DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 19(15), 1917-1930 (1993)

FORCE-TIME CURVES OF A MODERN ROTARY TABLET MACHINE II. INFLUENCE OF COMPRESSION FORCE AND TABLETING SPEED ON THE DEFORMATION MECHANISMS OF PHARMACEUTICAL SUBSTANCES

Peter J. Vogel and Peter C. Schmidt[1]
Pharmazeutische Technologie der Universität Tübingen
Auf der Morgenstelle 8
D-7400 Tübingen

ABSTRACT

Investigations on the compaction mechanisms of pharmaceutical substances using an evaluation method for force-time curves of a rotary tablet machine are presented. The machine speed is shown to have only little influence on the compaction behavior. Looking at the compression force, not only a quantification of plastic or brittle deformation behavior as well as a detection of elastic relaxation is presented but also a description of the disposition to porosity reduction.

INTRODUCTION

The segmentation of force-time curves into periods according to the punch head geometry and the following punch movements is enabled by the registration of the signal of an inductive sensor parallel to the registration of the force signals.

Each compression event consists of three parts. The first one is the compression phase, when punches are penetrating into the die caused by the movement of their head curvature in contact with the pressure rollers. The second one is the dwell time, when no vertical punch movements occur while the flat punch tops are moving over the

[1]to whom correspondence should be addressed

compression rollers. In the third phase, the relaxation phase, the punch heads are leaving the pressure rollers.

The middle of each compression event is indicated by a switch point of the registered signal of an inductive sensor. It occurs exactly when the centers of the punches and compression rollers are in line. The dwell time is calculated using the known punch geometry and the velocity, which is given by the distance of the switch points and the sample rate of the analog/digital-converter. The compression and relaxation phase are the time from the beginning of the force signal until the beginning of the dwell time and from the end of the dwell time until the end of the force peak respectively.

When maximum punch penetration is achieved at the beginning of the dwell time, any loss of compaction force in the following period without vertical punch movement must be caused by plastic deformation of the tableting material. In case of a totally brittle substance all deformation should occur in the compression phase and compaction force should be kept at a maximum until relaxation phase is reached. For the quantification of the amount of plastic deformation shown by the loss of force the dwell time is divided half. The areas under the force-time curve are calculated for each half. Both areas are decreased by the rectangles under the minimum compaction force in the dwell time. The remaining areas are called A5 and A6.

The quotient A6/A5 is an easy to handle parameter for the quantification of the deformation mechanism. Figure 1 depicts a hardcopy printout of the evaluation by a computer program.

MATERIALS

Table 1 comprises the materials used in the examinations. They are mixed with 1% of magnesium stearate for 15 minutes in a rotating drum mixer type "Rhönrad".

METHODS

The registration of force-time curves and the signal of an inductive sensor as a timebase for each compression event is described in an earlier paper [1].

For the examination of material behavior eight widely used substances are compressed. With the exception of acetaminophen always five different levels of compression speed from 25 up to 125 rpm and a variety of compression loads over a relevant range up to 25 kN (318 MPa), partially up to 40 kN are used. For the registration of the data sample rates of 11.111 kHz at velocities up to 75 rpm and of 22.222 kHz at higher speeds are used.

Usually a relative standard deviation of the compression forces of less then 3% is found. Only very low forces lead to higher values. All parameters derived from the curves are in the same or in a lower range of variation. At each level of compaction force between 150 and 450 compression events are registered, dependent on machine velocity, each with 500 in minimum up to 1500 data points.

