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RESEARCH PAPER

Investigation of the Mechanical Properties of Two Polyvinyl Alcohols and Their Influence on Drug Release

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ABSTRACT

The aim of this work was the investigation of the elastic behavior and the internal stress of two different polyvinyl alcohols (PVAs) and how their swelling behavior and drug release are influenced through internal stress. We used thermal mechanical analysis (TMA 202/1/F Netzsch-Germany) to make a qualitative evaluation of the internal stress and the elastic behavior of PVA 55/12 and 55/03. These two PVAs have the same molecular weight and different acetyl contents. The tablets were compressed with an instrumented eccentric tablet machine. Tablets from different PVAs showed different elastic behavior. The measured internal stress of PVA 55/12 was higher than that of PVA 55/03. By increasing the compaction force, the internal stress increased. The internal stress decreased as the humidity increased for both kinds of PVA. The expansion behavior in the diametrical and axial direction was significantly different due to the predominant orientation of the PVA crystals. PVA tablets that were thermal analyzed showed different swelling behavior from those that were not thermal analyzed. This can be caused by the released internal stress of thermal-analyzed tablets. The compaction behaviors of both PVAs were also investigated using different methods. PVA 55/03 had better compactibility and compressibility behavior. The drug release behavior was also investigated and showed that the drug release rate of PVA 55/12 was higher than that of PVA 55/03. This can be due to the different solubilities and elastic behaviors of the PVAs. TMA can be used to predict and evaluate elastic behavior and internal stress. Humidity can

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influence the internal stress of the tablet. The measured swelling of PVA was a combination of real swelling and the released internal stress. TMA also allowed prediction of the binding mechanism in tablets.
Key Words: *Compression; Fraser Suzuki function; Internal stress; Polyvinyl alcohol; Tablet; Thermal mechanical analysis.*

INTRODUCTION

The elastic deformation of compressed tablets plays a very important role in tablet production and during drug release. There are different methods to investigate and evaluate the elastic deformation during tableting of pharmaceutical excipients, for example, the energy distribution of force displacement curve and force-time course. Such methods are able to give only a qualitative evaluation of the elastic behavior. This study gives a rationale and description of a quantitative method for evaluating the elastic behavior of tablets.

Most pharmaceutical excipients are anisotropic; the compression of anisotropic substances leads to an anisotropic force distribution in the powder bed, so an anisotropic consolidation will be built. The predominant orientation plays a very important role in the production of tablets. In the preconsolidation phase, the particles do not bind. The individual crystals counter the compression force through turning or pushing their position. In this way, they build the predominant orientation. In the ideal case, it should be imagined that the punch force has different force vectors that act in different directions. In the powder bed, there are endless crystals, and every individual crystal meets a different force vector. When the values of the force vectors are equal, this will be the most important precondition for regular consolidation in the powder bed. Through the appearance of the predominant orientation, not every force vector has the same deformation effect since the force hits the crystals in different bar directions.

In some directions, a light plastic deformation occurs since the glide system can be activated with a low critical yield pressure. In other directions, only inconvenient systems can be activated, or only low plastic deformation takes place.

The consolidation of powders will be uneven because of the predominant orientation. Consequently, within the same tablet, there are strong consolidated areas with strong binding forces between the individual particles, and other areas have weak consolidation with weak binding forces. The area with the weak binding forces is responsible for capping since relaxation in this area will be very easy after the compression (1,2).

During normal compression, the powder part will be extremely claimed and generally will be partially plastically deformed and another one elastically deformed because of direct contact with the punches or with the die. There is another part of the tablet that is actually elastically deformed. However, relaxation of the elastically deformed part will be hindered because of the plastically deformed part around it. This is called the apparent plastically deformed part or the frozen elastic deformation, which builds the internal stress (Fig. 1).

Such phenomena can cause various kinds of instability phenomena for tablets such as a capping tendency or cracking of the sides of tablets during transport or during the friability test.

