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Research paper

The automatic micrometer screw

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Abstract

A new analytical method – the automatic micrometer screw – has been established to measure the edge height of tablets. The equipment offers many advantages compared with other methods. The precision is slightly increased compared to the traditional micrometer screw and the measurement with a small punch and a linear voltage transducer. No longer any touch of the tablet is necessary and influences results. The method works automatically and continuously, no manual measurement of the tablets is necessary. Up to ten tablets can be analyzed at the same time because of a rotary table on which they are positioned. Thus the method is not personal intensive. By combining the results from the measurement of punch displacement which means tablet height in the die and the results of the measurement with the automatic micrometer screw which means tablet height outside the die, a convenient measurement for the decompression process is possible.

Keywords: Tableting; Expansion; Elasticity; Elastic recovery; Decompression

1. Introduction

Elastic recovery after ejection of the tablet from the die and elastic recovery during unloading in the die have to be combined to analyze the process of decompression of a tablet completely [1]. This combination of elastic recovery is necessary to study the amount and time dependence of this factor. The tablet which gains energy during the decompression phase stores this energy. Van der Voort Maarschalk et al. [2] showed that the axial relaxation is dependent on the stored energy. This stored energy in the compact is the driving force for the expansion of the tablets; and bounding counteracts. Thus, the dimensional changes are the net effect of relaxation and bounding. The results from Picker [1] showed that this combination of relaxation and bounding leads to different decompression profiles with specific decompression mechanisms for various tableting materials. Therefore this elastic recovery should be analyzed for more materials. However, the methods used up to now were either personal intensive and had limitations in precision, e.g. the traditional micrometer screw, or they were very time consuming analyzing only one tablet at the time, e.g. the thermomechanical analysis. Therefore the aim of this study was to find or create a convenient and precise method to analyze several tablets at the same time.

1.1. Methods used up to now

Elastic recovery after ejection of the tablet from the die is determined from the edge height of the tablet. The methods used up to now to measure the tablet height are different. The most simple method is to measure the tablet height with a micrometer screw at various times after ejection. This micrometer screw is usually used for routine measurements. However this method is very personal intensive, the precision is low (0.005 mm) – especially when different persons are analyzing – and usually continuous measurement is impractical. Other attempts were made to measure the dimensions with a linear voltage transducer. Aulton et al. [3] remeasured in adequate time intervals by this method the tablet dimensions, Schierstedt and Müller [4] measured the tablet height continuously with a special apparatus based on this technique. These methods work on the same principle like thermomechanical analysis. With the thermomechanical analysis it is possible to measure the axial dimensional changes of a tablet with high precision (0.001 mm) for single tablets, but it is time consuming and inconvenient for routine measurements. For all these methods contact between the tablet and the measuring device is necessary. This contact is usually proven by a small resistance of the tablet and thus a force, even when it is low, is necessary to determine the edge height of the tablet. Thus tablets made of soft materials can be deformed easily.

An experimental apparatus has been described [5] to determine the strain recovery in compacts which works without touching the tablet. It consisted in a micrometer

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screw combined with a microscope which was aligned on an optical bench. The basic principle of the apparatus is the production of Fraunhofer diffraction fringes (helium neon laser) by two orthogonal slits formed between fixed edges and the edges of the compact, which permit small changes in compact dimensions to be monitored. York and Baily [6] used this non-contact method to measure the tablet dimensions. The method worked out very precisely, but it did not work continuously and the microscope had always to be adjusted manually.

These examples show that up to now a precise method to determine slow elastic recovery continuously has not been established for routine measurements and thus normally only partial data are available to look at the decompression process. Since by expansion the elastic component of the deformation process can be determined it seems worth to look at this process precisely and continuously.