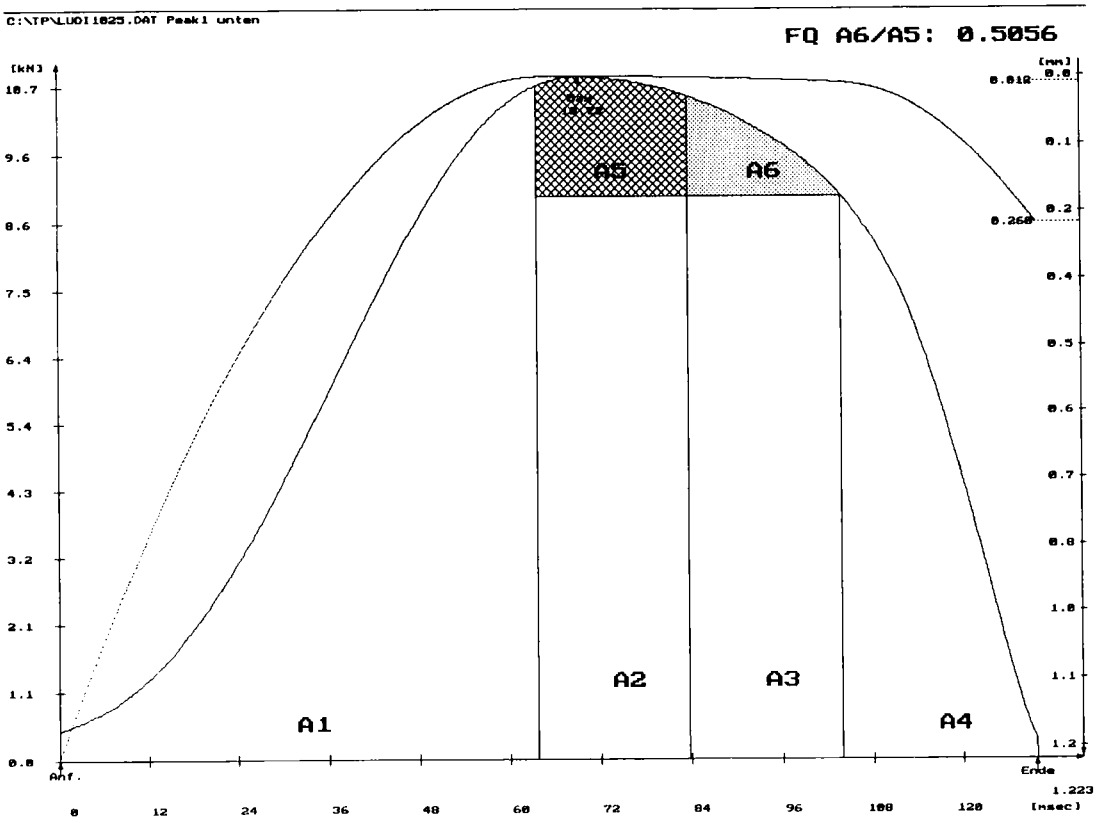

FIGURE 1
Hardcopy printout of a force-time peak of the compression of Ludipress with the areas used for the quantification of the deformation behavior

RESULTS AND DISCUSSION

Influence of velocity on the deformation behavior

The influence of the velocity on the plastic or elastic deformation behavior of the examined substances, described by the quotient of the areas A6/A5, is shown in the following pictures. Figure 2 presents the quotient for Starch 1500 as a function of compaction load at five different machine speeds ranging from 25 to 125 rpm. While there is only little influence of the machine speed on the quotient A6/A5, the compaction load has an unambiguous effect.

A comparison of the behavior of the different materials at a given compaction load is shown by figure 3, where interpolated values for a compression force of 10 kN are

TABLE 1

Material:	Supplier:
Avicel PH 101 (microcrystalline cellulose) Ch.-B.: 6943	FMC Co. distributed by: Lehmann & Voss & Co, D-2000 Hamburg 36
Bekapress D2 (hydrous dibasic calcium phosphate $CaHPO_4 \times 2\ H_2O$) Ch.-B.: 7 5132 230 / 36 90 7	BK-Ladenburg GmbH, D-6802 Ladenburg
Cellactose (cellulose / lactose - agglomerate) Ch.-B.: 065	Meggle Marketing GmbH, D-8090 Wasserburg 2
Karion Instant Pharma (spray dried sorbitol) Ch.-B.: M 374 303	Merck, D-6100 Darmstadt
Ludipress (α-lactose-monohydrate / povidone 30 / crospovidone) Ch.-B. 560191	BASF AG, D-6700 Ludwigshafen
Magnesium stearate Ch.-B.: 190151	Otto Bärlocher GmbH, D-8000 München
Paracetamol DC (acetaminophen, granulated with 3% povidone 30) Ch.-B.: 284VN1015	Mallinckrodt Speciality Chemicals (U. K.) Ltd., GB-Chesterfield
Starch 1500 (pregelatinized starch) Ch.-B.: 102046	Colorcon GmbH, D-6240 Königstein
Tablettose (α-lactose-monohydrate) Ch.-B.: 700	Meggle Marketing GmbH, D-8090 Wasserburg 2

