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The 3-D Model: Comparison of Parameters Obtained From and by Simulating Different Tableting Machines

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ABSTRACT

The aim of this study is to apply 3-D modeling to data obtained from different tableting machines and for different compression wheels on a linear rotary tableting machine replicator. A new analysis technique to interpret these data by 3-D parameter plots is presented. Tablets were produced on an instrumented eccentric tableting machine and on a linear rotary tableting machine replicator. The materials used were dicalcium phosphate dihydrate (DCPD), spray-dried lactose, microcrystalline cellulose (MCC), hydroxypropyl methylcellulose (HPMC), and theophylline monohydrate. Tableting was performed to different maximum relative densities ($\rho_{rel, max}$). Force, time, and displacement were recorded during compaction. The 3-D data plots were prepared using pressure, normalized time, and porosity according to Heckel. A twisted plane was fitted to these data according to the 3-D modeling technique. The resulting parameters were analyzed in a 3-D parameter plot. The results show that the 3-D modeling technique can be applied to compaction cycles from different tableting machines as different as eccentric and rotary tableting machines (simulated). The relation of the data to each other is the same even when the absolute values are different. This is also true for different compression wheels used on the linear rotary tableting machine replicator. By using compression wheels of different sizes on this simulator, mainly time plasticity changes. By using bigger compression wheels for simulation, the materials deform slower at lower densification and they deform faster at higher densification. For brittle materials, the stages of higher densification are influenced; for plastically deforming materials, the stages of lower and higher densification can be influenced.

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KEYWORDS: rotary tableting machine simulator, eccentric tableting machine, compression wheels, excipients, compression

INTRODUCTION

The 3-D modeling of tableting data has been successfully applied to characterize tableting materials by 3-D parameter plots.[1-3] The parameters *d* (time plasticity), *e* (pressure plasticity), and ω (the twisting angle, indicating fast elastic decompression) are presented. Materials that deform quickly show high *d*-values, and materials that deform easily and with low pressure show high *e*-values. Elastically deforming materials have much decompression already during tableting, and the ω-values are low.

However, most of these data have been gained by an eccentric single-punch tableting machine, which has different compaction characteristics compared with a rotary tableting machine. Its compaction performance is unilateral, whereas that of a rotary tableting machine is bilateral. Therefore, the model should be applied to data gained by rotary tableting machines. However, these machines need a high amount of material for compaction and cannot be easily instrumented for displacement measurement.[4-6] It has also been attempted to calculate displacement from machine geometries, but the results were not satisfactory.[7-10] Even for eccentric tableting machines, displacement measurement can always be improved.[11, 12]

The Presster (Metropolitan Computing Corp [MCC], East Hanover, NJ), a linear rotary tableting machine replicator, works with 1 single pair of punches and offers the possibility to simulate different rotary tableting machines by mimicking the mechanics of these machines.[13, 14] The same compression wheels and geometries as on a rotary tableting machine are used, and furthermore, different machines are simulated by exchanging the wheels. Working with only 1 single pair of punches reduces the consumption of tableting materials and facilitates instrumentation for displacement

measurement. The variables time, force, and displacement can be easily measured. Thus, the tableting data can be assessed with the 3-D model. In conclusion, by simulation of different machines using different compression wheels, the transfer from one machine to another should be possible to interpret using the 3-D model and its 3-D parameter plots.

The aim of this study is to apply 3-D modeling to data obtained from different tableting machines and for different compression wheels on the linear rotary tableting machine replicator Presster. The question is whether or not these data are comparable. A new analysis technique to interpret these data by 3-D parameter plots is presented.

MATERIALS AND METHODS

Materials

The materials used were microcrystalline cellulose (MCC; Avicel PH 101, lot # 14204, FMC Corp, Princeton, NJ), hydroxypropyl methylcellulose (HPMC 15 000; Metolose 90 SH, lot # 506825, Shin-Etsu, Tokyo, Japan), spray-dried lactose (FlowLac 100, lot # S0047, Meggle GmbH, Wasserburg, Germany), dicalcium phosphate dihydrate (DCPD; Emcompress, lot # R 19 K, Mendell, Patterson, NY), and theophylline monohydrate (TheoM; lot # 4072.2, Roth GmbH, Karlsruhe, Germany). Magnesium stearate (lot # 93810410, Caelo GmbH, Fröhlingsdorf, Germany) was used for internal lubrication.