The internal stress of tablets plays a very important role for tablet production, drug release, and stability of tablets produced.

The methods used to evaluate the internal stress of tablets are X-ray and polarization microscopy (3,4), measurement of the heat diffusion and the specific heat (5), and use of an instrumented Instron test apparatus (6).

These methods do not give a quantitative evaluation for the whole internal stress, but the evaluation of the measurement is place dependent. On the other hand, the tablet will be mechanically claimed. This mechanical claiming can cause the release of a part of the internal stress that cannot be measured. Consequently, another method that quantitatively measures all of the internal stress of tablets was needed.

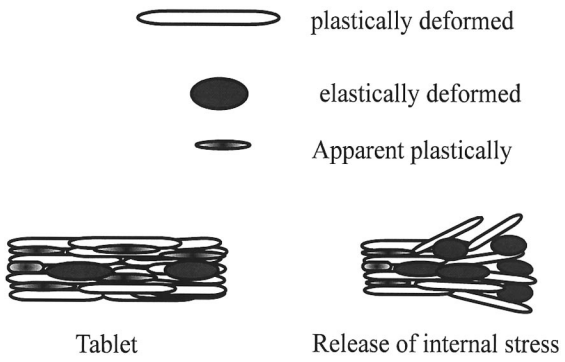

Figure 1. The release mechanism of the internal stress.

Our approach to method development began with the question: When can the internal stress be released? Internal stress can be released as follows:

1. During drug release, when the surface of the tablet will be eroded or dissolved. Once this occurs, the forces that hindered the relaxation of the frozen elastically deformed parts no longer exist, and it is possible for the internal stress to be released. Sometimes, a capping phenomenon could take place during the drug release, when the internal stress is very high.
2. During drug release when water is absorbed and the amorphous part reaches the glass transition temperature. When it reaches this point, the binding forces in the tablet will be weaker, and the internal stress can be released.
3. When the glass transition temperature is reached through heating.

Because of reason 3, we decided to use thermal mechanical analysis (TMA) directly on the tablet. Without load, TMA resulted in a dilatometrical measurement with a constant heating rate.

The displacement during measurements was measured two ways to see if the internal stress release is compaction force dependent.

Two kinds of polyvinyl alcohol (PVA) are often used as pharmaceutical excipients, especially as a binder, coating film, and a matrix former (7). Drug release from such matrix tables was characterized. Two kinds of PVA were investigated; they had the same molecular weight and different acetyl contents. The influence of the different acetyl contents on the compressibility using the modified Fraser-Suzuki function (8–10), energy distribution of force-displacement curve, and Heckel plot was investigated.

Polyvinyl alcohol shows a predominant orientation and can build the internal stress in the tablets. The internal stress of the two different kinds of PVA was measured, and its influence on the drug release was also characterized using TMA.

EXPERIMENTAL

Materials

Two different kinds of PVA (PVA 55/03 and PVA 55/12) were used; they have the same molecular weight and different acetyl contents. PVA 55/12 has the higher acetyl content (Chemie Werk Buna AG, Bund, Germany. Ch. no. 030786). The substances were a gift from Chemie Werk Buna in Germany. Theophyllin used was Carl Roth GmbH Ch. no. 1546638 (Karlsruhe, Germany).

Production of the Tablets

The tablets were produced using an instrumented single-punch machine (Korsch-EK0, Berlin, Germany) and an instrumented rotary machine (PH 100, Karsch, Berlin, Germany). The machines were connected with an amplifier (DMC-Plus, HBM GmbH, Darmstadt, Germany).

To evaluate the compressibility, compactibility, and internal stress, the polymers were compressed by different compression forces and different porosities without another excipient. For the investigation of drug release, tablets were produced using 70% polymer and 30% drug (theophyllin).

The diametrical crushing strength was tested using an Erweka strength tester (TBH-28, Erweka GmbH, Offenbach, Germany). The mean value of 10 determinations is reported.

