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FORCE-TIME-CURVES OF A MODERN ROTARY TABLET MACHINE I. EVALUATION TECHNIQUES AND CHARACTERIZATION OF DEFORMATION BEHAVIOUR OF PHARMACEUTICAL SUBSTANCES

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ABSTRACT

According to the geometry of punch heads and the interdependent punch movements force-time-curves of a rotary-tablet press are divided into periods by the aid of the signal of an inductive sensor. The decrease of compaction load in the interval of the flat punch top is mainly due to plastic flow of the compressed substances. Brittle or plastic deformation behaviour is easily distinguished and quantified by the combination of a standard press and a highly advanced data acquisition and off-line software evaluation.

Additionally it is shown that there is no need to use a complex equipment for displacement measurement to gather reliable data on compaction mechanisms. Even if the machine deformation is considered, calculated displacement data may surpass measured data in precision.

INTRODUCTION

Many attempts to characterize the deformation behaviour of pharmaceutical substances are found in literature. Some of them already gathered critical comments, other investigations lead to better data, but use unpracticable conditions. For example strain movements under constant stress examined with hydraulic presses seem to show only small accordance with material behaviour in a compaction event of a few milliseconds. Thus it is obvious that examinations should occur under production circumstances. Even compaction simulators cannot imitate these condi-

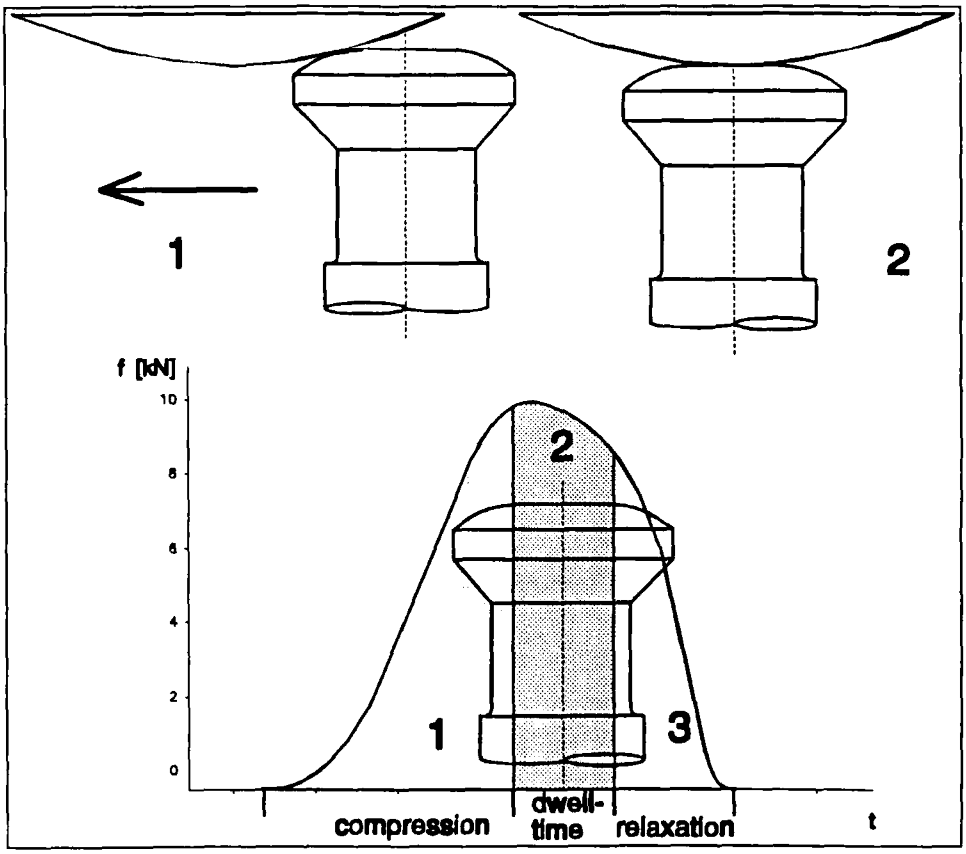

FIGURE 1
Phases of the compression event resulting from punch head geometry and application to the force time curve 1.) Compression: punch head moving against pressure roller. 2.) Dwell time: maximum deformation is kept 3.) Relaxation: punch head leaving pressure roller (similar to 1.)

tions because of their missing filling mechanism and a displacement-time profile calculated without any knowledge of the elastic tablet machine deformation.

In former studies the compression event is divided into periods, such as compression and decompression in case of eccentric-presses, or equivalent at rotary-presses, with an extra dwell-time between these two phases. Figure 1 depicts the intervals of the compression event of a rotary tablet machine.