Methods

True Density

The true density (ρ_{true}) of all materials was determined by Helium pycnometry (Accupyc 1330, Micromeritics, Norcross, GA). The equilibrated materials were analyzed in order to determine the true density of materials containing some moisture using the method described by Picker.[15] The results are given in **Table 1**.

Tableting and Data Analysis Using an Eccentric Machine

Tableting was performed on an instrumented eccentric tableting machine (EK0/DMS, No. 1.0083.92, Korsch GmbH, Berlin, Germany) with 11-mm diameter flat-faced punches (Ritter GmbH, Hamburg, Germany). Equal true volumes of the substances were tableted to 5 different maximum relative densities ($\rho_{rel,\ max}$) of the tablets (precision 0.001) between 0.70 and 0.90. The tablet height at maximum densification under load was held constant at 3 mm. Displacement of the punch faces was measured using an inductive transducer (W20 TK, Hottinger Baldwin Meßtechnik, Darmstadt, Germany) and corrected for elastic deformation of the punches. The depth of filling was held constant at 13 mm. The production rate was 10 tablets per minute. Lubricant (0.5% magnesium stearate) was used only for DCPD and spray-dried lactose. The amount of material necessary for each tablet with a given $\rho_{rel,\ max}$, and always the same apparent density, was calculated. The powder was manually filled into the die, and 1 compaction cycle was performed.

Five single tablets were produced at each condition. Data acquisition was performed by a DMC-plus system (Hottinger Baldwin Meßtechnik, Darmstadt, Germany), and data were stored by BEAM-Software (AMS, Flöha, Germany). Force, time, and displacement of the upper punch were recorded for each compaction cycle. For each compaction cycle, normalized time, pressure, and ln ($1/1\text{-}D_{rel}$) according to Heckel[16, 17] were calculated. The data were presented in a 3-D data plot. To this 3-D data plot, a twisted plane was fitted by the least-squares method according to Levenberg-Marquard (Matlab, The MathWorks Inc, Unterföhrung, Germany) with the following equation. The plane is twisted at $t = t_{max}$.

$$z = ln\left(\frac{1}{1-D_{rel}}\right) = (t - t_{max}) \cdot (d + \omega \cdot p_{max} - p) + (e \cdot p) + (f + d \cdot t_{max}) \quad (1)$$

$$d = \frac{\delta\, ln(1/(1-D_{rel}))}{\delta t},\ e = \frac{\delta\, ln(1/(1-D_{rel}))}{\delta p},$$

$$f = ln(\frac{1}{1-D_0})$$

where D_{rel} is relative density; t is normalized time; p is pressure; t_{max} is normalized time at maximum pressure; p_{max} is the maximum pressure; ω is the twisting angle at t_{max}; and D_0 is the relative density at t = 0.

Only the compression data above the 50% level of the maximum pressure were used for fitting. Since deformation of the particles mainly happens during the period of the compaction event, this procedure is deemed to be legitimate. The mean quality of the fits (R^2) was 0.0054.

The d, e, and ω of the 5 compaction cycles at each tableting condition (material, a given $\rho_{rel,\ max}$, and/or particle size fraction) were averaged, and means and stan-

Table 1. True Densities of the Materials*

Material	True Density (g/cm^{-1})
MCC	1.574 (0.001)
HPMC	1.331 (0.001)
spray-dried lactose	1.544 (0.002)
DCPD	2.342 (0.003)
TheoM	1.469 (0.001)

*MCC indicates microcrystalline cellulose; HPMC, hydroxypropyl methylcellulose; DCPD, dicalcium phosphate dihydrate; and TheoM, theophylline monohydrate. SD given in parentheses; mean, n = 3.

dard deviations were calculated. The mean standard deviation for time plasticity *d* was 0.02; for pressure plasticity *e*, 0.0001; and for fast elastic decompression indicated by ω, 0.0004.