2. Methods

2.1. Test conditions

All experiments were performed at room temperature (23–26°C). The water content of the tableting materials was determined by thermogravimetric analysis with two replicates (TG, Netzsch Gerätebau, Selb, Germany). To ensure that sorption and desorption did not influence the dimensional changes of the tablets, sorption isotherms of the materials used were recorded gravimetrically after equilibration over saturated salt solutions [7] in duplicate. The water content of the materials was referred to the relative humidity relevant and tableting and tablet height measurements were only performed when neither sorption nor desorption could influence the tableting experiments (Section 4). Relative humidity during analysis was measured by a hair-hygrometer and was measured to be relatively constant during the measurements (RH ± 2%)

2.2. Equipment

The present paper shows a new approach to measure tablet height including a new method for a convenient measurement. As shown in the photograph (Fig. 1) the measurement device consists of a micrometer screw (Mitutoyo Corp., Tokyo, Japan) driven by a motor. Parallel with the micrometer screw a laser is moving and the edge height of the tablet is measured by the laser light device. Ten tablets are moving on a rotary table and are passing the micrometer screw with the laser light device alternating. The micrometer screw is connected to the RS 232 port of a personal computer. This way data can be gathered and stored. Firstly, data analysis is performed without tablets (precision: 0.002 mm) that way that the height of each posi-

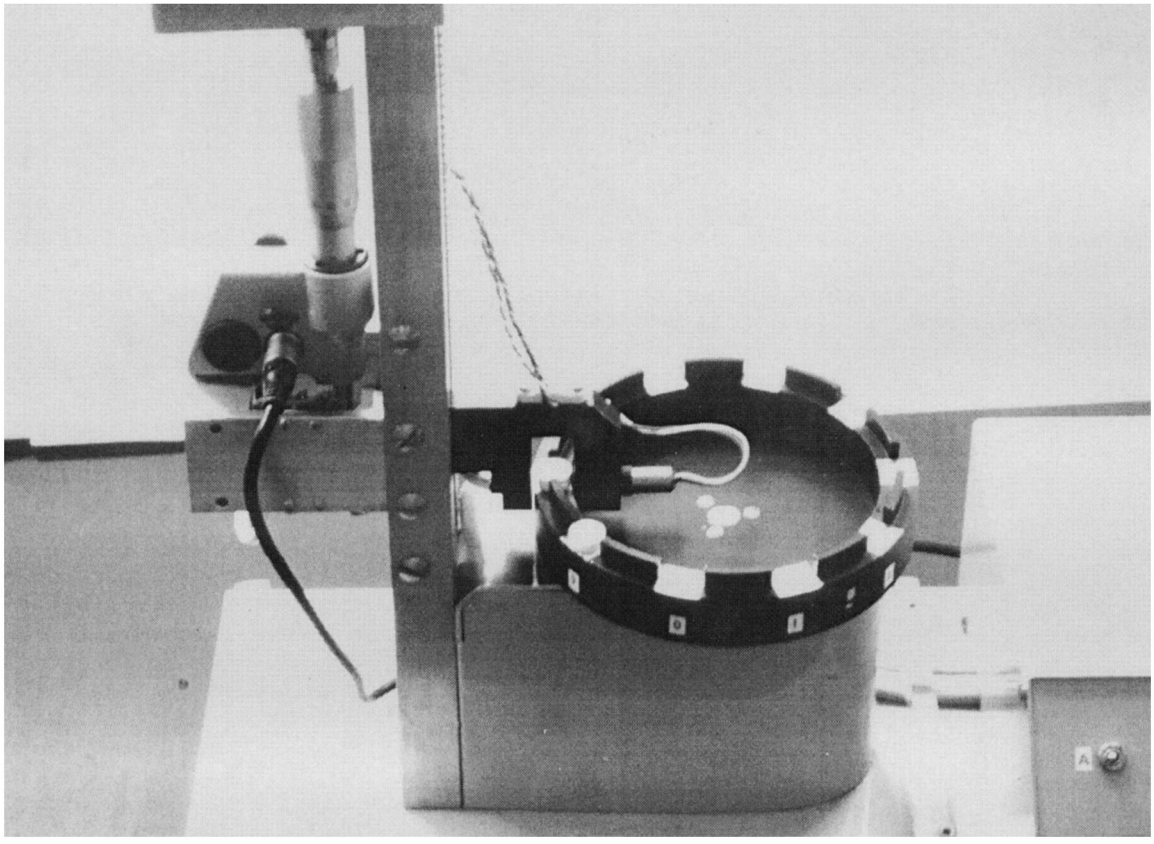

Fig. 1. The automatic micrometer screw.