Commonly the phases are applied on the force-time curves with the aid of a displacement measuring equipment. Despite of the generally low precision of dis-

TABLE 1

Material:	Supplier:
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

placement measurement if compared to the measurement of forces, acceptable accuracy is achieved at reciprocating presses. In case of rotary presses displacement-measurement is accompanied by an unacceptable expenditure and, due to bending effects of the tools, a very high error rate. Additionally it is not possible to work with a complete punch set on rotary machines with installed displacement measuring systems, because space is lost for the commonly used linear variable differential transformers (LVDT's) and a telemetric signal transmission.

The combination of measured force-data with calculated displacement is already published [1] under the assumption of a concurrence in time between maximum force and the beginning of the maximum displacement. The present paper is able to dispense with this assumption and therefore allows certain statements about punch movements at any time.

MATERIALS

The model substances used are listed in table 1. They are mixed with 1 % of magnesium stearate for 15 minutes in a rotating drum mixer type "Rhönrad".

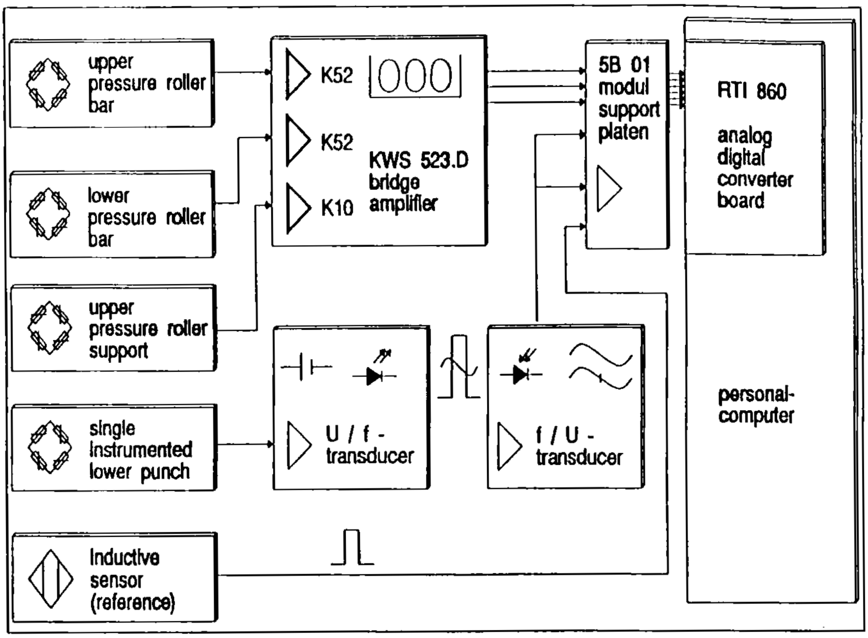

FIGURE 2

Survey on measuring chain with standard force measurement device at pre- and main compression rollers, an instrumented single lower punch with infrared telemetric signal transmission, an inductive sensor, the signal preparation and the analog to digital converter in a personal computer

METHODS

Tablet Press and Measuring Device

The rotary tablet press Korsch PH 230 (Korsch Maschinenfabrik, D-1000 Berlin) is a modern small-range machine with 17 pairs of punches and a production rate between 25 000 and 125 000 tablets per hour. It is fitted with strain gauges for measuring forces of lower and upper punches at the main compression rollers. Additionally forces on the upper precompression-roller can be measured by another set of strain gauges on the support of this roller. The signals are processed with carrier frequency bridge amplifiers (KWS 523.D; Hottinger Baldwin Meßtechnik GmbH, D-6100 Darmstadt) and registered with a microcomputer, interfaced to the tablet press with an analog to digital converter board (RTI 860, Analog Devices, Norwood, MA 02062-9106, USA), allowing a maximum sample rate of 250 kHz.

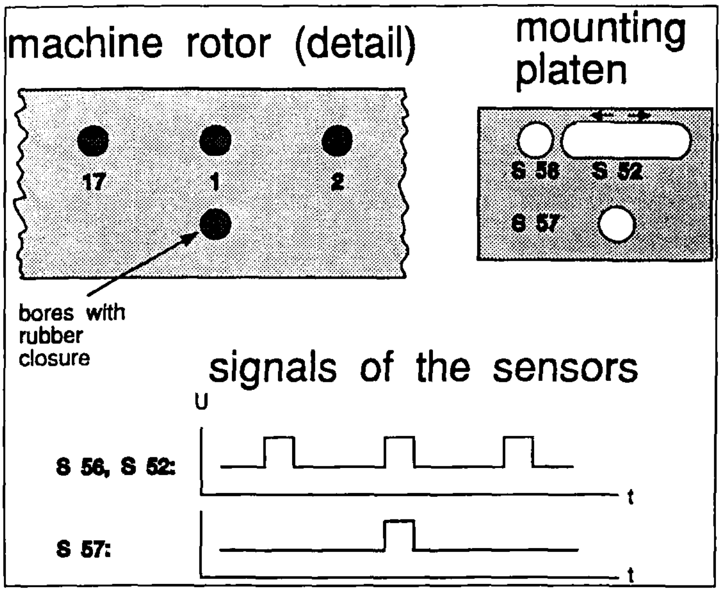

FIGURE 3
Modified mounting plate of the sensors, bores in the machine rotor and the corresponding signals