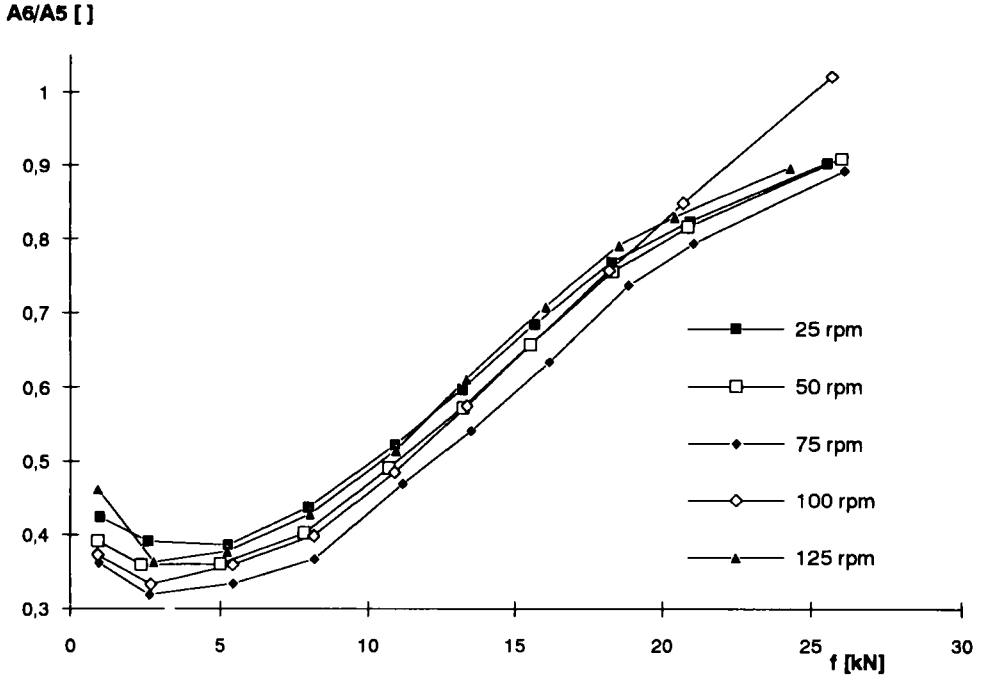

FIGURE 2
Influence of compaction velocity on the quotient of the areas A6/A5 as a function of the compression load for Starch 1500

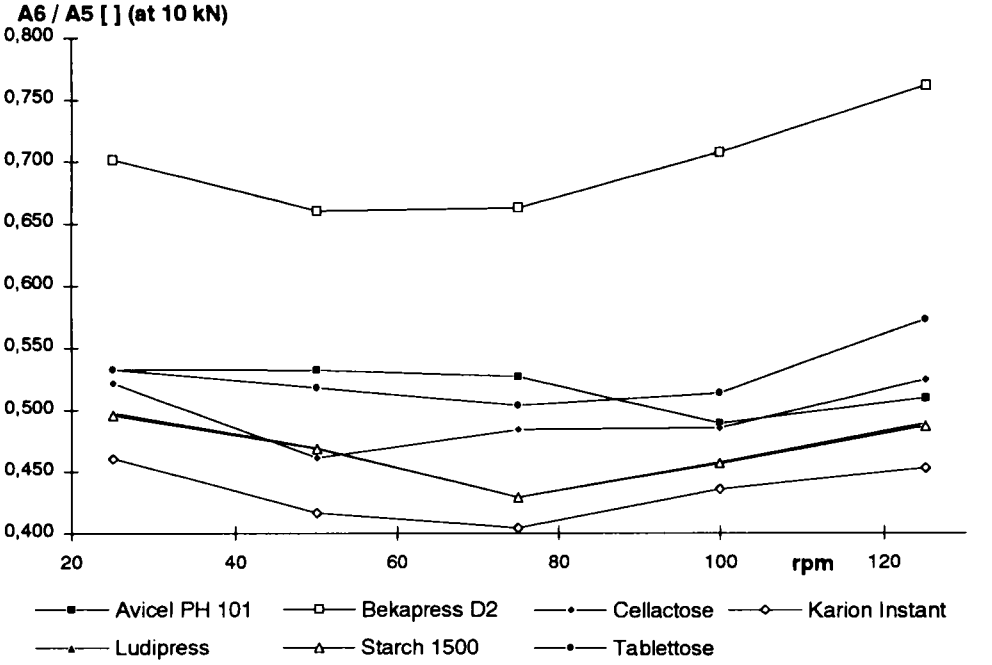

FIGURE 3
Deformation behavior of different substances described by the quotient of the areas A6/A5 for different machine velocities at a compression force of 10 kN (interpolated values)

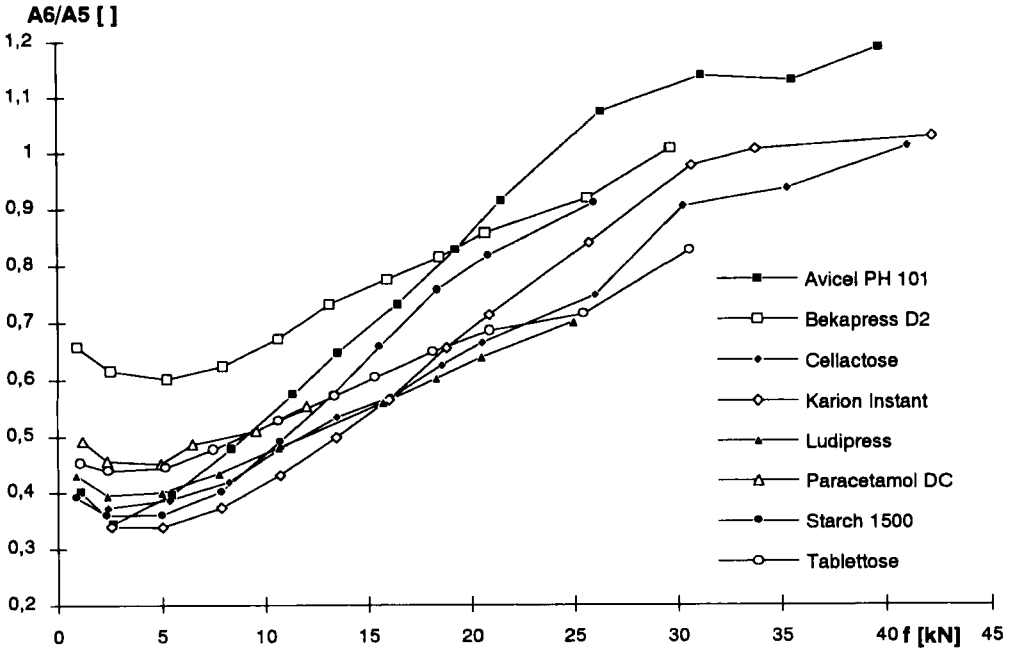

FIGURE 4
Differing response of the quotient A6/A5 to the compaction force for all examined materials at a machine speed of 50 rpm

used. Increasing the machine speed from 25 to 75 rpm a slight decrease of the quotient A6/A5 is found, indicating a more plastic deformation behavior.