Determination of the Drug Release

The USP paddle method was used to determine the release of theophyllin from the tablets. The samples were analyzed by measuring the UV absorption at 273 nm. The dissolution of the drug was reported as the mean of five determinations.

Determination of the Internal Stress

The determination of the internal stress was done using TMA (1–9). The measurements were performed with a TMA 202/1/F (Netzsch, Selb, Germany) using tablets exhibiting cylindrical shape (9 mm) using probes with spherical ends. There was no load on the sample during the measurement. The temperature range was 20°C to 150°C to 20°C. The extension as a function of temperature was measured applying a heating rate of 5 K/min. The expansion and the contraction of the tablets were measured in both vertical and horizontal (diametrical) directions (Fig. 2).

Determination of the Swelling Behavior

We measured the axial volume expansion of the tablets using a modified apparatus of List and Muazzam (11).

RESULTS AND DISCUSSION

PVA 55/03 and PVA 55/12 were compressed by different compression forces. The diametrical crushing

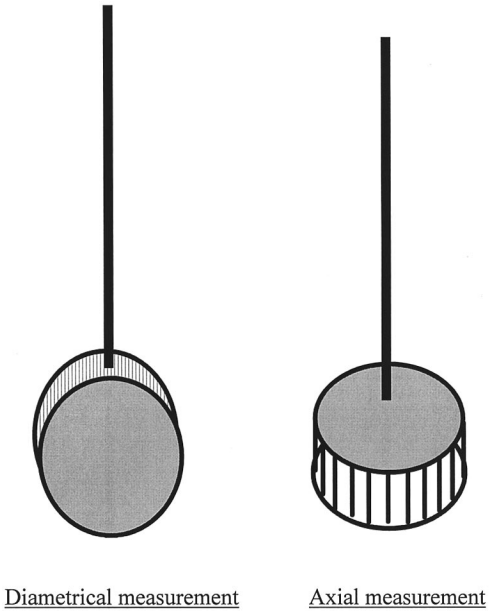

Figure 2. PVA 55/03 showed better compactibility than PVA 55/12.

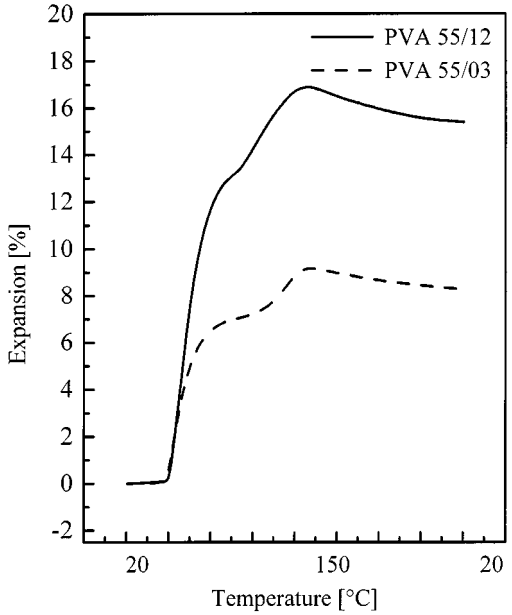

Figure 3. TMA of PVA 55/12 and 55/03 measured in the vertical direction.

strength increased by increasing the compression force for both kinds of PVA. The compactibility of PVA 55/03 was better than that of PVA 55/12 (12).

We used different methods to evaluate the compressibility of PVA: Heckel plot (13,14), energy distribution of the upper punch force displacement curve (15,16), and the modified Fraser-Suzuki function (Eq. 1) (8):

$$f(t) = H * \exp\left\{\left[\frac{-0.69315}{A^2}\right] * \left[\ln\left(\frac{\{1 + A * (tr - t)\}}{S}\right) * 1.17741\right]^2\right\}$$

where H is the peak maximum, A is the asymmetry factor, tr is the time by force maximum, and S is the standard deviation of the peak. The higher A and tr are, the better is the irreversible deformation.