For use with an optional available controlling unit the machine is equipped with inductive sensors, serving the unit with start- and stop signals for a hardware maximum-storage device.

Figure 2 gives an overview on the measurement equipment. An additional single punch instrumentation with an infrared telemetric system is also depicted, but not used in present work.

Two of the sensors are directed to a row of 17 bores in the turret indicating the beginning of the compaction event of each pair of punches. The position of one of these sensors can be adjusted to show the middle of the compaction event. At the switch point the median of the tool is exactly under the center of the pressure role. Another sensor, directed to a single bore, gives a signal on each completed rotation of the machine. Figure 3 shows their mounting near the machine turret, the bores in the rotor and the corresponding signals.

The exact position for the sensor called S 52 as a reference for the middle of the compression event is found pressing brass with moderate forces, which leads to a symmetrical force peak due to the totally elastic deformation. The area under the force curve before the switch point must be identical with that one after the switch point.

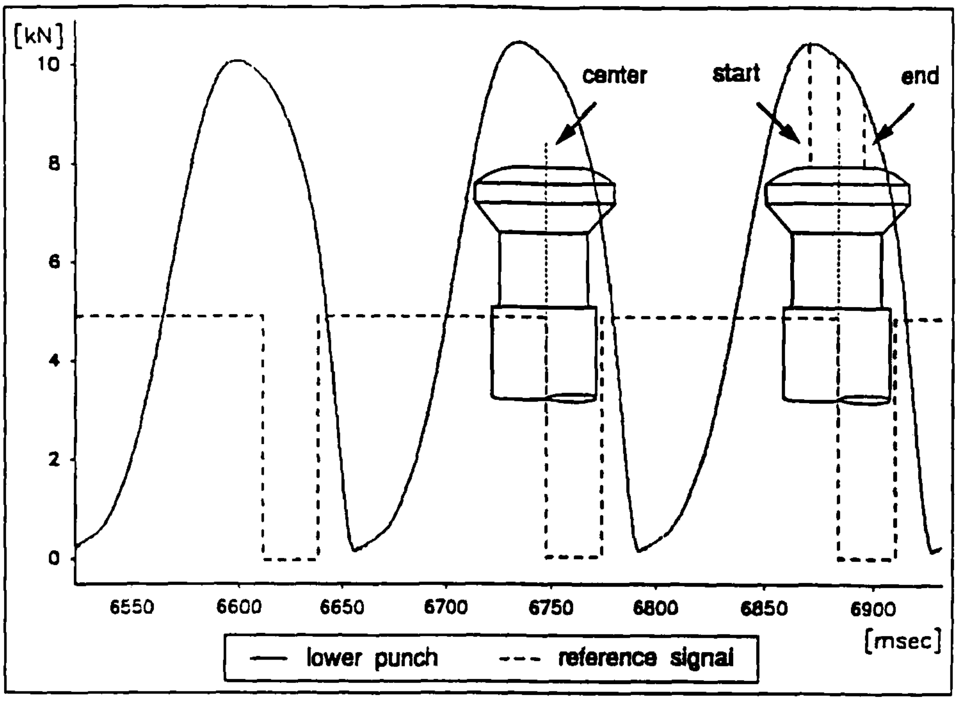

FIGURE 4
Force signal of the lower punch and the reference signal of the inductive sensor together with the punch head that indicates the limits of the dwell time

Data acquisition is controlled by a software package called Turbo-Lab (Stemmer PC-Systeme GmbH, D-8031 Puchheim; international version is available as "Global-Lab" and distributed by Data-Translation). Dependent on machine velocity sampling rates of 11.111 and 22.222 kHz per channel are chosen. Therefore each compression event is described with in minimum 500 up to 1 500 data points. Captured data are stored in the DAFF format (Data Acquisition File Format) on which the evaluation by a Turbo-Pascal program is based. This own program can be started as a subprogram of the Turbo-Lab shell. In most cases it is started as a stand-alone program from a batch program for overnight evaluation of higher amounts of data. A huge harddisk drive is used and accompanied by a tape streamer for permanent data storage.