At higher velocities of 100 or 125 rpm the quotient is rising again corresponding to a more brittle deformation with the exception of Avicel, which has a lower value at 100 than at 75 rpm. Due to a different and relative low expression of this effect an interpretation is avoided. In opposite to the small influence shown by the machine velocity, the influence of the compaction load seems to be of greater importance.

Influence of the compaction load on the deformation behavior

The influence of the compaction force on the deformation behavior described by the quotient of areas A6/A5 is already shown in figure 2. A survey on the response to the compaction force for different materials is given by figure 4, where a machine velocity of 50 rounds per minute is used.

All materials show a dependency of the quotient on the applied compaction load, but in a different amount. To enable a better differentiation the approximately linear ascending sections of the curves are described by a linear regression. As a result a discrimination into two groups is found both having nearly parallel courses of the resulting straights or matching slopes respectively.

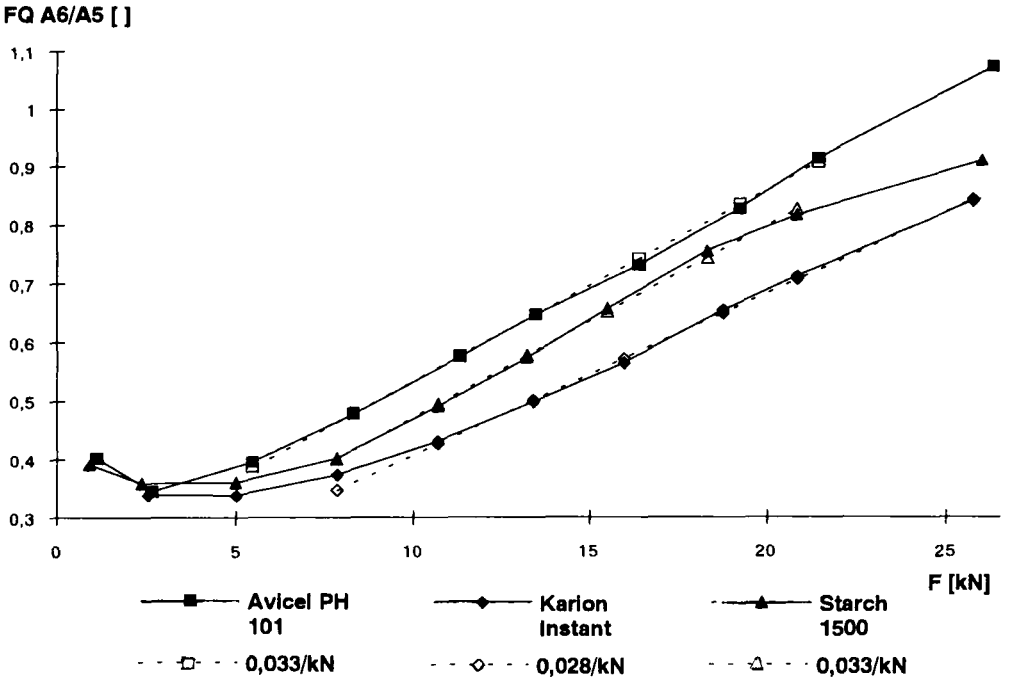

FIGURE 5
Ascending quotient of the areas A6/A5 as a function of the increasing compaction load and regression of the linear part of the curves with the corresponding slopes for plastically deforming substances

The first group includes Avicel PH 101, Starch 1500 and Karion Instant, which are known to deform almost plastically. They are shown together with their regression lines and the corresponding values for the slopes in figure 5. All other substances are combined in the second group and presented in figure 6.

The two facts, the increase of the quotient A6/A5 as a function of compaction load and the differing sensitivity to the force are rather interesting but on the other hand they seem to contradict the validity of the method as a tool for the characterization of the deformation behavior. Therefore it is necessary to give further explanations.

Disposition to porosity reduction

An interpretation can be found regarding the porosity examinations of [2] or [3]. Plastically deforming substances lead to remarkably lower porosities than brittle ones at equivalent compaction loads. As a consequence of reduced porosity, the resistance against further deformation is increasing, followed by a higher portion of elastic deformation. Resulting from this elastic deformation the symmetry of the force-time peak also increases and consequently the quotient A6/A5 comes up to higher values.