tion is measured for each of the ten positions. Then the tablets are positioned on the rotary table and analysis of the tablet height is performed with the same procedure. Both data with and without tablets are stored and the final tablet heights for the different times for each tablet are calculated. For validation procedure see Section 2.4.2. By the laser measurement no touching of the tablet by the screw is necessary and thus the height of the tablet is measured without force. By this method the precision of the primary micrometer screw can be increased, because no longer force is influencing the measurement. Beside this continuous measurement, the analysis of ten tablets directly after ejection of the die becomes possible not only for several hours but for several days, and thus the elastic recovery of the tablet can be determined up to the final expansion.

2.3. Tableting

Tableting was performed on an instrumented single punch tableting machine (EK0/DMS, No. 1.0083.92, Korsch GmbH, Berlin, Germany) with 11 mm diameter flat faced punches. Equal true volumes of the substances were tableted to a maximum relative density of the tablets, $\rho_{rel,\,max}$, of 0.950 (precision: 0.001) with

$$\rho_{rel,\,max} = \frac{\rho_{max}}{\rho_{true}} \quad (1)$$

$\rho_{rel,\,max}$ = maximum relative density; ρ_{max} = density at minimum height of the tablet under load; ρ_{true} = true density.

This high maximum relative density was used to have a lot of deformation and thus expansion of the different materials. The true density of the materials was determined by a difference pressure pycnometer using helium (Accupyc 1330, Micrometrics, Norcross, USA) in triplicate.

The tablet height and therefore the volume at maximum densification under load was held constant at 3.000 ± 0.001 mm (corrected for elastic deformation of the punches). This precision is valid for the absolute tablet height. The inductive tranducer was calibrated with small parallel shaped steel tablets with exact heights for a range of 1mm. For this range this precision is valid and the transducer is acting linear.

The depth of filling was constant (13 mm) and the compression rate was ten tablets/min always. Forces were measured by the calibrated strain gages and displacement of the upper punch was measured using an inductive transducer (W 20 TK, Hottinger Baldwin Meßtechnik, Darmstadt, Germany). The amount of material necessary for each tablet with a given maximum relative density was calculated. After filling the powder manually into the die, one compaction cycle was performed. Five tablets were produced for each material. Lubricant was only used in case of dicalciumphosphate dihydrate (0.5% magnesium stearate) to avoid its influence on the microstructure of the tablets. Sorption and desorption did not influence the production of the tablets, since this process was controlled during tableting (see Section 2.1).

2.4. Dimensional changes after compression

2.4.1. In the die

The calibrated inductive transducer transducer (W 20 TK, Hottinger Baldwin Meßtechnik, Darmstadt, Germany) was used to measure the position of the upper punch and thus the axial expansion in the die. Calibration was performed with tablet shaped parallel plates (steel) with a basic height of 2, 3 and 5 mm. Radial dimensions of the die are constant to 11 mm.

2.4.2. Outside the die

For 5 days the height of the tablets was measured by the automatic micrometer screw (Fig. 1) continuously at controlled climatic conditions (see Section 2.1). The use of the micrometer screw was validated by measuring the six steel tablets of different heights (1, 2, 3, 4, 5, 6 mm) each 50 times at 3 independent days on the rotary table. The mean of the standard deviations of these measurements is 0.003. Linearity of the actual range is given. Validation of the manual use of a micrometer screw resulted in a precision of 0.005 mm.

2.4.3. Total dimensional changes and correspondence of in-die to out-die measurements

The total dimensional changes are the sum of the dimensional changes in the die and outside the die. In-die and out-die measurements were confirmed against each other by measuring the tablet shaped parallel plates of 1, 2, 3, 4, 5 and 6 mm height inside and outside the die. The measured values were corresponding referring to the statistical error.