Tableting Using the Presster

Tablets were produced on the Presster, a single-station linear rotary tableting machine replicator.

The Presster offers the possibility to measure time, force, and displacement, and to use only small amounts of material for formulation development. Using the Presster, the compression process can be simulated by mimicking the mechanics of a rotary machine; ie, by using the same compression wheels used on rotary machines and the same geometries.

The equipment is instrumented with inductive displacement transducers (Macro Sensors, Pennsauken, NJ) for the upper (model CD375-100) and the lower (model CD375-250) punch. The transducers were calibrated. Strain gages (N2A-06-T031P-350, Measurements Group Inc, Raleigh, NC) were applied at the upper compression roll pin. Measurement was temperature compensated. Calibration was performed up to 50 kN using a load cell (model 42/8378-01 s/n 331148, Sensotec, Columbus, OH). Compression rolls with the geometries of the high-speed rotary tableting machine Fette PT 2090 (Fette GmbH, Hamburg, Germany) and the rotary tableting machine Manesty Betapress (Casburt Ltd, Stoke-on-Trent, UK) were used for simulation. Dwell time was set to 10.6 milliseconds referring to 55.8 rpm (Fette PT 2090) and 100 rpm (Manesty Betapress) of the original machine.

Standard PCT B tooling with 10-mm flat-faced punches was used throughout the study. Internal lubrication (0.5% magnesium stearate) was only used in the case of DCPD and spray-dried lactose. All other substances were tableted without lubrication to avoid its influence on material characteristics. Feeding of the die happened automatically using a feeding shoe with gravimetric force. The height of the tablets at the minimum distance between upper and lower punch was adjusted to 3 mm. The error for this determination was estimated to be 25 µm. Equal true volumes of the substances were tableted to different $\rho_{rel,\,max}$ between 0.75 and 0.95. The weight of the final tablets was recorded. By using tablet weight, true density, tablet height under load, and the diameter of the die, the $\rho_{rel,\,max}$ of the final tablets was calculated.

New Data Analysis

The 3-D modeling was applied as for the data obtained with the eccentric machine. In this case, the quality of the fits R^2 was between 0.0001 and 0.0037. Two examples of 3-D data plots with a fitted twisted plane are given in **Figure 1** for HPMC and DCPD.

The resulting different characteristic parameters for each tableting excipient *d*, *e*, and ω were plotted in a 3-D coordinate system. A quadratic polynomial regression in the 3-D space was performed. For this procedure the least-squares method according to Levenberg-Marquard was applied. A 3-D parameter plot resulted (**Figure 2**), which gives a simple, yet characteristic description of the tableting properties. In the 3-D parameter plot, the calculated parameters *d*, *e*, and ω as well as the resulting values after polynomial fitting are given. This polynomial fitting method allows application of the 3-D model to data from tablets with all different $\rho_{rel,\,max}$, which can be calculated if the tablet weight, true density of the material, and apparent density of the tablet are known. No mean values are calculated, and the scattering of the values is best approximated by the polynomial fit.

Using this method it is not necessary to produce tablets with a preliminary defined $\rho_{rel,\,max}$. It becomes possible to use all data obtained from all types of tableting machines, which allows continuous measurement of the height of the tablets by displacement measurement. The possibility of the determination of tablet weight and true density of the materials is taken for granted. In conclusion, this method enables broad application of 3-D modeling.