All methods gave nearly the same result: PVA 55/03 was more compressible than PVA 55/12. This could be because of the better plastic deformation and the lower elastic deformation of PVA 55/03. Table 1 shows the evaluated Parameter of modified Fraser-Suzuki function.

The A parameters and tr parameters of PVA 55/03 are significantly higher than those for PVA 55/12. This demonstrates the better consolidation behavior of PVA 55/03 (Table 1).

The TMA showed that the internal stress of PVA 55/12 was higher than the internal stress of PVA 55/03. Figure 3 shows the curve course done in the vertical direction of the tablet.

Table 1

Modified Fraser-Suzuki Function Parameters for PVA 55/03 and 55/12 Compressed to the Same Porosity of 15%

PVA	*A*	*S*	*tr*
PVA 55/03	0.4751 ± 0.0004	0.2001 ± 0.0003	0.7036 ± 0.0008
PVA 55/12	0.4517 ± 0.0005	0.2010 ± 0.0003	0.6841 ± 0.0007

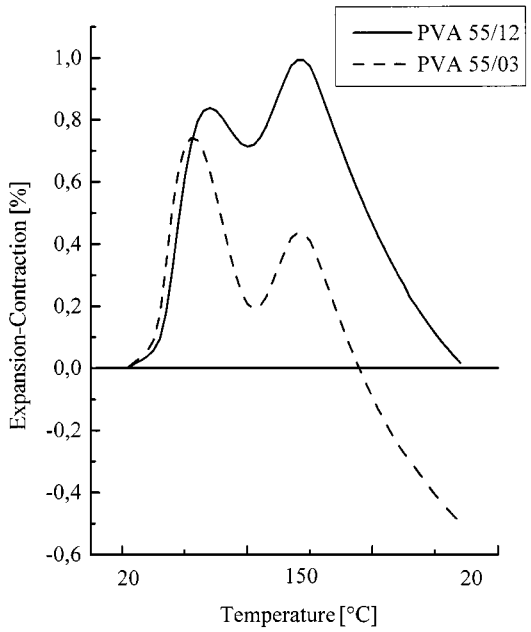

Figure 4. TMA of PVA 55/12 and 55/03 tablets measured in the diametrical direction.

The total expansion of PVA 55/12 was greater than the total expansion of PVA 55/03. This result correlates with the compression behavior and demonstrates that PVA 55/12 behaves more elastically than PVA 55/03. PVA 55/03 produced tablets with lower internal stress and higher binding energy.

The TMA in the diametrical direction of both PVA kinds was different, especially in the cooling phase (Fig. 4).

Comparing the relaxation in both vertical and diametrical directions shows that the relaxation behavior of PVA tablets was compression force dependent. This is an improve for the predominant orientation of PVA. Figure 5 shows the TMA of two different PVA 55/03 tablets in both directions.

Figure 6 shows that the total expansion of tablets during TMA was humidity content dependent during storage. It can be seen that a decrease in the total expansion can be observed by increasing the humidity content during storage. By increasing the humidity content, an increase of the released internal stress was decreased.

Investigation shows that PVA 55/12 swelled much more than PVA 55/03 (Fig. 7). The swelling is due both to the real swelling process and relaxation of the tablet. During water absorption by the tablet, the binding forces between the particle weaken, and the internal stress is released. Consequently, the measured swelling is a combination of real swelling and released internal stress. To