The signal of the sensor S52 (see figure 3) is always registered together with the force signals. Usually 1.4 Mbytes of data are sampled comprising among 150 and 350 compaction events dependent on velocity and sample rate.

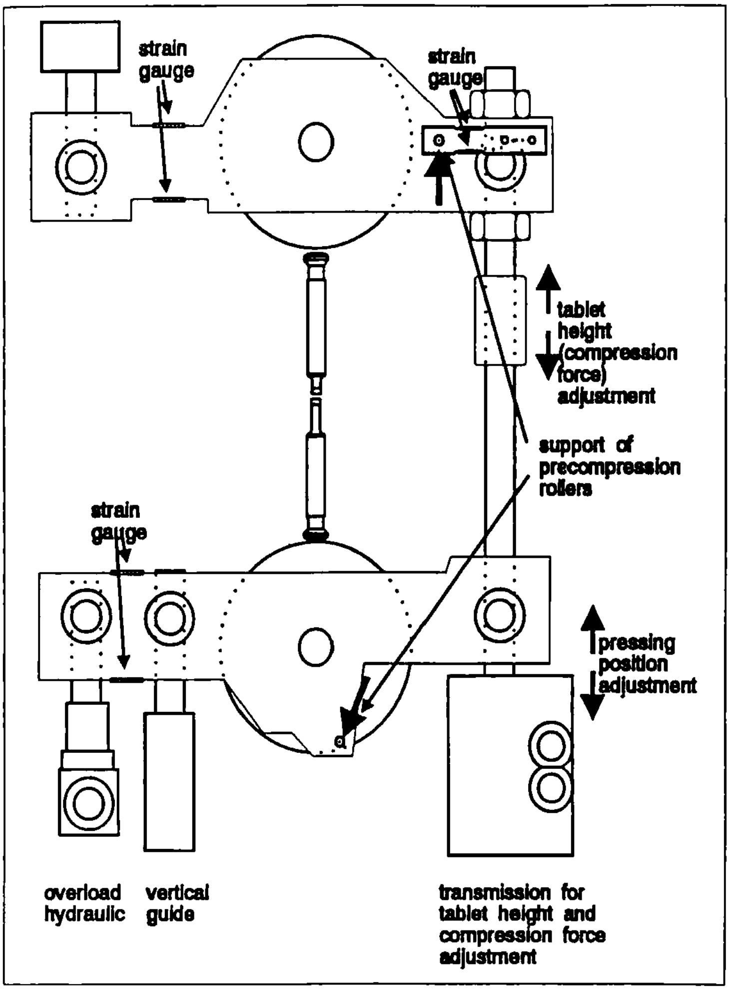

FIGURE 5
Position of the compression rollers at a pair of parallel arms, mechanisms for changing penetration depth and tablet thickness, position of the force measuring device and the attachment of precompression rolls

Figure 4 gives a survey on the stored signals. According to the switch point in the signal of the inductive sensor and the machine velocity that is given by the distance between the switch points and the constant sample rate beginning and end of the dwell-time can be calculated.

Calculation of the punch movements

In opposite to elder machine types using eccentric bearings for pressure rollers, there is, independent of the given vertical position, no or only a neglectable horizontal distance between the centers of the two compression rollers, due to their mounting on a pair of parallel arms. Figure 5 shows the construction of compression roller rocker arms for the used tablet press. It also depicts the position of the strain gauges and the mechanisms for changing the pressing position and tablet thickness respectively compaction force.

The vertical movements of both upper and lower punch can be calculated by the following equation [2]:

$$z = \sqrt{(r_1 + r_2)^2 - (r_3 * \sin\omega t - x_2)^2}\ .$$

z	=	vertical distance between punch head and the center of the compression roller at time t
r_1	=	radius of the compression roller
r_2	=	radius of the punch head curvature
r_3	=	active radius of the machine turret
ω	=	angular velocity
x_2	=	radius of the flat punch head flat radius

Determination of the elastic machine deformation

The elastic machine deformation is determined with the aid of mechanism for changing the tablet thickness. A pair of preferably flat faced punches has to be positioned between the compression rollers. If the distance between the rollers is decreased at a certain point the punches get in contact and a compaction force can be registered. A further decrease of distance leads to an elastic deformation of the machine, punches etc., together with a corresponding force. For the knowledge of the exact movements of the compression rollers the hand wheel scale of the mechanism for changing tablet height has to be calibrated. Therefore a dial gauge is used. Figure 6 depicts the correlation between the values of the hand wheel scale and the compression roller movements.

The movements of the compression roller are linear to the values of the hand wheel scale with a coefficient of correlation of 0.9999 to a linear regression but the slope of the straight is only 0.9034. Corrected with this factor the stretch of the machine gathers the values shown in Figure 7.