3. Materials

Dicalciumphosphate dihydrate (Emcompress®, Lot # R 19 K, Mendell, NY), κ-carrageenan (Gelcarin® GP-911 N, Lot # ZC502, FMC Corporation, USA), microcrystalline cellulose (Avicel® PH 101, Lot # 14204, FMC Corporation, USA), hydroxypropylmethyl cellulose (Metolose® 90 SH, Lot # 506825, Shin-Etsu, Tokyo, Japan), cellulose acetate (Lot # AC-62505, Eastman Chemical Company, Tennessee, USA) and theophylline monohydrate (Lot # 4072.2, Roth GmbH, Karlsruhe, Germany) were used as materials with different deformation mechanisms.

4. Results and discussion

In Fig. 2 sorption isotherms of the materials are given. The substances were very different in sorption behavior, however the influence of sorption and desorption was elimi-

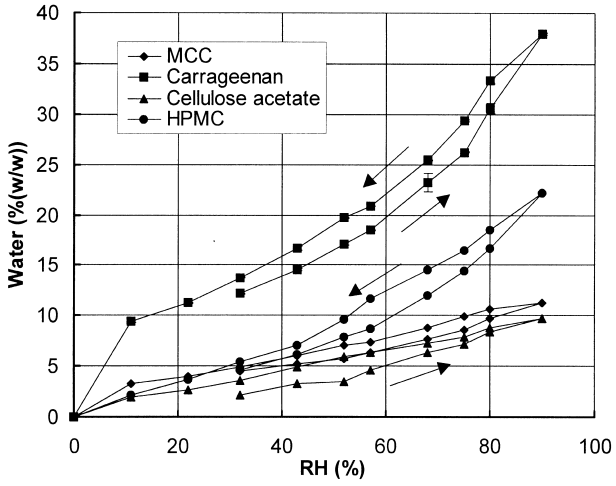

Fig. 2. Sorption behavior of the different materials (mean of $n = 3$).

nated as much as possible. The content of water was determined by TG. The results were 12.10 ± 0.66% (w/w) for carrageenan (30% RH), 4.67 ± 0.14% (w/w) for MCC (30% RH), 4.84 ± 0.26% (w/w) for HPMC (30% RH) and 2.53 ± 0.05% (w/w) for CAC (35% RH). Dicalciumphosphate and theophylline showed no sorption up to 80% RH (50% RH). The relative humidities given in brackets were the measurement conditions used for the different tableting materials.

The results of the decompression process measured by the automatic micrometer screw are given in Figs. 4–9.

As shown in Fig. 3 there is some fluctuation of the data points measured. This effect is due to the movement of the rotary table, the movement of the micrometer screw and small fluctuations in current intensity. This can be avoided by further improvement of the equipment. Another reason can be differences in tablet height of the measured tablets, since they are not absolutely smooth [6] and will be measured at slightly different positions due to moving. To eliminate this influence adjacent averaging (30) was performed. The resulting smoothed lines were fitted with different polynomial functions. The best fit was performed

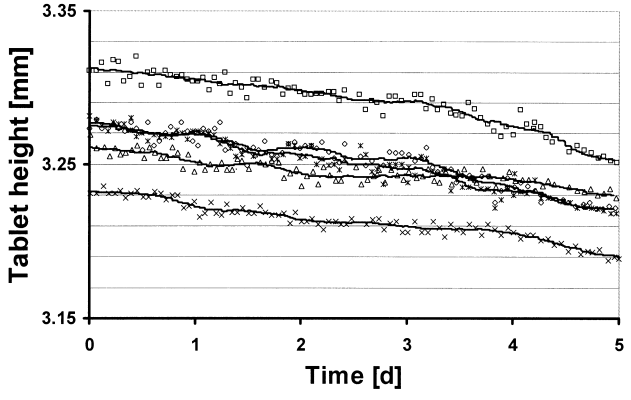

Fig. 3. Tablet height measured for five tablets made from theophylline monohydrate at a maximum relative density of 0.950 (raw data and adjacent averaging).