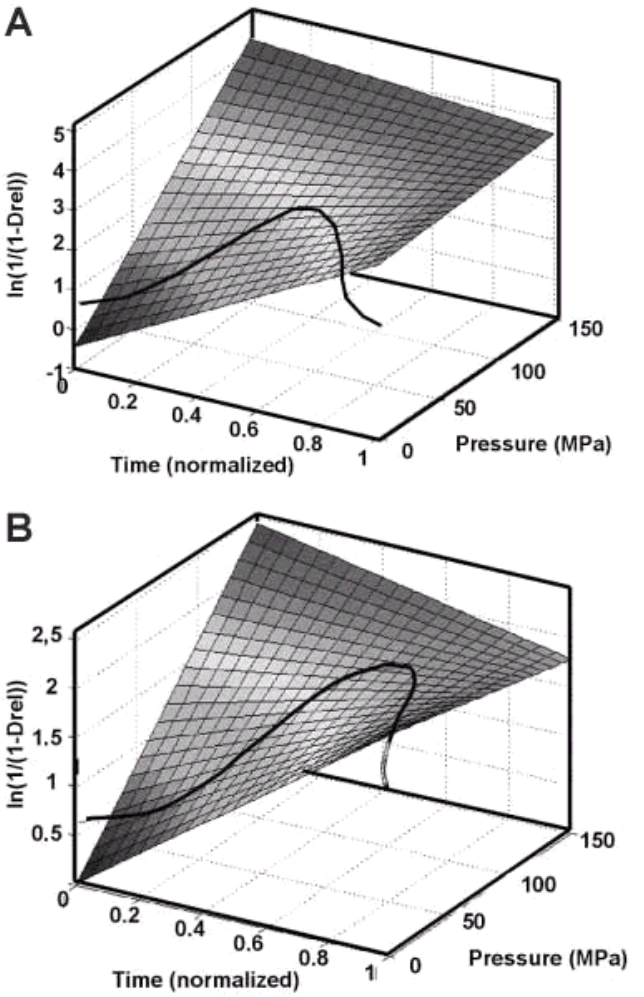

Figure 1. 3-D data plots of (A) HPMC and (B) DCPD for data gained with the linear rotary tableting machine replicator Presster and compression wheels of a Fette 2090.

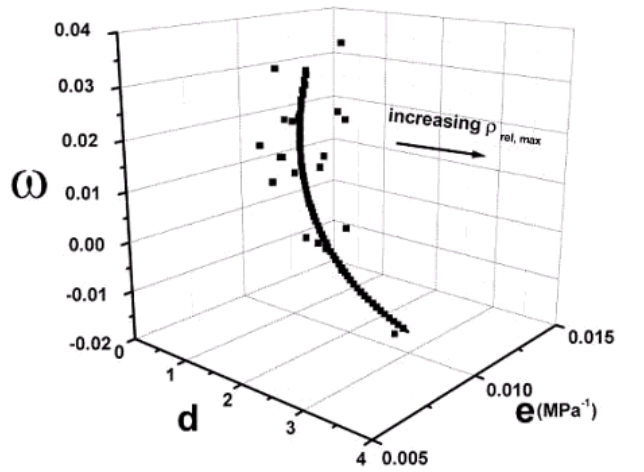

Figure 2. 3-D parameter plot of MCC for data gained with the linear rotary tableting machine replicator Presster and compression wheels of a Fette 2090.

RESULTS AND DISCUSSION

Comparison of Different Tableting Machines

Figure 3A shows the 3-D parameter plot for data obtained with the Presster and compression wheels of the high-speed tableting machine Fette 2090. The speed was 55.8 rpm. For spray-dried lactose and DCPD, the *d* and e-values are low, which means that time and pressure plasticity are low, and the materials deform neither easily nor fast. The ω values are strongly decreasing with increasing $\rho_{rel, max}$. This is typical for brittle materials as described for the eccentric tableting machine.[3] The fast elastic decompression, indicated by ω, increases due to further densification. MCC shows much higher time plasticity *d* and pressure plasticity *e*. This material is much easier and faster deforming than DCPD. The ω values are medium but less decreasing; thus overall the material is more plastically deformable. Finally, HPMC shows high pressure plasticity *e* and the lowest fast elastic decompression as indicated by high ω values. This material is fairly easily deformable. The following order for deformability (*D*) can be set up:

D (HPMC) > *D* (MCC) > *D* (DCPD) > *D* (spray-dried lactose).