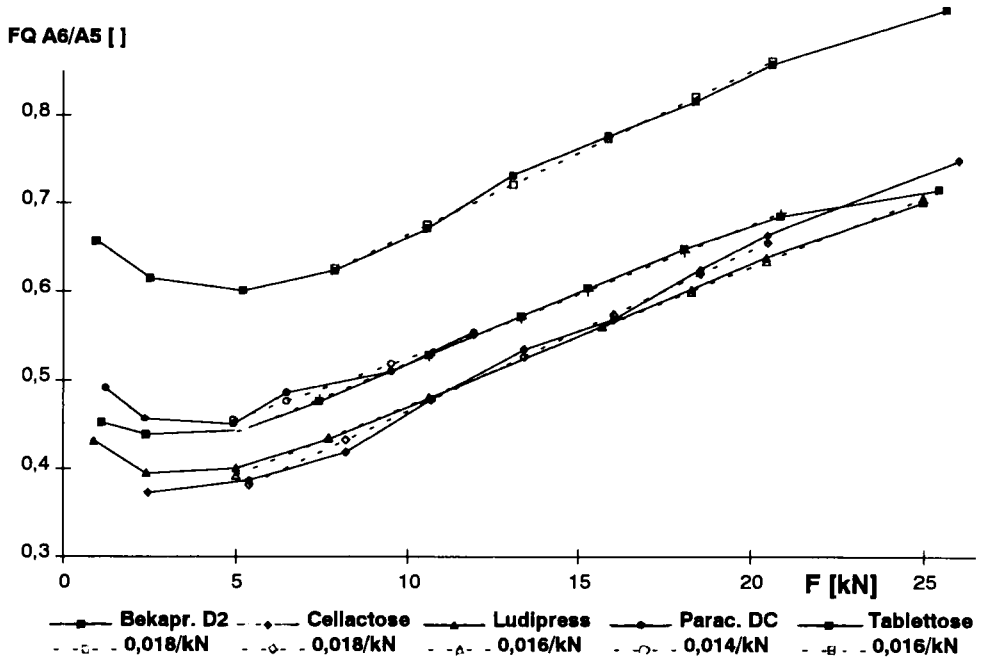

FIGURE 6
Increase of the quotient of the areas A6/A5 with rising compaction load and regression of the nearly linear part of the curve for the remaining substances (differing y-scales).

Most of all this is obvious for Karion Instant in figure 4. After the strong increase during compression forces between 30 and 35 kN the slope is declining to a course nearly parallel to the x-axis. The remaining porosity is minimized, a further volume reduction nearly impossible.

The Heckel equation [4] used by the authors named above leads to porosity diagrams, the so-called Heckel plots.

$$\ln \frac{1}{1-D} = K*P + A$$

D is the relative density,
P is the pressure,
1-D is the pore fraction and
K is a proportionality constant.

Equally to the slope K of the Heckel plot, the porosity reduction or the resistance against volume reduction is reflected by the slopes in figure 4. Unlike the method of Heckel in this case no displacement measurement is needed.

TABLE 2:

Quantification of plastic or elastic deformation characteristics by the minimum values found together with the according values of compaction load ordered in the row of increased brittleness; machine velocity 50 rpm

substance	compression force [kN]	quotient of the areas A6/A5	interval of confidence (p = 0.01)
Karion Instant	2.55	0.3389	± 0.00221
Avicel PH 101	2.66	0.3448	± 0.00329
Starch 1500	2.36	0.3593	± 0.00326
Cellactose	2.42	0.3719	± 0.00383
Ludipress	2.39	0.3946	± 0.00311
Tablettose	2.41	0.4386	± 0.00287
Paracetamol DC	4.93	0.4504	± 0.00269
Bekapress D2	5.22	0.6008	± 0.00318

Only at very high compression forces a falsification induced by bending effects of the tableting tools cannot be excluded. The variations in this part of the curve of Avicel PH 101 in figure 4 can be put down to this fact. Values higher than 1 have to be linked up with elastic relaxation expressed here by capping at high forces and velocities.

Another effect, which has to be regarded in connection with the porosity of the compact, is evident in figures 2, 4 and 5. At very low forces all examined substances show a decrease of the quotient down to a minimum. Coincidentally this is the force that is necessary to produce tablets with a remarkable mechanical stability. Lower forces lead to shaped compacts without any measurable hardness. Obviously a change in deformation mechanism comes along with the formation of stable bindings. A reduction of volume by rearrangement of particles cannot appear furthermore. Any additional volume reduction is due to a modification of particles that is fracture or deformation.

The phenomenon of the variation of the slope agrees to the hypothesis of the percolation theory [5] [6] explaining sharp modifications of the properties of compacts by the percolation of components that is the formation of coherent frameworks. This theory defines three so-called percolation thresholds.

The first one is the formation of a compact with bindings of undestructed particles but only minimal stability. This compact is composed of a coherent phase of particles, which is penetrated by the also coherent inner phase, the porosity. Volume reduction can occur by a rearrangement of particles.

At the second threshold an optimum arrangement is reached. The compact cannot be reduced in volume furthermore without a change of shape of the particles. This induces a higher resistance against volume reduction. Modification of the particles occurs as fragmentation or plastic deformation, reducing the volume of the pores.