Linear values with a high coefficient of correlation (0.9992) for a regression are obtained at compaction loads above 2.5 kN with a slope of 0.0244 mm/kN and if calculated above 0.64 kN the slope is 0.0249 mm/kN with a coefficient of correlation of 0.9977.

RESULTS AND DISCUSSION

The different behaviour of materials under the compaction load is already known. Precondition for formation of bindings is an approximation of the particles

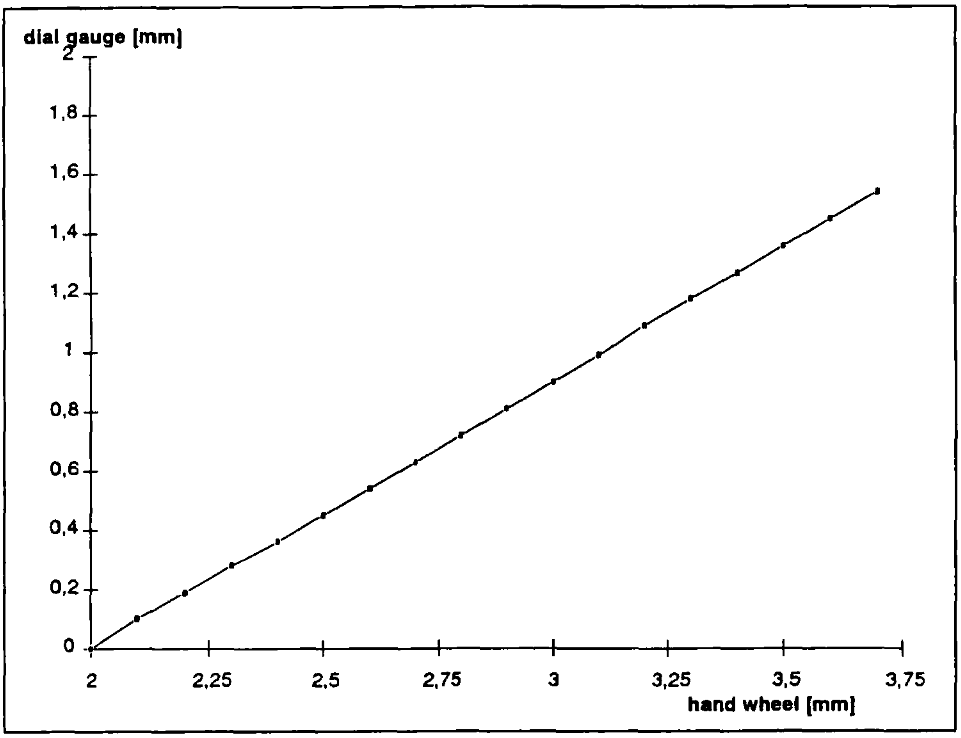

FIGURE 6
Distance reduction between the compression rollers measured with a dial gauge according to the hand wheel scale

that arises from a plastic deformation or the brittle fracture of the single component of the powder bed. Measurement of the particle size [3] is able to show the occurrence of fragments induced by the compaction load. Microscopic examinations show the deformation of the particles or their elastic recovery after the compaction event [4]. Additionally the occurring deformation mechanism is dependent from the initial particle size [5].

"In situ" examinations are impossible using these methods. Therefore the row of attempts to characterize the deformation mechanism by examining measured force-time and deformation-time data seems to be endless. Very often the Heckel Plots [6] which are porosity diagrams are used. The inconsistent results [7,8] should keep off anybody from using this method. Using calculated data it is easy to show the great influence of minimum errors in displacement measurement on the obtained parameters indicating compaction mechanisms.