The 3-D parameter plot is similar to that of data obtained with the eccentric tableting machine (**Figure 3B**). The relationship of the parameters to each other and the order of deformability is the same, even when the absolute values are not identical. But, it has also to be kept in mind that the same punch diameters could not be used. This means that the 3-D modeling method is applicable to data from different tableting machines as diverse as an eccentric and a high-speed rotary tableting machine (simulated in this study). The underlying material properties can be analyzed and compared with each other.

Comparison of Different Rotary Tableting Machines Simulated by the Presster

Figure 3C shows the 3-D parameter plot for data obtained with the Presster and compression wheels of a Manesty Betapress. The speed was 100 rpm, which means that the dwell time was 10.6 milliseconds as for simulation of the high-speed tableting machine Fette 2090.

Again spray-dried lactose and DCPD show the lowest time and pressure plasticity and the lowest ω values. Spray-dried lactose has even higher ω values. The plot of MCC is slightly flatter; pressure plasticity is a lot higher than for the brittle materials. HPMC is more plastically deforming than MCC. The *e* and ω

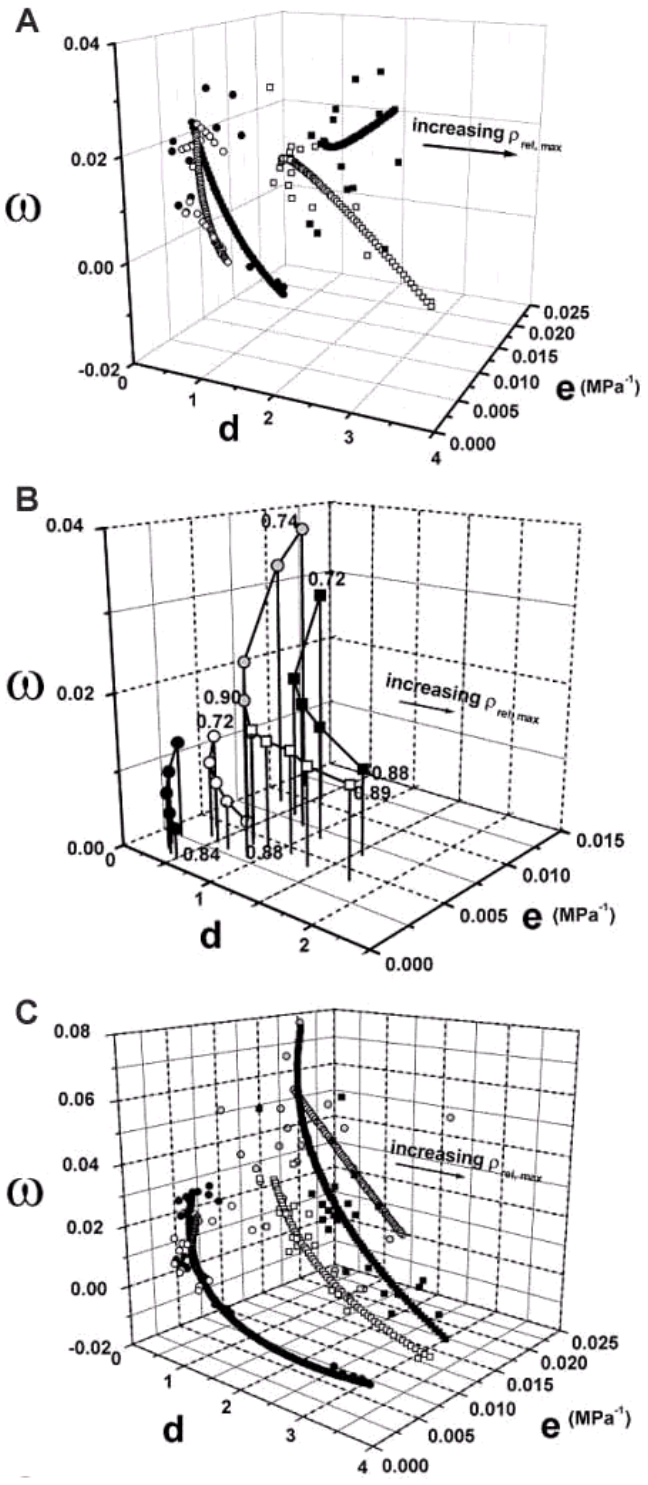

Figure 3. 3-D parameter plot of ● DCPD, ○ spray-dried lactose, □ MCC, ● theophylline monohydrate, and ■ HPMC for data gained (A) with the linear rotary tableting machine replicator Presster and compression wheels of a Fette 2090, (B) with the linear rotary tableting machine replicator Presster and compression wheels of a Manesty Betapress, and (C) an eccentric tableting machine.

values are higher. Finally, TheoM is more plastic because of pressure plasticity *e*; however, time plasticity *d* is lower than for the other materials, and the material is more slowly deforming.

The following order for deformability can be set up:

D (TheoM) ≥ *D* (HPMC) > *D* (MCC) > *D* (DCPD) > *D* (spray-dried lactose).