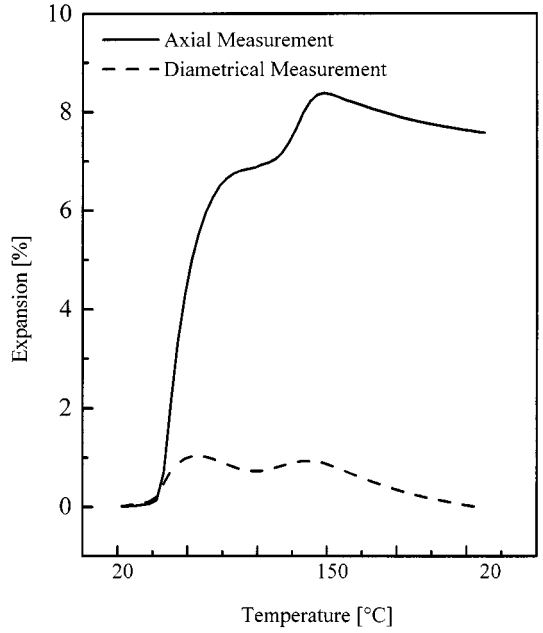

Figure 5. TMA of two PVA 55/03 tablets in different directions.

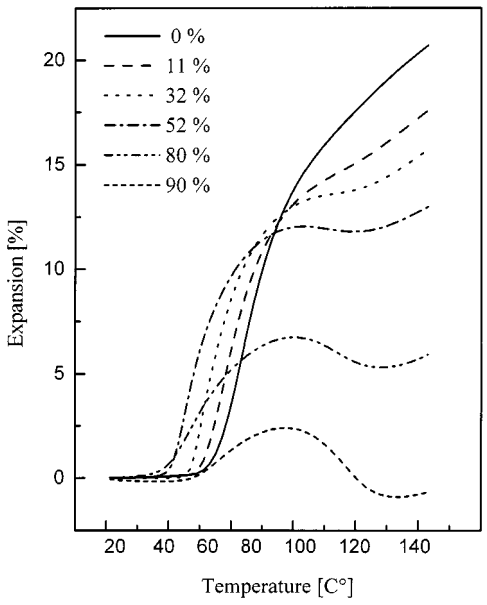

Figure 6. TMA of 55/03 tablets stored in different humidities.

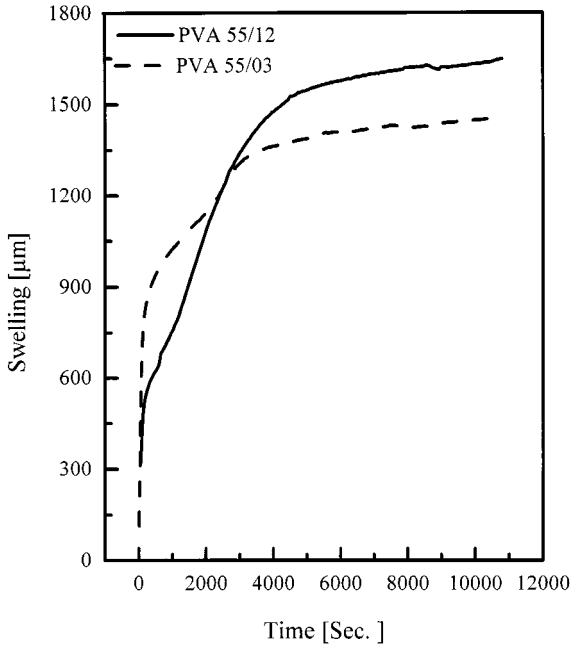

Figure 7. Swelling behavior of PVA 55/12 and 55/03.

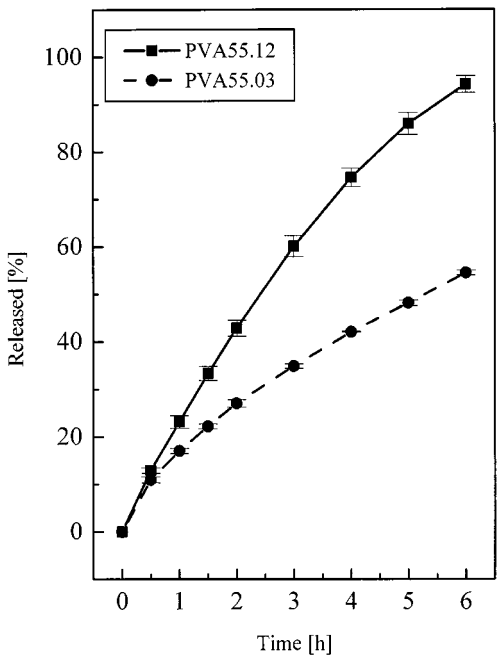

Figure 9. Drug release rate of PVA 55/03 and PVA 55/12.