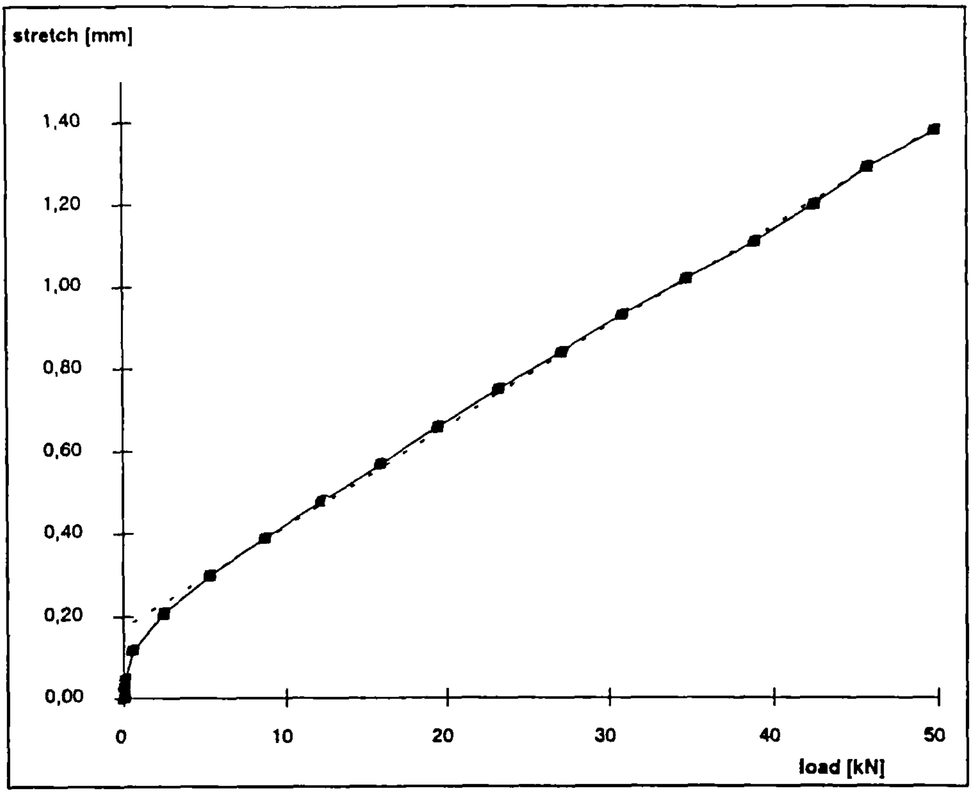

FIGURE 7
Elastic machine deformation as a function of compaction load

Other attempts [9,10] try to determine deformation behaviour from the force time curves using viscoelastic models or the Weibull function for the adaptation of curves. Curve parameters obtained from quotients of areas under the force-time curve [11,12,13] are easier to handle and offer better possibilities to quantify material behaviour.

As a survey figure 8 shows the different course of the force time curves for three materials with differing deformation mechanisms. The signals are brought into line with the aid of the reference signal. Bekapress is known as a mainly brittle substance, the sorbitol Karion Instant is deforming plastically. Cellactose, consisting of lactose and cellulose, should show an intermediate behaviour.

The decrease of compaction force in the period without deformation movements is due to the timedependant plastic deformation that is more distinct for Karion Instant than for Cellactose. The typical brittle dicalcium phosphate Bekapress shows

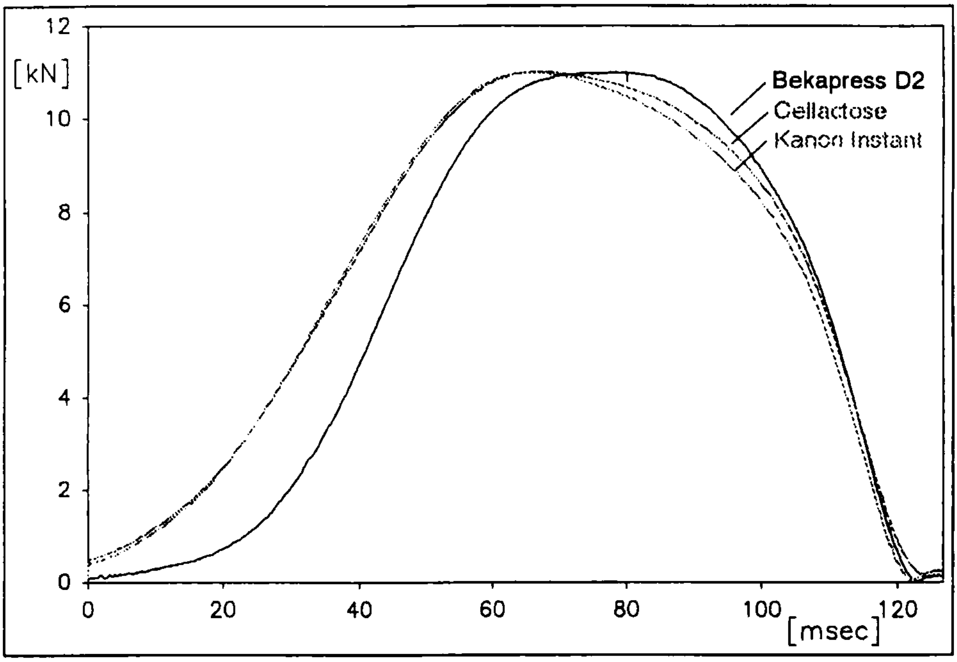

FIGURE 8
Force time curves of three materials with differing deformation mechanisms at corresponding compaction forces and -velocity and equal masses

no loss of force during the dwell time. The complete compaction work is done during the compression phase. No further deformation occurs later on.