This is the same order as obtained using the compression wheels of the high-speed tableting machine Fette 2090. The underlying material properties are visible.

Detailed Comparison of Data from Simulation of Fette 2090 and Manesty Betapress

Figure 4A shows the 3-D parameter plots of the data from Fette 2090 and Manesty Betapress simulation for DCPD. The deformation is compared at the same dwell time of 10.6 milliseconds for both machines in order to eliminate the influence of speed. The results show that the deformation process mainly changes due to time plasticity *d*. Using the bigger compression wheels of Fette 2090, *d* is lower and ω is higher at the highest $\rho_{rel, max}$. The pressure plasticity *e* is similar for both machines. This finding means that the bigger compression wheels of Fette 2090 mainly influence the deformation process of a brittle material such as DCPD at higher densification. The material deforms more slowly, and fast elastic decompression is lower for the bigger compression wheels.

Figure 4B shows the results for the compaction cycles of MCC. For this plastically deforming material at higher densification, the *e* and ω values are nearly similar with both machines. However, for the data from Fette 2090 at lower densification, the *e* values and thus pressure plasticity are higher, and the ω values are lower. This finding means that the bigger compression wheels influence mainly the deformation process of a plastically deforming material such as MCC at lower densification. The material deforms more easily, and fast elastic decompression is higher for the bigger compression wheels of Fette 2090.

Figure 4C shows the 3-D parameter plot for data from spray-dried lactose. Here, no influence of machine type is visible. Spray-dried lactose consists of crystalline and amorphous lactose. The crystalline lactose deforms by brittle fracture, and the amorphous part adds plastic deformation. Thus, spray-dried lactose shows a 3-D parameter plot similar to DCPD. However, since at higher densification some plastic deformation exists, no influence of the compression