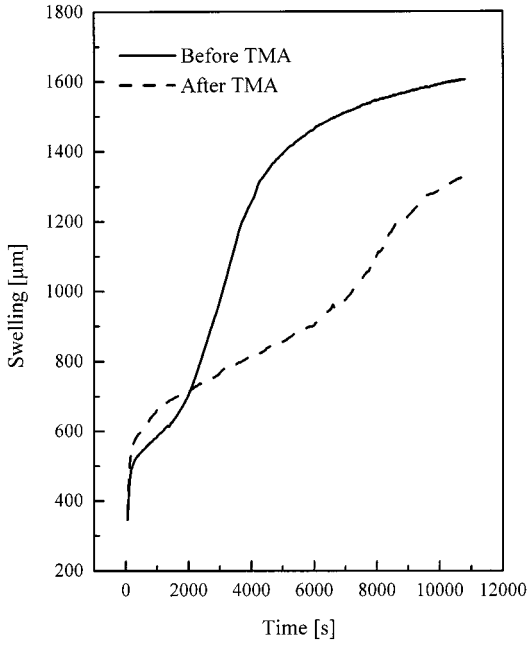

Figure 8. The swelling behavior of both thermal-treated and nontreated PVA tablets.

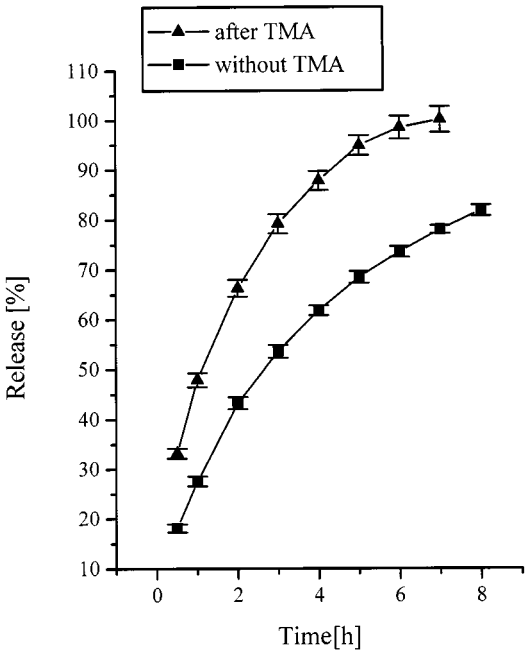

Figure 10. The drug release rate from PVA tablets with and without thermal treatment.

prove this, we measured the swelling of thermal-treated tablets, and we compared it with values for tablets that were not thermal treated.

Figure 8 shows that thermal-treated tablets swelled less than those that were not treated. This phenomenon can influence the drug release, which can be affected and controlled through the swelling behavior.

The drug release from such tablets shows that PVA 55/03 tablets have a lower rate than PVA 55/12 (Fig. 9). The reason for this can be the distinctive erosion rate of PVA 55/12 because of its better solubility.

We investigated the drug release of thermal-treated tablets and compared it with tablets that were not thermal treated. Figure 10 shows that the drug release of thermal-treated tablets was higher than those tablets that were not thermal treated, especially the initial dose released. This difference in thermal treated and untreated tablets can be important during therapy.

CONCLUSION

The TMA can be used to predict and evaluate elastic behavior and to make a qualitative evaluation of the internal stress. Humidity can influence the internal stress of the tablet. The measured swelling of PVA was a combination of real swelling and the released internal stress. The internal stress can influence the drug release of matrix tablets.

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