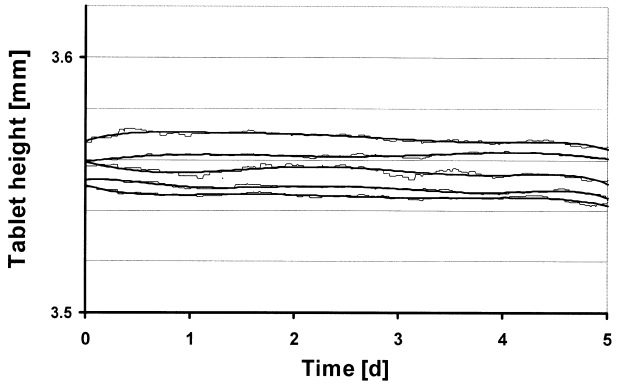

Fig. 4. Tablet height measured for five tablets made from dicalciumphosphate dihydrate at a maximum relative density of 0.950 (smoothed data and polynomial fit).

by a polynom of sixth order. The results from adjacent averaging and the polynomial fitting are given in Figs. 4–9. The quality of the polynomial fits was evaluated by correlation coefficients. The following mean correlation coefficients ($n = 5$) were calculated: dicalciumphosphate dihydrate 0.81, carrageenan 0.87, microcrystalline cellulose 0.84, hydroxypropyl methylcellulose 0.93, cellulose acetate 0.92 and theophylline monohydrate 0.99. The polynomial fits were only used to visualize 'general trends'.

Since the tablets were all tableted to the same tablet height of 3.000 mm differences in the total height of the tablet are the first difference. It is astonishing that tablets of one material have slightly different tablet heights. This can be explained by the fact that the powder samples used for one tablet consist of different particles which can be different in particle form and size distribution. Following that, every tablet is an individual and statistics will be of limited value. However, different tablets of one material can be regarded as a set according to the set theory of G. Cantor [8]. Different materials can be regarded as sets which are in linear order. For these sets a linear order relation [9] can be proposed.

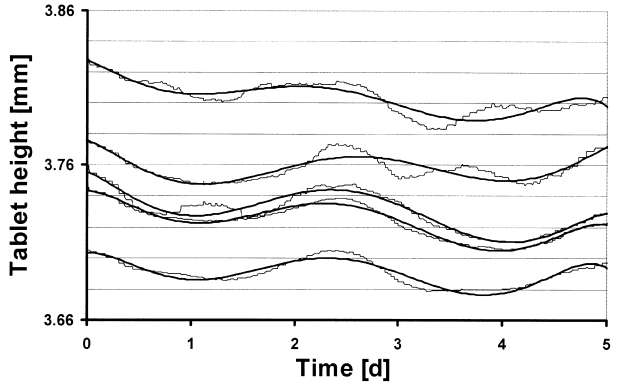

Fig. 5. Tablet height measured for five tablets made from carrageenan at a maximum relative density of 0.950 (smoothed data and polynomial fit).

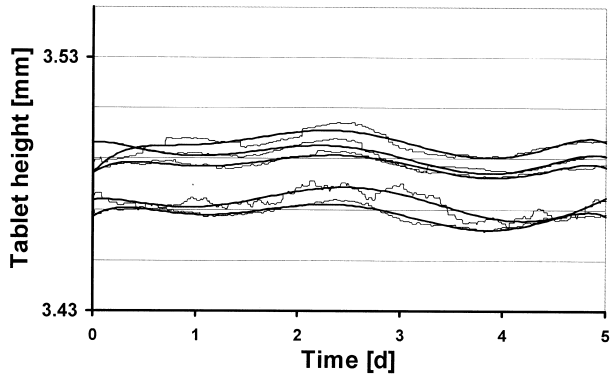

Fig. 6. Tablet height measured for five tablets made from microcrystalline cellulose at a maximum relative density of 0.950 (smoothed data and polynomial fit).

For the different materials used the following rank order is given for the total height (measured at time = 0): theophylline monohydrate < microcrystalline cellulose < hydroxypropyl methylcellulose < dicalciumphopshate dihydrate < cellulose acetate < carrageenan. Theophylline monohydrate shows the lowest elastic recovery and carrageenan the most. Even when the relative humidity was not always the same this rank order is valid for the materials because materials with a high influence of humidity were measured at similar conditions.