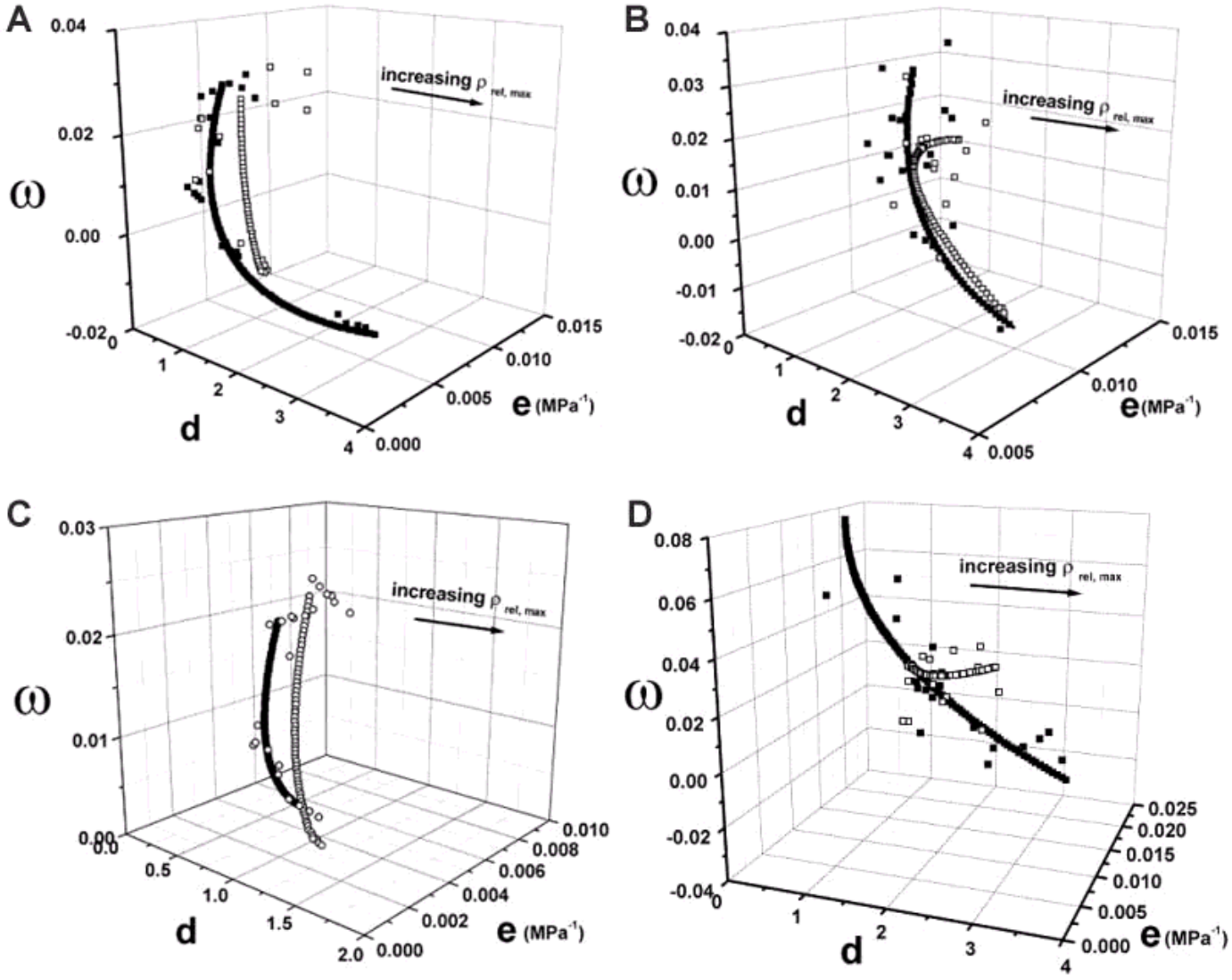

Figure 4. 3-D parameter plot of (A) DCPD, (B) MCC, (C) ○spray-dried lactose, and (D) HPMC for data gained with the linear rotary tableting machine replicator Presster and compression wheels of ■ a Fette 2090 or □ a Manesty Betapress.

wheels is visible at higher densification as it is for DCPD.

Finally, **Figure 4D** shows the 3-D parameter plot for HPMC densified with different compression wheels on the Presster. The *e* values are similar. However, the parameters *d* and ω obtained for this material change at higher and also at lower densification. At lower $\rho_{rel, max}$, the *d* values are higher and the ω values are lower for the bigger compression wheels of Fette 2090. Thus, as a result time plasticity and fast elastic decompression are higher and the material deforms faster. At higher $\rho_{rel, max}$, the *d* values are lower, and the ω values are higher for the data from Fette 2090. The material deforms more slowly, and fast elastic decompression is lower. Thus, for HPMC, a very plastically deforming material, the bigger compression wheels of the Fette 2090 change the compression process the most.