The quantification of the amount of plastic deformation, respectively the decrease of force is done with the aid of the computer program. For this, the area under the force-time curve is divided into subareas. In conformity to the nomenclature of [14] two further areas are called A5 and A6. They are created by dividing the dwell-time area half. According to the trapezoid rule the subareas are integrated. To eliminate the influence of the amount of compression force both areas are decreased by the rectangles under the minimum compression force in the dwell time. Dividing the remaining areas A6/A5 a dimensionless parameter is obtained showing very sensitively even little differences in deformation behaviour.

Figure 9 depicts an original hardcopy printout of the computer program showing the force-time curve of Ludipress, an α-lactose that is coprocessed with pvp, leading to a more plastic deformation.

Despite of the high sensitivity only very low values for the standard deviation of this parameter are found. It is in the order of the magnitude of that for the

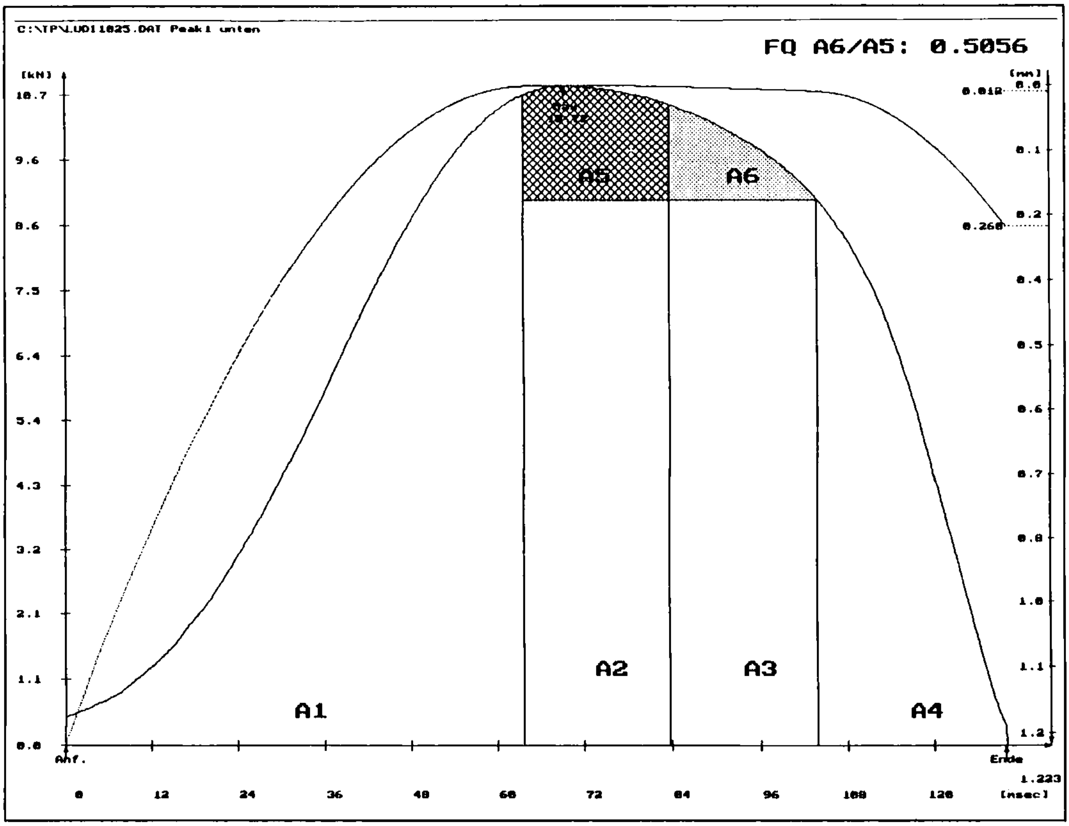

FIGURE 9
standard force-time depicture of an evaluated peak including the filename, the number of the peak, the name of the channel, the different subareas, the position and amount of maximum force and the parameter A6 / A5

maximum compression force which means in most of the cases less than 3 % relative standard deviation. Regarding the amount of data very small confidence intervals are obtained.

Combining the measured force data with the calculated punch movements displacement-, velocity- or force-displacement diagrams can be obtained. Both, calculation with or without regarding machine deformation, is possible to show the remarkable influence on parameters like compaction energy.

Figure 10 gives an example of the difference between those two possibilities. Here it is important to know that the correct volume reduction of the powder bed cannot be measured due to the impossibility of determining the punch tip movements. In most cases the elastic deformation of the punches leaves unregarded.