This means that theophylline monohydrate is the most plastically deforming material and carrageenan the most elastically deforming material. Dicalciumphosphate dihydrate shows a lot of elastic recovery, this means this brittle material [10] or the small particles of this material, created at high densification, give a lot of resistance against densification. They are deforming elastically. This elasticity is more than for the polymers microcrystalline cellulose and hydroxypropyl methylcellulose. These polymers show more plasticity at this high densification than dicalciumphosphate dihydrate and they show more than cellulose acetate. Finally, all derivatives of cellulose show less elastic recovery than carrageenan.

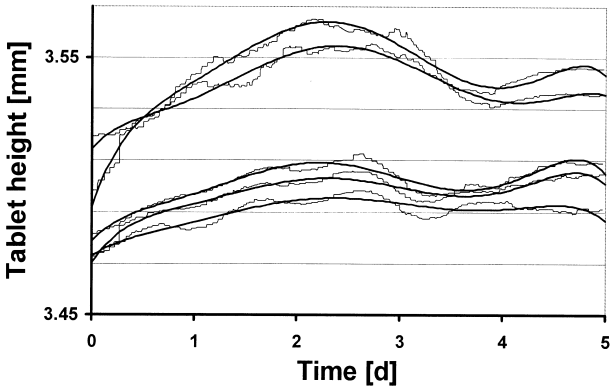

Fig. 7. Tablet height measured for five tablets made from hydroxypropyl methylcellulose at a maximum relative density of 0.950 (smoothed data and polynomial fit).

However not only the amount of expansion is different, the decompression profiles are different as well. One might think that these decompression profiles are due to slight differences in humidity and temperature. However, the climatic conditions were controlled as much as possible and the experiments were repeatable.

Dicalciumphosphate dihydrate (Fig. 4) expands fast and then tablet height remains constant. Following that, the total elastic recovery is the same as fast elastic recovery. Fig. 4 shows that the profiles are not absolutely constant. They appear to be rough. A reason can be internal stress in the tablet which tries to be solved. The carrageenan (Fig. 5) shows a fast high expansion, shrinking, again some expansion and shrinking. The resulting profile seems to be the result of stress relaxation. Shrinking can be interpreted as a reorganization of the material as consequence of relaxation. Carrageenan is a totally amorphous material. It is in the rubbery state at room conditions [11], because its glass transition temperature is 0°C for the dry material. One main bonding mechanism is mechanical interlocking of the long threads of the material [11]. This allows the fast expansion. Microcrystalline cellulose (Fig. 6) shows some fast expansion, then small changes in tablet height occur. They seem to be similar to those of carrageenan. However stress relaxation is more suppressed since this material is more plastically deformed. Another reason may be the glassy properties of this material. Hydroxypropyl methylcellulose (Fig. 7) shows a similar fast expansion compared to microcrystalline cellulose, however expansion is continuing over the time. The resulting profile may be the result of relaxation and reorganization as well. However, this glassy material may not allow fast expansion like carrageenan. Cellulose acetate (Fig. 8) shows much more fast expansion than microcrystalline cellulose and hydroypropyl methylcellulose. This material resists more against densification than even dicalciumphosphate dihydrate. The expansion continues for 1 day, then tablet height remains mainly constant. The small changes in the decompression profile show that still some energy is stored inside the tablet which 'tries to escape'. A reason could be a partial fusion in the

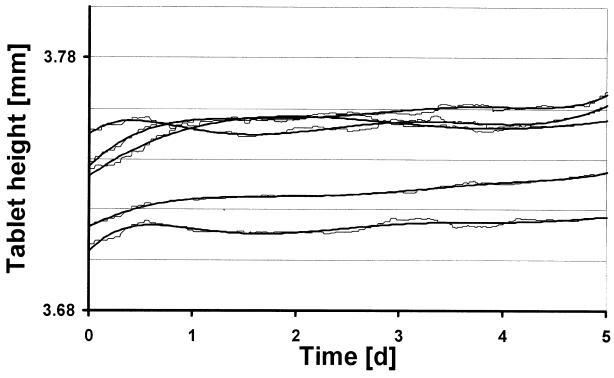

Fig. 8. Tablet height measured for five tablets made from cellulose acetate at a maximum relative density of 0.950 (smoothed data and polynomial fit).