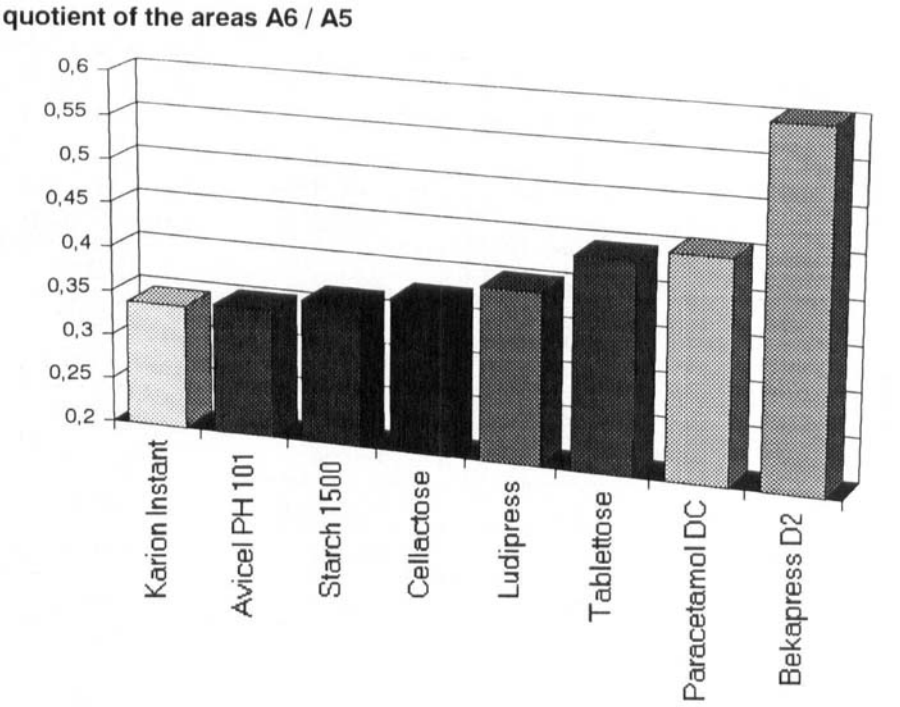

FIGURE 7
Deformation behavior of the examined substances quantified by the minimum of the quotient of the areas A6/A5

A third percolation threshold is reached when the remaining porosity is reduced to such a degree that the pores do not percolate any more.

It is possible to transfer this theory to the curves represented in figure 4. The first threshold is the first formation of a compact, the second one is corresponding to the minimum of the quotient. A third threshold, the deflection point at high compression forces, can be detected particularly for Karion Instant.

Quantification of plastic or elastic deformation

For the differentiation of the substances according to their plastic or brittle deformation type it is necessary to consider the minimum values of the quotient A6/A5 as a result of their different slopes.

Table 2 lists the minimum values of the quotient A6/A5 for the examinations at 50 rpm. Figure 7 presents them graphically. The minimum values and the corresponding forces may not be determined exactly because the compaction forces are chosen in levels of about 1.25, 2.5 and 5 kN. A more distinct examination of this area might lead to slightly decreased values.

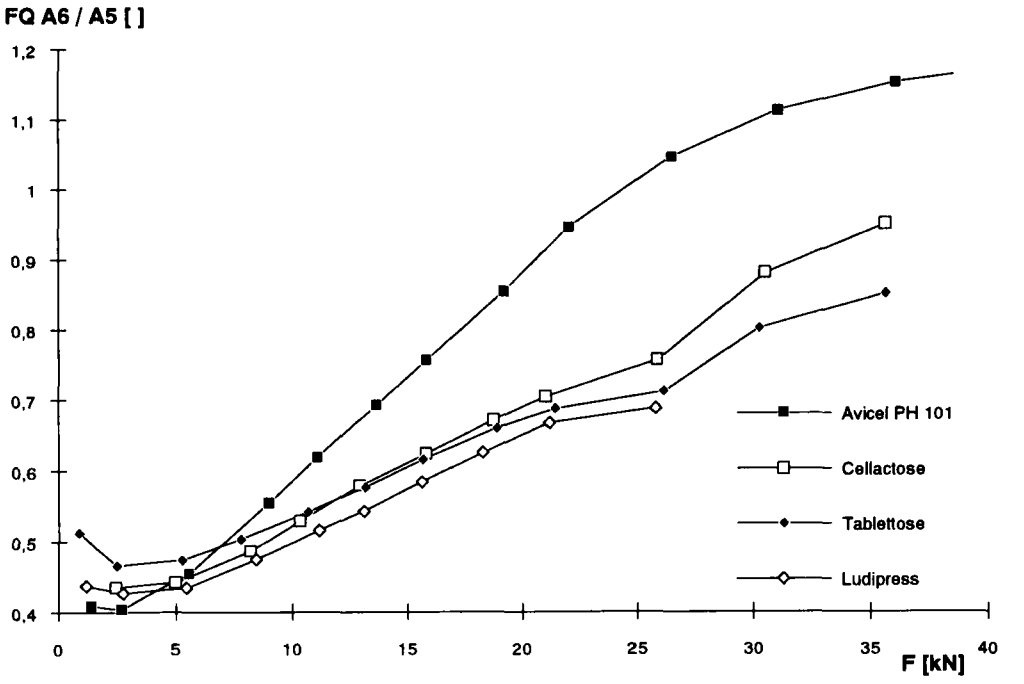

FIGURE 8
Deformation behavior of the coprocessed materials Cellactose and Ludipress in comparison to Avicel PH 101 and Tablettose at 25 rpm

Hence the quotient A6/A5 enables a significant differentiation of the deformation characteristics of the substances. Ludipress, an α-lactose plastified by added PVP, differs clearly from Tablettose. By analogy Cellactose shows characteristics intermediate between Tablettose and the microcrystalline cellulose Avicel PH101, not only at the minimum but also at the entire range of compaction forces, as depicted in figure 8.

