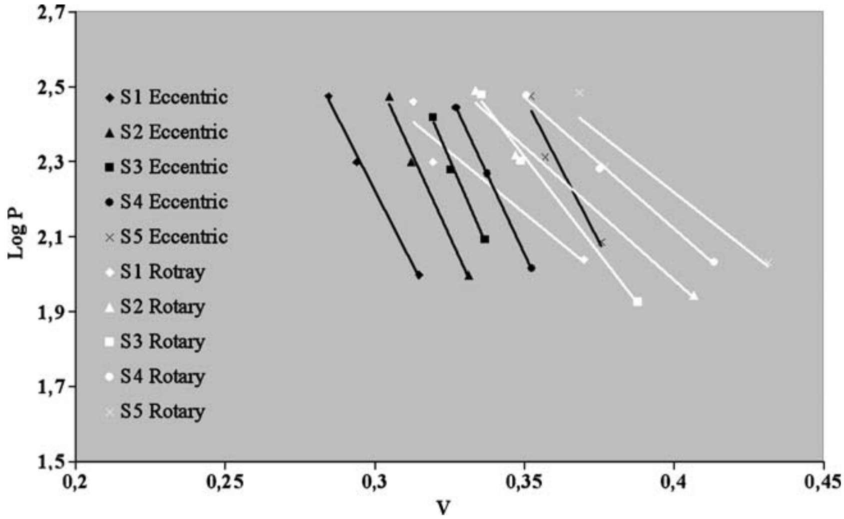

Fig. 5. Walker plot based on Eq. 4

initial rearrangement of the powder bed (D_a) according to the following equation:

$$D_a = 1 - e^{-A} \quad (7)$$

With the application of D_a, the densification due to the fragmentation of particles (D_b) can be calculated:

$$D_b = D_a - D_0 \quad (8)$$

where D_0, related to the initial die filling, is defined as the apparent density of the powder bed at zero pressure.

As compared with the other methods, Heckel analysis does not give such unanimous results (Table III). The mean yield pressure does not display a characteristic change; the differences between the machines are clear. The larger values of D_a and D_b demonstrate that a greater proportion of the particle densification is due to the initial rearrangement and particle fragmentation in the eccentric press. The differences in initial rearrangement and fragmentation may result from the differences in the method of die filling and the compression cycle.

The parameters discussed above all influence the post-compressional properties of tablets. Table IV demonstrates that the tensile strength is almost two times higher for the tablets formed with the eccentric press. It can be seen that the tensile strength decreases with increasing amount of Pearlitol, the small adhesion and cohesion forces and the fewer contact points between the particles greatly reducing the tablet hardness. This parameter is probably the most important influencing factor of the breaking. A strong relationship can be observed between tensile strength of tablets and halving properties (Table V). The results suggest that tensile strength at about 3.00 MPa is required to the acceptable halving on eccentric press, and even higher values are necessary on rotary one.

DISCUSSION

The primary aim of this study was to establish relationships between powder densification on different tablet presses and the halving properties of the resulting tablets. The calculations with the equations suggest that the longer