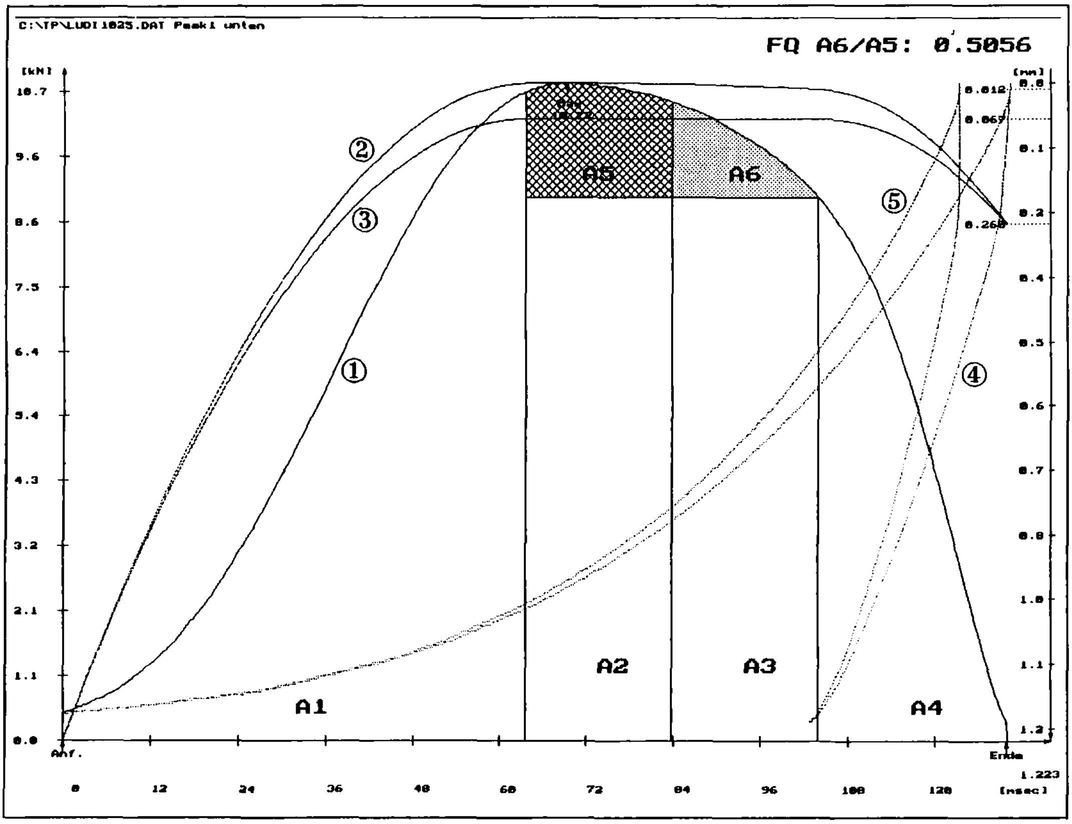

FIGURE 10

Force-time (①), displacement-time (②, ③) and energy diagram (④, ⑤) with (②, ④) and without (③, ⑤) consideration of elastic machine deformation. Right y-axis: displacement, energy diagram with hypothetical second x-axis for punch movements

Also there is no differential measurement of punch movements causing errors by neglecting the deformation of the machine frame.

Along with the quotient of the areas A6/A5 further parameters are calculated for the exact characterization of the behaviour of the materials in the compression event. They include the already mentioned machine velocity and maximum forces together with the position of the maximum relative to the dwell time. Others are the areas under the curve and duration of the compression and relaxation interval and descending from the maximum force the position of 90, 80 etc. percentage of the maximum force down to the beginning and the end of the peak. This enables for example the precise examination of the elastic relaxation process of the materials, indicating the capping tendency.

The evaluation is repeated for each compression event and each measured force signal (commonly upper and lower punch). During this evaluation statistical parameters and additionally an average compression event are calculated, the latter as a base for efficient data compression and storage without hundreds of megabytes as used at time.

CONCLUSIONS

A method for determining the compaction mechanism of a compressed substance relinquishing on any displacement data is presented. With the aid of the signal of an inductive sensor, originally fitted to the machine, a timebase is applied to each compression event. This allows to determine the deformation type from material behaviour during the dwell time, as well as occurring relaxation during the decompression phase, indicating capping tendencies. Using a tablet press with a pressure rollers mounted on a pair of parallel arms, the movements of the punches can be calculated precisely. If these data are completed with the easily determinable elastical stretch of the machine, high accuracy is achieved. The given examples show a remarkable influence of the elastic machine deformation on compaction parameters.

The studies on the influence of compaction load and velocity on the deformation mechanisms will be presented in a further paper.

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