In case of Ludipress it is possible to talk, starting from Tablettose, of a parallel shifting of the deformation qualities to more plastic behavior. Cellactose is less plastically than the pure cellulose Avicel. The slope is significantly lower than that one of Avicel but higher than that of Tablettose. The deformation behavior seems to be composed additvely of the corresponding parts of the original materials.

Tendency to elastic recovery

In practice the detection of elastic recovery of the compacts is of same or even greater importance than the definition of the deformation behavior. Very often capping or laminating of the tablets is limiting the production rate of modern high speed machines while variation of tablet weight is only a minor problem, if mechanical forced feeders are used.

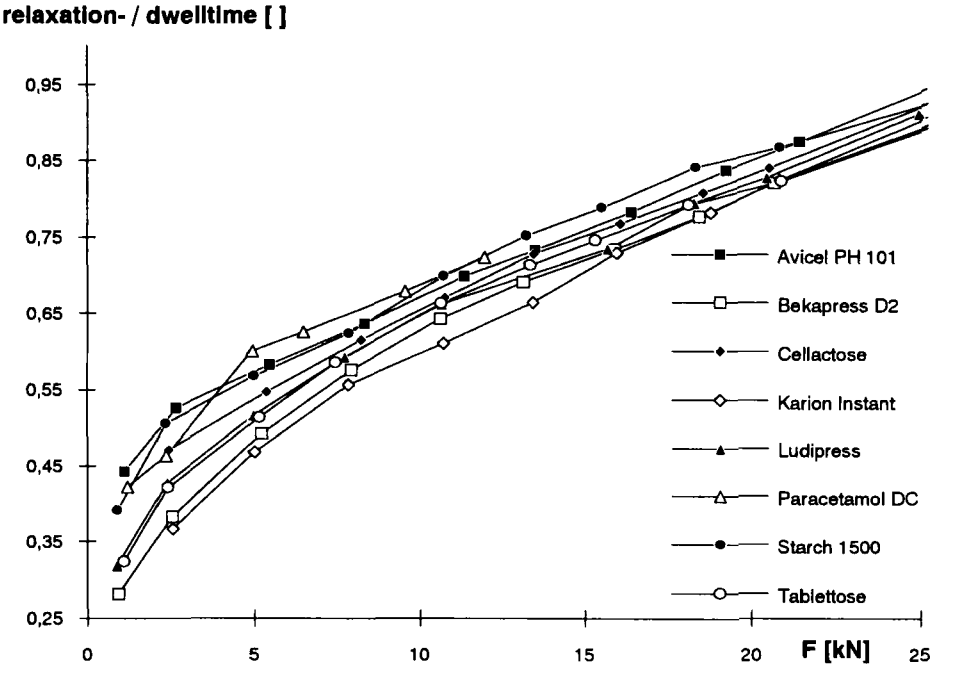

FIGURE 9
relaxation time relatively to the dwell time as a function of compaction force for eight different materials at a machine speed of around 50 rpm

Obviously elastic relaxation occurs during the decrease of the compaction load. Since the acoustic examinations of [7] it is proofed that capping already can occur in the die of the tabletting machine. Hence it is expected that capping tendencies can be recognized by a relaxation phase, which is prolonged in comparison to uncritical tableting processes, or by a sustained decrease of the measured force because of a buffering action of the tablet.

With the aid of the used method of evaluation it is principally possible to calculate the duration of the relaxation phase as a part of the compaction event. In practice, some difficulties arise, because each pair of punches reaches the compression rolls before the proceeding has left it. For this reason the force-time peaks are not totally separated and the detected relaxation time may be shorter than it is in origin. On the other hand the final part of the force-time curve decreases very steep with the consequence that only a very small error can occur.

Figure 9 presents the values of the relaxation time for the different materials as a function of the compaction force. To eliminate the influence of the differences in machine velocity they are calculated relative to the duration of the dwell time.