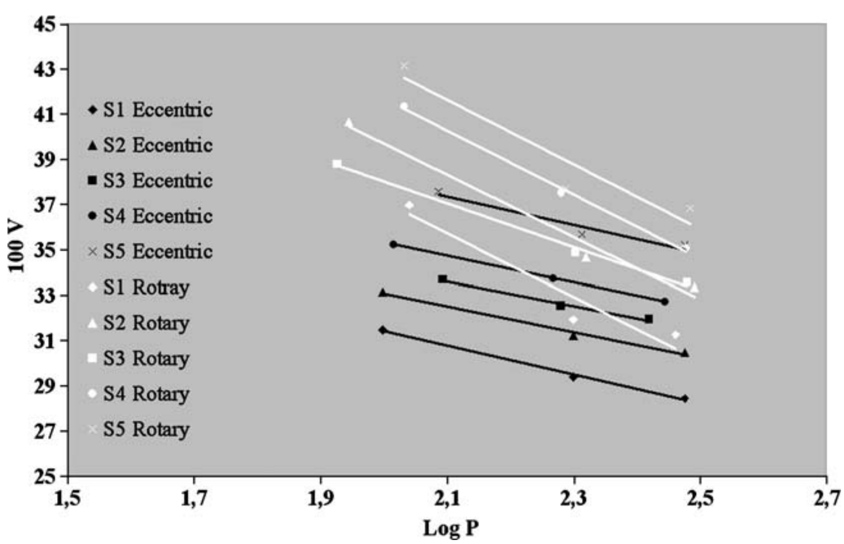

Fig. 6. Walker plot based on Eq. 5

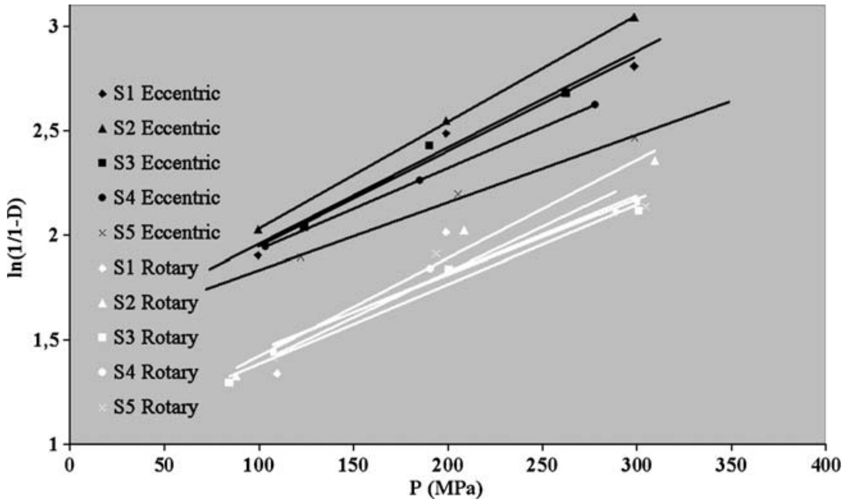

Fig. 7. Heckel plot based on the out-of-the-die method

time of compression causes a two- to threefold higher stress on use of the eccentric machine at the same compression force. This causes a greater proportion of particle fragmentation, but the bonding between particles becomes much stronger, resulting to greater hardness.

The tablet hardness and the properties of the materials are strongly related to the breaking properties of the tablets. Postcompressional examination of the halving of the scored tablets is very important because it is necessary to verify it in the pharmaceutical file. The axial stress acting on the bisecting line gives rise to elastic stresses in the tablets, resulting in different degrees of deformation, depending on the properties, deformability, and bonding of the tablets. In this case, elastic deformation is advantageous. The change in the deformation can be measured through the application of strain gauges. When the elasticity predominates, the force–time curve rises with increasing axial stress and collapses at the moment of breaking of the tablet (Fig. 8a). The tablets break well when the masses of the two halves are closely similar. We chose a 50±5% tolerance limit in this study. The breaking result depends mainly on the hardness of the tablets and was better at higher tensile strength. However, it is additionally influenced by the internal structure of the tablets.

Table V. Amounts of Well-halved Tablets

	Compression pressure (MPa)		
Sample	100	200	300
Eccentric press			
1	50%	90%	100%
2	50%	100%	60%
3	60%	100%	80%
4	50%	80%	70%
5	30%	80%	90%
Rotary press			
1	10%	30%	40%
2	0%	10%	40%
3	0%	10%	30%
4	0%	0%	0%
5	0%	0%	10%

When the tablet hardness is low or internal structural defects exist, the breaking surface crumbles or the tablets break into more than one piece. The new breaking surfaces are associated with extra stress that does not act on the bisecting line. This type of breaking often proceeds through several steps, which are seen in the curves as extra peaks (Fig. 8b). When the structure of the tablet is free from defects, a lower tensile strength may be sufficient for good breaking, as in the case of sample 3. The results allow the conclusion that the tablet hardness must be relatively high for good halving. However, when the internal structure of the tablets is free from defects, a lower hardness may be sufficient. Nevertheless, the application of a higher compression force on a rotary

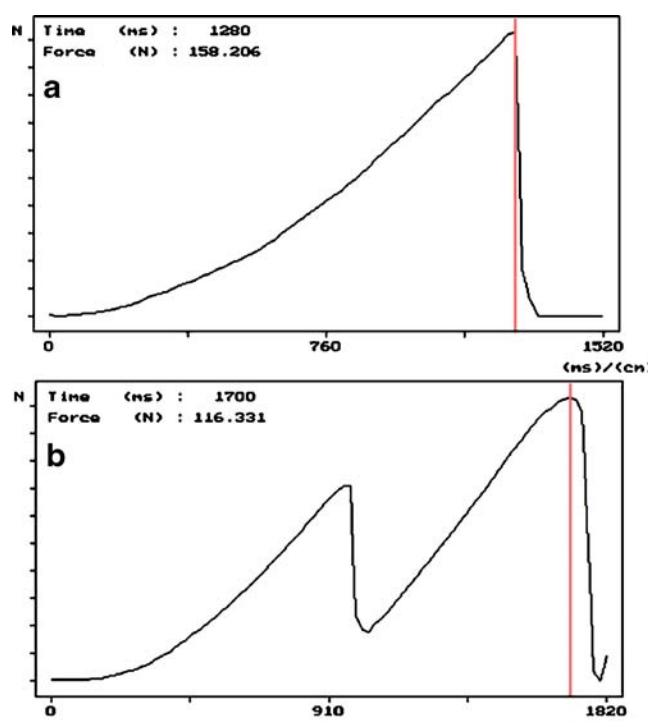

Fig. 8. Breaking curves of a well-halved (**a**) and a not-well-broken tablet (**b**)

machine is needed to equal the better results on tablets compressed on eccentric machines. No structural defects are formed during compression when the powder is well compressed and undergoes low adhesion to the die wall, and the bonding between the particles is formed quickly. The models of Walker and Kawakita describe these processes better than the Heckel model and furnish a better prediction of the halving properties. The results obtained with the Heckel equation should be utilized with caution.

CONCLUSIONS

Overall, it can be stated that the properties and the densification behavior of the powders strongly influence the halving properties of scored tablets. The relationships between the densification behavior of powders and the applied compression force can be characterized well with the use of the equations of Heckel, Walker, and Kawakita. They also can give useful information to the comparison of the behavior of materials on different tablet presses. Comparing these results, with the properties of compressed tablets, conclusions can be drawn about the probable halving properties.

ACKNOWLEDGMENT

The work was supported by a Sanofi-Aventis scholarship.

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