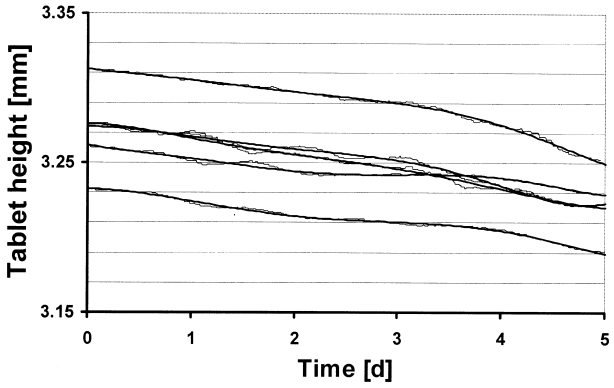

Fig. 9. Tablet height measured for five tablets made from theophylline monohydrate at a maximum relative density of 0.950 (smoothed data and polynomial fit).

tablet [12]. Tablets made from theophylline monohydrate (Fig. 9) are expanding little but very fast, within the first 2 min, then they are shrinking continuously. A process of rehardening of the tablets may have started due to stabilization of hydrogen bands [13].

5. Conclusions

The results show that the automatic micrometer screw offers the possibility to measure the edge height of the tablets, the slow elastic recovery, (a) precise, (b) touchless, (c) continuously, (d) for up to 10 tablets at the same time and (e) without the necessity of extra personal. The equipment is especially designed for this purpose and the advantages prevail the disadvantages. The disadvantages will be avoided by a future improvement of the equipment. By this method new insights in the deformation and relaxation behavior of tableting excipients become possible and thus a new evaluation of tableting materials.

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References

[1] K.M. Picker, Analysis of elastic recovery during and after tableting, Int. World Meeting Pharm. Biopharm. Pharm. Technol. 2 (1998) 203–204.
[2] K. Van der Voort Maarschalk, K. Zuurman, H. Vromans, G.K. Bolhuis, C.F. Lerk, Porosity expansion of tablets as a result of bonding and deformation of particulate solids, Int. J. Pharm. 140 (1996) 185–193.
[3] M.E. Aulton, D.N. Travers, P.J.P. White, Strain recovery of compacts on extended storage, J. Pharm. Pharmacol. 25 (1973) 79P–86P.
[4] D. Schierstedt, F. Müller, Rückdehnung und Relaxation während der Tablettierung mit Exzentermaschinen, Pharm. Ind. 44 (1982) 932–937.
[5] E.D. Baily, P. York, Apparatus for the study of strain recovery in compacts, J. Mater. Sci. 11 (1976) 1470–1474.
[6] P. York, E.D. Baily, Dimensional changes of compacts after compression, J. Pharm. Pharmacol. 29 (1977) 70–74.
[7] L. Greenspan, Humidity fixed points of binary saturated aqueous solutions, J. Res. Nat. Bur. Stand 81A (1977) 89–96.
[8] A. Fraenkel, Einleitung in die Mengenlehre, Springer Verlag, Berlin, 1973.
[9] B. Picker, in: M. Glatfeld, E. Joachim, B. Picker (Eds.), Mengenlehre 1. Tutorial Reihe Mathematik, Schwann Verlag, Düsseldorf, 1973.
[10] J.E. Rees, P.J. Rue, Time-dependent deformation of some direct compression excipients, J. Pharm. Pharmacol. 30 (1978) 601–607.
[11] K.M. Picker, Matrix tablets of carrageenans – a compaction study, Drug Dev. Ind. Pharm. 25 (1999) 329–337.
[12] K.M. Picker, F. Bikane, Tablet formation and release from matrix tablets manufactured with cellulose acetate, Int. J. Pharm. 175 (1998) 147–164.
[13] P. York, Crystal engineering and particle design for the powder compaction process, Drug Dev. Ind. Pharm. 18 (1992) 677–721.