CONCLUSSION

The results show that the 3-D modeling technique can be applied to compaction cycles from different tableting machines. The relation of the data to each other produced on one tableting machine is the same, even when the absolute values are different. This is true for machines as different as eccentric and rotary tableting machines (in this study simulated) and also for differ-

ent compression wheels used on the rotary machine simulator Presster.

By using compression wheels of different sizes on the Presster, the stages of higher densification are influenced for brittle materials. For plastically deforming materials, the stages of lower and higher densification can be influenced. Mainly, time plasticity *d* changes, and the materials deform by using bigger compression wheels; eg, Fette 2090, slower at lower densification and faster at higher densification.

In conclusion, the results of this study allow the use of 3-D modeling for all data obtained from very different types of tableting machines, which allow continuous measurement of the height of the tablet by displacement measurement. Thus, 3-D modeling is a useful tool for transfer of tableting formulations from one tableting machine to another, and 3-D modeling aids in formulation development and scale-up.

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REFERENCES

1. Picker KM, Bikane F. An evaluation of three-dimensional modeling of compaction cycles by analyzing the densification behavior of binary and ternary mixtures. Pharm Dev Technol. 2001;6:333-342.

2. Picker KM. A new theoretical model to characterize the densification behavior of tableting materials. Eur J Pharm Biopharm. 2000;49:267-273.

3. Picker KM. New insights into the process of tablet formation - Ways to explore soft tableting [Habilitationsschrift]. Halle, Germany: Martin-Luther-University Halle-Wittenberg; and Görich und Weiershäuser Verlag, Marburg, 2002.

4. Schmidt PC, Tenter U. Force and displacement characteristics of rotary tableting machines. Pharm Ind. 1987;49:637-642.

5. Matz C. Evaluation einer IR-telemetrischen Kraft/Weg-Instrumentierung für Rundlauftabletten-pressen Differenzierung des Verformungsverhaltens direktkomprimierbarer Tablettierhilfsstoffe [Dissertation]. Freiburg, Germany: University of Freiburg; 1999.

6. Matz C, Bauer-Brandl A, Rigassi T, Schubert R, Becker D. On the accuracy of a new displacement instrumentation for rotary tablet presses. Drug Dev Ind Pharm. 1999;25:117-130.

7. Rippie EG, Danielsson DW. Viscoelastic stress/strain behaviour of pharmaceutical tablets: analysis during unloading and postcompression periods. J Pharm Sci. 1981;70:476-482.

8. Oates RJ, Mitchell AG. Calculation of punch displacement and work of powder compaction on a rotary tablet press. J Pharm Pharmacol. 1989;41:517-523.

9. Oates RJ, Mitchell AG. Comparison of calculated and experimentally determined displacement on a rotary tablet press using both Manesty and IPT punches. J Pharm Pharmacol. 1990;42:388-396.

10. Oates RJ, Mitchell AG. A new method of estimating volume during powder compaction and the work of compaction on a rotary tablet press from measurements of applied vertical forces. J Pharm Pharmacol. 1994;46:270-275.

11. Krumme M. Entwicklung rechnergestützter Verfahren zur Kompressions: und Festigkeitsanalyse von Tabletten [Dissertation]. Berlin, Germany: Free University of Berlin; 1992.

12. Krumme M, Schwabe L, Frömming KH. Development of computerised procedures for the characterization of the tableting properties with eccentric machines. High precision displacement instrumentation for eccentric tablet machines. Acta Pharm Hung. 1998;68:322-331.

13. Levin M, Tsygan L, Dukler S, inventors. Press simulation apparatus. US patent 6 106 262. December 23, 1998.

14. MCC Corp. The Presster Binder [technical information]. East Hanover, NJ: The MCC Corp; 2000.

15. Picker KM, Mielck JB. True density of swellable substances at different relative humidities - a new approach to its determination. Eur J Pharm Biopharm. 1996;42:82-84.

16. Heckel RW. Density-pressure relationships in powder compaction. Trans Metall Soc AIME. 1961;221;671-675.

17. Heckel RW. An analysis of powder compaction phenomena. Trans Metall Soc AIME. 1961:221:1001-1008.