The highest values are found for Avicel, Paracetamol DC and Starch. In opposite to the latter substances, which are well-known as candidates for capping, it may be

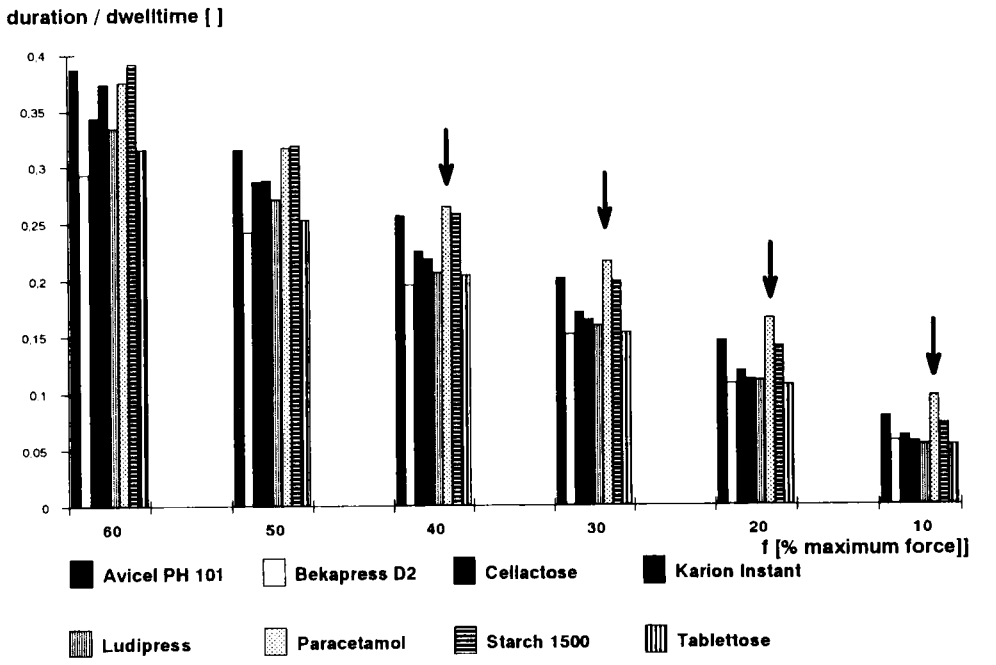

FIGURE 10

Duration of relaxation from different fractions of the maximum compression force to the end of the compression peak relative to the dwell time for different materials at a compression force of 5 kN and a velocity of 50 rpm (Paracetamol DC marked by arrows)

surprising to find Avicel in this series. In fact, in the examinations Avicel turns out to be very problematical at high compaction loads and velocities. The high sensitivity of microcrystalline cellulose against lubricants and the concentration of 1% magnesium stearate used here might be an explanation. Very low values for the relaxation are calculated for Karion Instant and for Bekapress D2, which agrees to the fact that these substances do not show any capping tendencies.

On further consideration it can be demonstrated that the extended relaxation for substances, which show capping tendencies, becomes apparent especially in the last third of the relaxation phase. While there is no difference in comparison with other substances looking at the duration of relaxation from 60 or 50% of maximum force to the end of the compression peak, there is a remarkable prolongation from 30% on.

This leads to the knowledge that only the final part of the compression event is of importance for the detection of excessive relaxation, which is in conflict with the overlapping of the force-time peaks. Therefore this detection of capping tendencies has to be done at low compaction forces preferably, where the overlapping of the peaks is only of minor importance.

CONCLUSIONS

Using a modern data acquisition equipment it is possible to examine the force-time peaks of a rotary tablet press precisely. The additional registration of the signal of an inductive sensor gives the time-base for the division of the compaction event into phases. This enables the separated examination of the material characteristics under increasing, constant or decreasing stress.

The behavior under constant stress is indicating the deformation mechanism, which is quantified by the quotient of calculated areas under the force-time curve. The deformation type does not show remarkable dependence on machine velocity. The influence of the compaction load is interpreted as an increasing portion of elastic deformation. Characteristic changes of the calculated quotient in dependence from the force can be explained with the theoretical reflections of the percolation theory. The resistance against porosity reduction can be derived from the plotted values. A porosity reduction examination is given indirectly, but without any requirement of displacement measurement.

If the part of the compaction event with decreasing force is regarded, knowledge on the elastic relaxation tendencies can be derived. The final part of this phase is shown to be of main importance for the detection of capping trends, which is only in conflict with the fact that compaction events are overlapping, if higher compression forces are used.

ACKNOWLEDGMENTS

We thank the Deutsche Forschungs-Gemeinschaft for financial support of the work as well as O. Bärlocher GmbH, BASF AG, BK-Ladenburg GmbH, Colorcon GmbH, FMC Co., Meggle Marketing GmbH and Fa. E. Merck for the tableting substances.

REFERENCES

1. Part I (in press)
2 M. Duberg, C. Nyström, Acta Pharm. Suec. 19, 421 (1982)
3. M. Çelik and K. Marshall, Drug Dev. Ind. Pharm. 15, 759 (1989)
4 R. Heckel, Trans. Metall. Soc. Aime 221, 671 (1961)
5 D. Blattner, M. Kolb and H. Leuenberger, Pharm. Res. 7, 113 (1990)
6 H. Leuenberger, R. Leu, conference paper on "Sitzung des Fachausschusses 'Agglomerations- und Schüttguttechnik' der GVC-VDI-Gesellschaft Verfahrenstechnik und Chemieingenieurwesen" Würzburg (1992)
7. P. J. Rue, P. M. R. Barkworth, P. Ridgway-Watt, P. Rough, D.C. Sharland, H. Seager and H. Fisher, Int. J. Phar. Tech. & Prod. Mfr. 1, 2 (1979)